

оказывает слабое угнетающее действие на белую пульпу селезенки крыс периода полового созревания.

Ключевые слова: ксеногенная цереброспинальная жидкость, селезенка, белая пульпа, период полового созревания.

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STRUCTURE FEATURES OF SPLEEN OF PUBERTY RAT AFTER XENOGENEIC CEREBROSPINAL FLUID ADMINISTRATION

The article describe the structural features of rat's spleen after three and ten time injection of xenogeneic cerebrospinal liquid. The experiment was carried out in immature Wistar rats. Six of them was subjected by three-time injection of liquor and six one was subjected by ten-time injection in doze 2ml/kg of weight. The histomorphological characteristics was evaluate on slim sections stained by hematoxilin and eosin. It is found that after the threetime injektion of CSF spleen capsule and walls of blood vessels were not different from control, red pulp is characterized by hyperemia. The relative area of the white pulp of the spleen almost doubled due to the forming and differentiation of new lymphatic nodules, increased due to the expansion of their periarterial area and marginal zones. There was also an increase in the diameter of periarterial lymph sheaths. After tentime repeated administration CSF capsule of the spleen and the vessel walls become more dense. The red pulp is unchanged. The white pulp is increase in the number of primary nodules on the background of a slight decline in the absolute size of the lymph nodules and their zones. At the same time, an increase in T-zone of white pulp was observed.

Thus, three-CSF administration leads to the induction of immune processes in the spleen of rats; tentime repeated administration of CSF has little inhibitory effect on the white pulp of the spleen of immature rats.

Key words: xenogenic cerebrospinal fluid, spleen, white pulp, puberty.

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Dynamic of epithelial cells' mitotic activity in the structures of rat's major salivary glands after intrauterine antigenic action depending on the lymphocytes quantity

The work is the fragment of SRW of the chair of Anatomy, Operative Surgery and Topographic Anatomy and the chair of Histology, Cytology and Embryology of Zaporizhzhya State Medical University «Lectinhistochemical characteristics of

morphogenesis of the organs and tissues in early postnatal period in norm and experiment» (2008-2013, № state Registration 0109 U 003986).

Key words: salivary glands, lymphocytes, epithelial cells, mitosis, rats.

Aim – to determine the dynamic of epithelial cells mitotic activity in the structures of rat's major salivary glands after intrauterine antigen action depending on the lymphocytes quantity. It was investigated 252 submandibular glands of white laboratory rats through the histological and statistical methods. **Conclusions.** Newborn animals, after intrauterine antigen action determined the increased content of major salivary glands' epitheliocytes with mitosis figures, compared intact group. Quantity of mitotic activity epithelial cells is directly proportional to lymphocyte quantity and these indicators in antigenpremiun animals exceed the same parameters in intact group. Observed changes remains to the fourteenth day, gradually manifestation decreasing to the 45th day of postnatal formation.

Background. Lymphocytic infiltrates of the major salivary glands are involved in a spectrum of diseases that range from reactive to benign and malignant neoplasms. In many cases, the lymphocytic infiltrate is a minor inflammatory component that is easily distinguish from the primary disease processes. In some cases, however, the lymphocytic infiltrate is a major component of the disease, and histopathologic features that distinguish reactive and benign lesions from malignant lesions are often subtle [3].

Branching morphogenesis is a complex and dynamic embryonic process that creates the structure of many adult organs, including the salivary gland. During this process, many cellular changes occur in the epithelial cells, including changes in cell-cell adhesions, cell-extracellular matrix (matrix) adhesions, cell proliferation, and cellular contraction, resulting in formation of clefts in the epithelial cells of the organ [7].

The salivary gland metaplasia was accompanied by varying degrees of proliferation of basaloid and luminal epithelial cells [1]. Various cellular factors affect morphodynamic pattern formation. Immunohistochemistry revealed that the lymphocytic infiltrates form around epithelial structures of affected organs - for example, around the glandular epithelium of the exocrine glands [5]. Salivary gland epithelial cells (SGECs) may promote the formation of lymphoid follicles by attaching and activating both B and T cells [8]. The study of lymphocytes' influence as a cause of morphogenesis on formation of the organs' structures as the action of antigens, which come into to the organism of fetus and cause the lymphocytes' migration to the peripheral organs of immune system [9]. Lymphocytes have the proved influence to cells histogenetic and mitotic activity. At the present study, we investigated the correlation between a lymphocytes quantity and the number of SGECs in mitotic activity condition in rats' salivary glands after intrauterine antigenic action.

