

## STATE OF APUD- SYSTEM OF LUNG IN CONDITIONS OF ORGAN DEVELOPMENT AND PATHOLOGY



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### АЪЗОНИНГ ТАРАҚҚИЁТИ ВА ПАТОЛОГИК ШАРОИТЛАРИДА ЎПКА АПУД-ТИЗИМИНИНГ ҲОЛАТИ

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### СОСТОЯНИЕ АПУД-СИСТЕМЫ ЛЕГКИХ В УСЛОВИЯХ РАЗВИТИЯ ОРГАНА И ПАТОЛОГИИ

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**Резюме.** Тадқиқотнинг мақсади эмбрионал тараққиётнинг турли босқичларида ҳамда яллиғланиш ва ўсма ўсиш ҳолатларида одам ўпкасининг АПУД-тизими тузилишининг хусусиятларини аниқлашдан иборат. Гистологик усуллар ёрдамида инсон ҳомиласи ва янги туғилган чақалоқларнинг, шунингдек, нафас олиш тизими аъзолари касалликларидан вафот этган болалар ҳамда онкологик беморларнинг ўпкалари ўрганилди. Ўпка бўлақлари Буэн суюқлигида фиксация қилинди ва парафинга қўйилди. Умумий гистологик усуллар: Ван-Гизон ва Вейгерт усули бўйича гематоксилин ва эозин билан бўйиш қўлланилди. Аргирофил нейроэндокрин тузилмалар Гримелиус усули бўйича қумуш нитрат билан импрегнация қилинди. Ўпка гистогенезининг найсимон ва альвеоляр босқичларида яқка нейроэндокрин ҳужайралар (апудоцитлар), кейинчалик нейроэпителиал таначалар аниқланди. Бола туғилгандан сўнг барча нейроэндокрин тузилмалар сони камаяди. Деадаптив ремоделлашишга келтирувчи ўпканинг яллиғланиш жараёни ва айниқса ўсма ўсиш ҳолатларида, асосан ёпиқ турдаги апудоцитларнинг пролиферацияси ва нейроэпителиал таначаларнинг шаклланиши кузатилади.

**Калит сўзлар:** ўпка, апудоцитлар, нейроэпителиал таначалар, онтогенез, деадаптив ремоделлашиш.

**Abstract:** The aim of the study was to determine the features of the structural organization of the APUD-system of human lungs at different stages of embryonic development, as well as during inflammatory and tumor processes in them. The lungs of human fetuses and newborns, as well as children who died from respiratory diseases and in cancer patients were studied by histological methods. Fragments of the lungs are fixed in Bouin's fluid and embedded in paraffin. General histological methods were used: hematoxylin and eosin, according to the method of Van Gieson and Weigert. Argyrophilic neuroendocrine structures are impregnated with silver nitrate according to the Grimelius method. Already at the tubular and alveolar stages of lung histogenesis, single neuroendocrine cells (apudocytes), later neuroepithelial bodies, are determined. After birth, the number of all neuroendocrine structures decreases. With inflammation and especially tumor growth in the lungs, leading to maladaptive remodeling, the proliferation of apudocytes of a predominantly closed type occurs, and neuroepithelial bodies are also formed.

**Key words:** lungs, apudocytes, neuroepithelial bodies, ontogenesis, maladaptive remodeling.

**Relevance.** In the context of the widespread spread of lung diseases, the study of their morpho-functional properties under various conditions, both in norm and in pathology, is becoming increasingly important. Understanding the cellular and molecular mechanisms that control the morphogenesis of this organ provides a basis for understanding the pathogenesis of acute and chronic lung diseases. At present, there has been a revived interest in the study of

fundamental issues related to the diversity of lung cells, and recent advances in the field of cellular and molecular pathways involved in lung organogenesis are being analyzed [8]. Due to this, the basic concepts of the cellular and molecular mechanisms that control the development of the lungs begin to form [5]. An important role in these mechanisms is played by biogenic amines and peptide hormones produced by neuroendocrine cells. Cells of the diffuse endocrine sys-

