# CONTENTS

## Part IV. Special Histology

# Chapter 1

# SUBJECT AND AIMS OF HISTOLOGY. LEVELS OF STRUCTURAL AND FUNCTIONAL ORGANIZATION OF LIVING BEINGS

*Histology* (derived from the Greek word *histos* meaning "tissue", and *logos* meaning "study") is a scientific study exploring patterns of development, structure and functioning of tissues, interstitial interactions during historical and individual evolution of humans and other multicellular organisms. The focus of Histology is to study tissues, which are topographically and functionally related cell systems and their derivatives with common phylogenetic background that form organs.

Histology as a scientific and educational subject includes several sections.

*Cytology* is the study of the cell as a key histological element within tissues. Here, we will discuss the general and specific principles of cell structure, cytophysiology, reproduction and death mechanisms, reactive changes and regenerating capacity in case of cell damage. *Embryology* is the study of embryogenesis, patterns of developing germ layers, tissues and organs, critical periods of human development; embryology is closely linked to teratology (the study of congenital disorders) *General histology* is the study of tissue development, structure, functions, and regeneration. *Specific histology* deals with the microscopic structure of organs and organ systems, interstitial interactions during organogenesis, reactive and regenerative properties of organs, age-related changes during ontogenesis.

The human and animal organisms are holistic biological systems in which it is conditionally possible to distinguish several interrelated, interacting and subordinate levels of organization: molecular, subcellular, cellular, tissue and organ. Each of these levels is to a certain extent autonomous and includes structural units of subordinate levels.

The organismal level (i.e., the organism itself) is formed as an integral biological system in the process of an individual organism's development called ontogenesis.

The organ level comprises a complex of interacting tissues in the process of performing inherent functions of the given organ or organ system.

The tissue level integrates cells and their derivatives. Tissues may consist of cells developing from different genetic sources; however, the main properties of tissues are determined by the prevailing cells.

The cellular level is represented by the cell and its derivatives as the basic functional tissue unit.

The subcellular level comprises structural and functional components of the cell, which are the cell membrane, the nucleus, the cytosol, organelles, cytoplasmic inclusions and so forth.

Finally, the molecular level is characterized by the molecular composition of the cell components and the mechanisms of their functioning.

A basic understanding of the levels of organization and interconnections of different levels allow us to view the organism as an integral and yet hierarchically subordinate complex system. The structural components of various levels of organization of living things are the object of study of various biomedical disciplines. In recent years the science has developed an integrated approach for studying animal organisms using the full set of methods and techniques available to these disciplines. These allowed planing and performing of the fundamental studies and achieve a high level of knowledge about structural and functional organization of living matter including that of the human body.

The substantive content of histology as a branch of science and educational subject comprises the patterns of histogenesis, morphofunctional organization, tissue reactivity and regeneration, which were identified by examining a large amount of factual material. Here are the most important theoretical achievements of histology: cell theory, theory of germ layers, tissue evolution, histogenesis, and regeneration.

The urgent problems in the field of histology are:

- developing a general theory of histology which would reflect the evolutionary dynamics of tissues and the patterns of embryonal and postnatal histogenesis;
- studying histogenesis as a set of coordinated both in time and space processes of proliferation, differentiation, determination, integration, adaptive variability, programmed cell death and so on;
- clarification of homeostatic mechanisms and tissue regulation (nervous, endocrine, immune) and age-related tissue dynamics;
- studying the patterns of reactivity and adaptive variability of cells and tissues caused by exposure to adverse environmental factors, extreme conditions of functioning and development or transplantation;
- working on the problem of posttraumatic tissue regeneration and methods of tissue replacement therapy;
- revealing the mechanisms of molecular genetic regulation of cell differentiation and inheritance of genetic developmental defects of the organ systems in humans, developing methods of gene therapy and embryonic stem cells transplantation;
- elucidation of embryogenetic processes in humans, a critical period of fetal development, reproduction and fertility challenges.