Objective. To determine the dynamic of epithelial cells' mitotic activity in the rat's major salivary glands' structures after intrauterine antigen action depending on the lymphocytes quantity.

Methods. The object of the research was 252 salivary glands of white

laboratory rats. Due to impossible qualitative materials taking, in the early periods of postnatal life parotid and sublingual salivary glands, the investigation done on the submandibular salivary glands. The submandibular salivary gland (SMG) is a classical model system to study morphogenesis and differentiation that undergoes branching morphogenesis during embryonic and post-natal development [6]. Rats divided into three groups. First group is intact rats. Second group is rats, which were introduced 0,05 ml solution of antigen in the amniotic fluid on the 18th day of pregnancy by the method of N. Voloshyn [10], the third group – control, the animals were introduced intrauterine 0,05 ml of physiological solution on the 18th day of pregnancy. The feeding of animals was twice a day at the same time. For the study of lymphocytes quantities and quantities of epithelial cells with mitotic figures after antigen's action on the fetus, chosen the model of transuterine, transmembrane introduction of antigen in amniotic waters by the method of N. Voloshyn [10]. The antigen was rare (killed) split - vaccine Vaxigrip 2009. Keeping the animals and experiments were carried out accordingly to regulations of European convention about the defense of spine animals', which are used due to the experimental and other scientific aims (Strasbourg, 18.03.86), law of Ukraine "Animal Protection from Cruel Appeal" (№ 1759 from 15.09.2009). The animals' killing and taking of the material done from 13-00 till 14-00 on the 1st, 5th, 7th, 11th, 14th, 30th, 45th day of postnatal life. On every term in all groups of the animals were examined 5 - 6 animals from 2 - 3 afterbirth. For the investigation, the submandibular salivary glands used during some minutes after killing. The samples fixed in 10% solution of formalin, dehydrated, filled in paraffin mixture and produced serial paraffin sections 4 μ m thick, stained by Felgen. The lymphocytes and mitotic activity epitheliocytes quantities counted per one thousand cells through A. Glagolev's ocular grid and designated in promille (‰), 1000 magnifications. Processing of the obtained numerical results conducted through statistical methods - STATISTICA® for Windows 6.1 (StatSoft Inc., № AXXR712D833214FAN5). Comparison of variables performed using Student's test. To verify existence of relationship between obtained variables used correlation analysis (Pearson coefficient of correlation). The difference between the variables was considered statistically significant at the $p \leq 0,05$.

Results. For all observed terms and experimental animals' groups counted the correlation of quantities of cells in different mitotic cycle phases to the intraepithelial lymphocytes total quantity.

Newborn intact animals, the cells with mitosis figure are detecting in parenchymal zone of major salivary glands. It quantities in intact group is $26,66 \pm 0,11\%$. Correlation cells in mitotic activity phase – intraepithelial lymphocytes is 0,81. Animals, that received antigen in antenatal period, the number of cells with mitosis figure is $29,7 \pm 0,08\%$, that is more compared intact group. The intraepithelial lymphocytes number is significantly increase in this group. The mitotic-lymphocytic coefficient of a current term – 0,59 and is significantly less, than in intact animals.

Indicators of intact group do not differ from control group. Intact rats on 5th day after birth, among the epithelial cells, a number of cells with

mitotic activity is significantly more relatively indicators of newborn animals (Fig.1). Coefficient mitosis-lymphocyte increased to 0,9 compared indicators of previously observed term. Against this background, in antigenpremium group on 5th day after birth, the quantity of epitheliocytes with mitosis figures is $39,2 \pm 0,11$, that statistically significantly more than in control group of current observed term. Correlation of mitotic active epitheliocytes to the number of intraepithelial lymphocytes 0,72, that is significantly less as compared with the indicators of newborn animals and intact group.

Compared to the previous period, in the control animals group at the 7th day of postnatal life, the quantities of cells with signs of mitosis increased to $40,37 \pm 0,22$ (Fig.1), but the mitotic-lymphocytic coefficient decrease 0,83. In antigenpremium animals, the mitosis quantity prevails over indicators of control animals of current period. Correlation of mitosis-lymphocyte continues to decrease, relatively the data of intact group (Fig.2). At the 11th day of postnatal life, the quantity of epitheliocytes at different stages of the mitotic segmentation is more relatively previous observation term (Fig.1). The ratio – cells in the mitotic activity phase to the total number of intraepithelial lymphocytes decreases by 0,12. Antigenpremium group, in comparison to control, the quantity of mitotic activity cells and ratio indicator mitosis/lymphocyte statistically significantly increases and is $56,66 \pm 0,1$ ($p \leq 0,05$), and 0,77 ($p \leq 0,05$) accordingly.