tem - apudocytes (APUD - Amine Precursore Uptake and Decarboxylation) absorb precursors of biogenic amines introduced from outside, subject them to decarboxylation to form biogenic amines and peptide hormones. The APUD-system of the lungs also includes innervated clusters of endocrinocytes – neuroepithelial bodies (NEB). In the respiratory system, apudocytes appear at various stages of embryogenesis, and the biologically active substances produced by them are directly involved in the development of the lungs. The cells of the endocrine apparatus are often implicated in the development of inflammatory and oncological diseases of the lungs, leading to maladaptive remodeling of the organ [2]. These cells can also regenerate secretory and ciliated cells after damage, although this ability may be limited [4]. The secretion of the hormone by apudocytes can change the hormonal status of patients with respiratory diseases [1].

**Aim of the study:** to reveal the features of the structural organization of the APUD-system of human lungs at different stages of embryonic development, as well as in inflammatory and tumor processes in them.

**Material and research methods.** We have studied histological preparations of lungs in 22 human fetuses at 9-36 weeks of embryogenesis and 5 full-term newborns. In addition, a comparative study of histological preparations of 19 children who died from respiratory diseases at the age of 7 months to 2 years (acute bronchitis, polysegmental bronchopneumonia, septic pneumonia) was carried out. In addition, the morphological and functional state of the components of the APUD-system of the lungs was studied in 15 cancer patients (surgical and sectional material). At the same time, histological preparations of areas of the lung not affected by the tumor were examined. The fixation was carried out in Bouin's fluid. Paraffin sections were stained by general histological methods: hematoxylin and eosin, according to the method of Van Gieson and Weigert. To identify argyrophilic endocrine cells, the sections were impregnated with silver nitrate according to the Grimelius method.

**Research results and discussion.** The study of histological preparations showed that within 9-13 weeks of development, the lungs of human fetuses are at the glandular stage of histogenesis. During this period, branching of the bronchial tubes is observed, the airways develop. At 11-13 weeks of embryogenesis, intralobular bronchi are detected, which pass into epithelial tubes, blindly ending in the mesenchyme. In the lobar and segmental bronchi, cartilaginous plates are determined. The mucous membrane of these bronchi is lined with multi-row non-ciliated prismatic epithelium, in the intralobular bronchi the epithelium is single-row prismatic. Neuroendocrine cells in the lungs of fetuses at an early stage of devel-

opment (9-10 weeks) are not yet detected. At the 11th week of embryogenesis, argyrophilic apudocytes are detected in the epithelium of large bronchi. Open apudocytes are more common, since their apical process reaches the lumen. In small bronchi, closed apudocytes are mainly determined, the apical part of which does not reach the lumen of the bronchus. In addition to single apudocytes, NEB is rarely detected.

In the tubular and alveolar stages of histogenesis, the number of neuroendocrine structures in the lungs increases. At the same time, there are more of them in the distal parts of the bronchial tree than in the proximal ones. The components of the neuroendocrine apparatus of the lungs appear some time after the formation of bronchial tubes, i.e. the most distal branches of the bronchial tree do not yet contain apudocytes and NEB. The cells of the open type are determined more often in the more formed proximal parts of the bronchial tree, while the closed type – in the distal ones (Fig. 1).

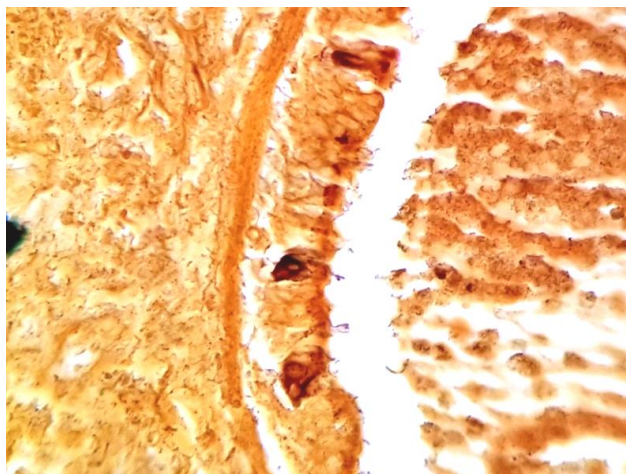


**Fig. 1.** Lung of the fetus 11 weeks of development. Open apudocytes in the epithelium of the bronchi. Grimelius impregnation. x400.