Medical university histology course must give the future doctors a concept about the levels of structural and functional organization of the human body, their interconnection and continuity. In-depth knowledge of the human body's structure and functions at all its organizational levels is essential for modern doctors as only on this basis can authoritative analysis of a disease etiology (from the Greek word *aitiología* which means "cause" + *logos* meaning "study" which is the study of what causes the disease) and pathogenesis (from the Greek word *pathos* which means "suffering" + *genesis* meaning "creation" which is a field of medicine studying the disease occurrence and progression) can be performed as well as pathogenetically justified therapy assigned. For the medicine of the future which should become preventive, knowing the structural basis and patterns of ensuring stability and integrity of living systems (in particular tissues) is especially important since the progressive development of human civilization inevitably leads to creating new factors with a negative impact on animals including the human.

## TEST QUESTIONS

1. Substantive content of histology, cytology and embryology.
2. Levels of structural organization of living beings.
3. Urgent problems of histology.

# Chapter 2

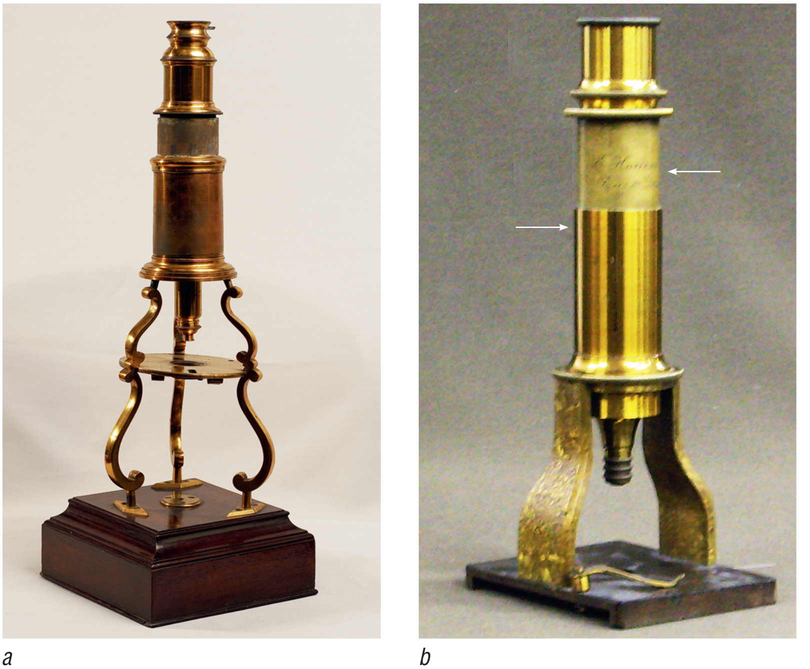
# A BRIEF HISTORICAL SKETCH OF THE DEVELOPMENT OF MICROSCOPY, HISTOLOGY AND EMBRYOLOGY

Histology started to emerge as a distinct discipline during the early part of the 19th century. It evolved as a result of multiple microscopic (visual) studies of different animals and plants. The crucial factor in the emergence of histology as the study of tissue structure was the invention of a magnifying device that was first created in the early 17th century (H. and Z. Janssens, Galilei, Drebbel et al.). One of the earliest scientific studies using a microscope of his design was undertaken by English physicist Robert Hooke (1635–1703). He studied the microscopic structure of various objects. All the objects of his studies Hooke described in a book called "Micrographia: or some Physiological Descriptions of Minute Bodies made by Magnifying Glasses..." that was first published in 1665. His observations led him to conclude that vesicular compartments, or cells, are common in plants and thus made him the first to suggest the term "cell".