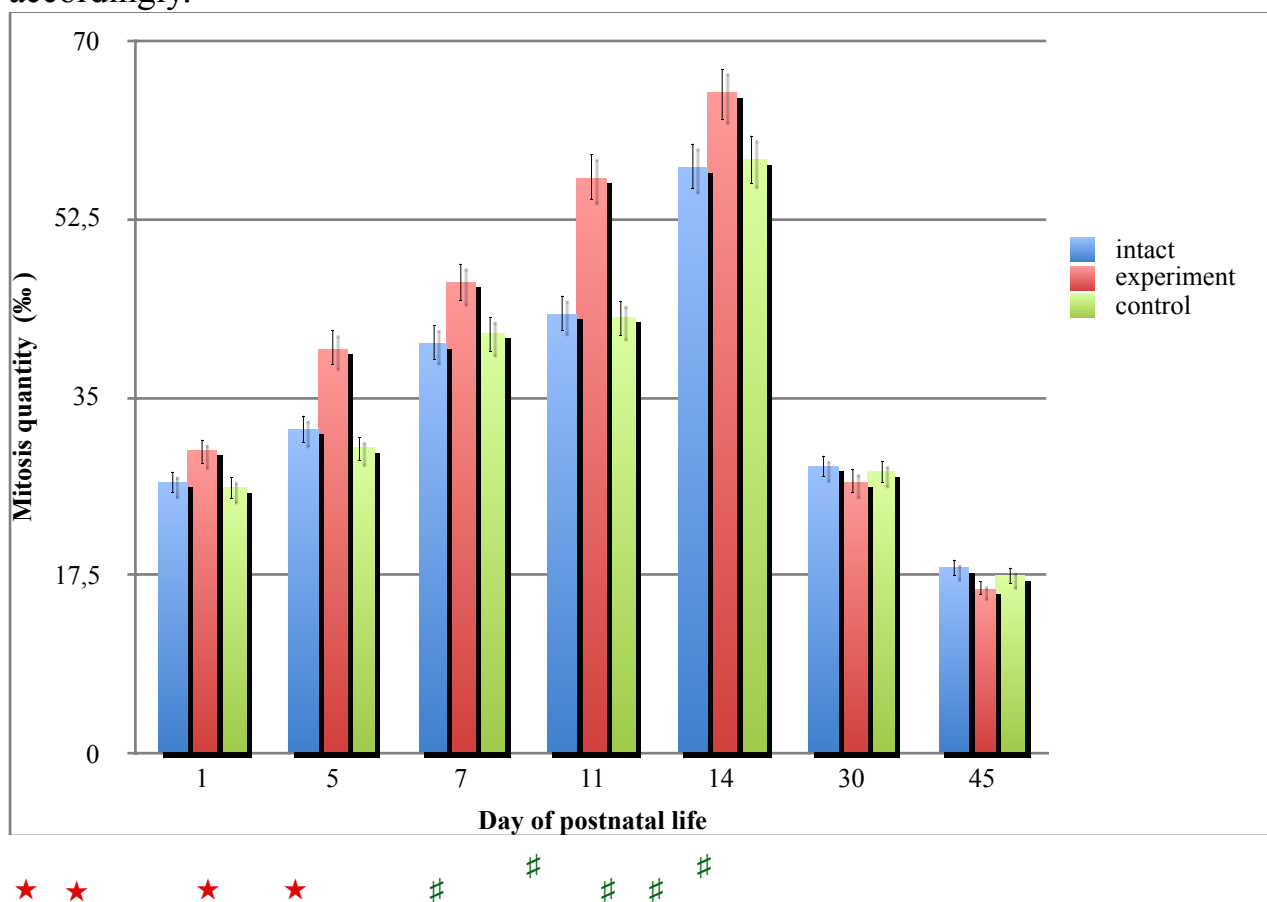
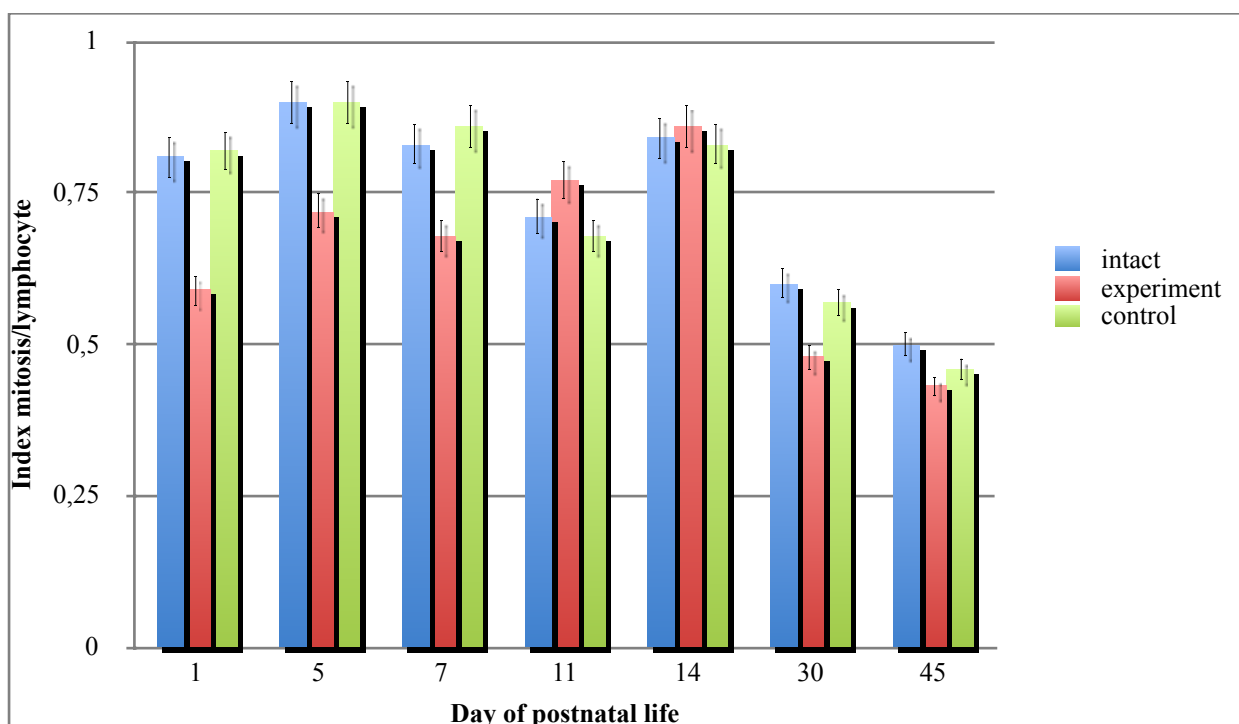