In inflammatory diseases of the lungs in children, a large number of both apudocytes and NEBs are found. There are much more of them than in the lungs of children who died from diseases not related to the respiratory system. In the lungs of children with pneumonia, apudocytes of the closed type predominate in quantitative terms. Often, NEBs are deeply immersed in the epithelium, i.e., they also consist of closed cells.

The largest number of apudocytes was found in lung cancer in organ tissue perifocal in relation to the tumor. The cells are usually round or oval in shape. They sometimes occupy a significant part of the bronchus. Usually apudocytes are located in the basal part of the epithelial lining of the bronchus and do not reach the lumen of the airways. In some cases, along with single apudocytes, isolated groups of argyrophilic cells resembling NEB are revealed (Fig. 2). In the lungs of cancer patients with extrapulmonary localization of the tumor, apudocytes are very rare. NEB in these cases cannot be detected.

Our comparative study of the cellular composition of the endocrine apparatus of the lungs during its morphogenesis and maladaptive remodeling made it possible to reveal some general patterns. We have found that open apudocytes during the development of the lungs appear in large bronchi, i.e., in earlier generations of branching of the airways.



**Fig.2.** Hyperplasia of apudocytes and the presence of NEB in lung cancer in adults. Grimelius impregnation. x400.

Closed apudocytes are more characteristic of newly formed bronchial tubes. During the development of the lungs, NEBs appear later than apudocytes and there are also more of them in the developing small bronchi and respiratory section. In newborns, there is a significant decrease in the number of both apudocytes and NEB. In lung diseases leading to maladaptive remodeling of organ structures, an increase in the number of neuroendocrine structures is observed [3,7]. With pneumonia in children, there is an increase in the number of apudocytes and NEB. Closed cells predominate among apudocytes. Also, NEBs appear, which are normally not detected after birth. Severe hyperplasia of apudocytes occurs during a tumor process in the lung and the restructuring caused by it. In this case, proliferation of mainly closed cells is observed, as well as the formation of NEB. Apparently, the proliferative processes occurring in the lungs in inflammatory and oncological diseases lead to maladaptive remodeling of lung structures and changes in the morphofunctional properties of its neuroendocrine apparatus.

#### Conclusions:

1. Neuroendocrine cells (apudocytes) of the lungs are determined at the tubular and alveolar stages of organ histogenesis. Closed apudocytes and neuroepithelial bodies predetermine branching of the bronchial tree. After birth, their number decreases.

2. In case of maladaptive remodeling of the lungs caused by inflammation and especially by the tumor process, proliferation of apudocytes of predominantly closed type occurs, and neuroepithelial bodies are also formed.

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**Резюме.** Целью исследования явилось определение особенностей структурной организации АПУД-системы легких человека на разных стадиях эмбрионального развития, а также при воспалительных и опухолевых процессах в них. Гистологическими методами изучены легкие у плодов человека и новорожденных, а также детей, умерших от заболеваний органов дыхания и у онкологических больных. Фрагменты легких фиксированы в жидкости Буэна и залиты в парафин. Применены общегистологические методы: окраска гематоксилином и эозином, по методу Ван-Гизона и Вейгерта. Аргирофильные нейроэндокринные структуры импрегнированы азотнокислым серебром по методу Гримелиуса. При воспалении и особенно опухолевом росте в легких, приводящих к дезадаптивному ремоделированию, происходит пролиферация апудоцитов преимущественно закрытого типа, формируются также и нейроэпителиальные тельца.

**Ключевые слова:** легкие, апудоциты, нейроэпителиальные тельца, онтогенез, дезадаптивное ремоделирование.