In 1671 English scientist Nehemiah Grew (1641–1712) wrote about cellular structure as a general principle of plant organization. Grew was the first to introduce the term "tissue" to denote plant microstructure as the latter resembled fibers that were used to produce clothes. In the same year, Italian biologist Marcello Malpighi (1628–1694) gave a systematic and detailed description of the cellular structure of various plants. Later, the evidence of the cellular structure of animal tissues gradually kept on accumulating. In the second half of the 17th century, Antonie van. Leeuwenhoek (1632–1723) through his mastery in lens grinding designed microscopes providing up to 300–400 times magnification. This enabled him to discover the world of microscopic creatures and be the first to describe red blood cells and male germ cells.

Throughout the 18th century, the evidence of the cellular structure of animals and plants was building up. Czech scientist Jan Purkyně (1787–1869) and his students thoroughly examined and described animal cells in the early 18th century.

The microscope technology improvement has had a huge impact on the further advancement of knowledge about the microscopic structure of organisms. Already in the 18th century, microscopes were produced in large number. The early compound microscopes consisted of a pillar mounted on a base (Fig. 2.1) the focusing was achieved by sliding the tube. The most popular model up until the 1820s was a Culpeper type microscope produced by English optician E. Culpeper (1660–1740). The round base supported the tripod that held a tube with a sliding microscope body inside and had a round aperture in the center turning it into the stage (Fig. 2.1, *a*). The stage itself was mounted on a tripod secured to a small wooden box for accessories.



*a* *b*

Fig. 2.1. Culpeper-Style microscope from the museum of the Department of Surgery of the S.M. Kirov Military Medical Academy (*a*); a simple microscope designed by the German optician E. Gartnak exhibiting in the museum at the Department of Histology with a course of embryology at S.M. Kirov Military Medical Academy (the 1830s–1840s). The inscription on the tube says: E. Hartnach Paris & Potsdam (upper arrow); the focusing is reached through direct movement of the tube (lower arrow) (*b*)

Imperor Peter the Great was the first to bring the microscope to Russia from Holland. Later, the St. Petersburg Academy of Sciences opened a mechanical workshop for producing microscopes and, in 1725, employed I.P. Kulibin and I.I. Belyaev. Russian scientist and naturalist M.V. Lomonosov (1711–1765), regarded as a founder of national science, made a great contribution to the development of microscopy in Russia by proposing a number of technical improvements to the construction and optical system of the microscope.

The second half of the $19^{th}$ century was marked by a significant improvement in the microscopy techniques. New models of microscopes were designed (Fig. 2.2). Fine focusing was made possible by introducing a screw.

The invention of immersion objectives (water immersion was first introduced in 1850, oil immersion — in 1878) increased resolving power of optical instruments tenfold. The microscopes are becoming more and more comfortable to work with. The stage is equipped with a device for moving the slides around and a rotating nosepiece holds objectives that are easy to change (Fig. 2.3).

The design of microscopes continues to improve throughout the $20^{th}$ century. Microscopes come with a binocular head, knobs of fine and coarse focus placed in the lower part of the arm, the image quality increases significantly due to using new lenses and techniques of manufacturing objectives (Fig. 2.4).

**Fig. 2.2.** Enhanced microscope made by Hartnack (1860–1870s); arrow — fine focusing screw; coarse focusing is achieved through the direct movement of the tube

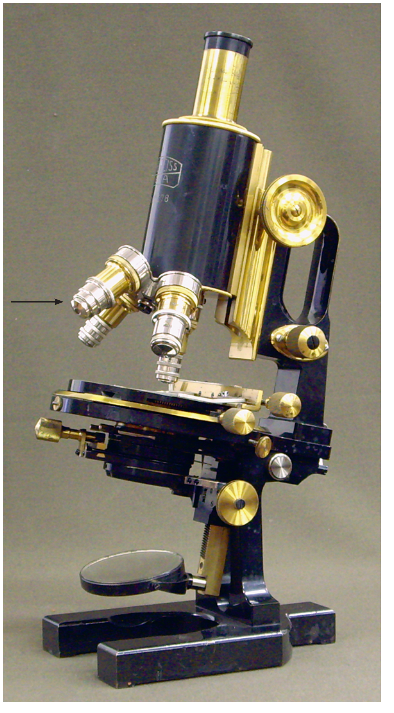


**Fig. 2.3.** Carl Zeiss Jena microscope with a revolving nosepiece for changing objective lenses (arrow)

In the late 1920s, the first production models of the Russian microscopes come out. Modern Russian microscopes are multifunctional, both light and dark-field, phase-contrast, allow the use of a camera and monitor (Fig. 2.5).

Currently, the greatest improvement of light microscopy is the confocal laser-scanning microscope (Fig. 2.6). However, the image of the slide here is digital, not optical (see Chapter 3).

Alongside improving microscopes, the technique of preparing histological slides was also developing. If earlier objects were examined under the microscope immediately after their isolation from plants or animals without any preliminary preparation, now the researchers began to resort to various preparation techniques, which made possible to preserve the structure of biological objects. Different methods of material fixation were proposed. A wide range of substances such as chromic, picric, osmic, acetic and other acids and their mixtures found their application as fixatives. Simple and often irreplaceable fixative formalin was first used for fixation of biological samples in 1893.

Preparing slides in a form suitable to be examined visually in transmitted light became possible with the introduction of a new technique of placing samples into dense embedding media, thus facilitating the preparation of thin sections. The invention of special instruments for sectioning called microtomes in the Purkyně's laboratory

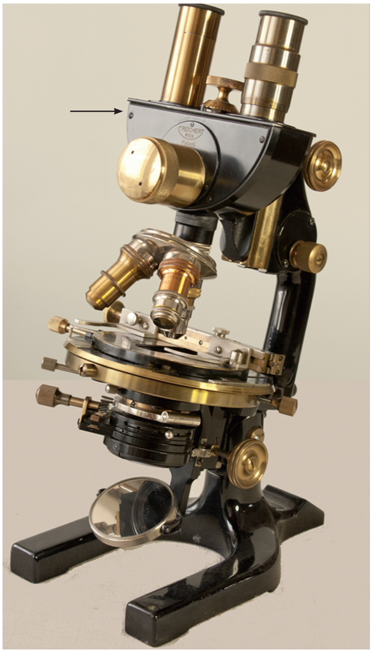


Fig. 2.4. Reichert microscope (Austria) with binocular head (arrow)

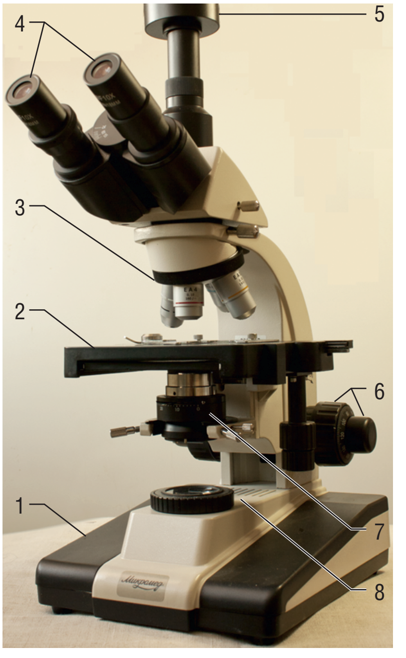



Fig. 2.5. Light microscope for biological research: 1 — base; 2 — stage; 3 — revolving nosepiece with several objective lenses; 4 — eyepiece lenses of the binocular; 5 — microscope camera; 6 — fine and coarse focus; 7 — condenser with an iris diaphragm; 8 — illuminator


Fig. 2.6. Confocal microscope: 1 — light microscope; 2 — objectives; 3 — control unit of the scanning device that moves the light beam along the *X*, *Y*, *Z* axes; 4 — digital image processed by a computer program