Figure 1 - Dynamics of cells with mitosis figures total quantity per 1000 SGEs

Notes: ★ - result is significant compared intact group;

- result is significant compared previously observations term.

In animals of 14th day, control group, the epitheliocytes proliferative activity and the intraepithelial lymphocyte number are peaks. The cells with mitosis figures occur in an amount $57,6 \pm 1,1\%$ – that is significantly more than in animals of previous observation term. Index mitosis/lymphocyte in comparison previously observation term in intact group increase to 0,84. Two weeks later after birth, the animals, which undergo an antigenic action, the quantity of cells with mitosis figures significantly exceeds the indicator of control group and it is $64,8 \pm 0,1\%$ per 1000 SGECS. The ratio of the mitotic activity epitheliocytes to the intraepithelial lymphocytes number almost does not differ from indicators of intact group. At the 30th day of postnatal life, observed the epitheliocytes mitotic activity decline in all animals group at the background of intraepithelial lymphocyte total quantity decrease. That is significantly in comparison with previously observation term (Fig. 1). Coefficient mitosis/lymphocyte in intact animal group is decreased to 0,6. In antigenpremium group, the quantity of cells with mitosis figures is slightly higher compared the control group. Index mitosis/lymphocyte is 0,48, that significantly differ from control.



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Figure 2 - Dynamics of mitosis/lymphocyte index

Notes: ★ - result is significant compared intact group;

- result is significant compared previously observations term.

For all animals group at the 45th day of postnatal formation, characteristically

statistically significantly reduction of salivary gland epithelial cells' mitotic activity, compared to results of 30th day. The difference in values of the ratio – mitotic activity epitheliocytes to the number of intraepithelial lymphocytes – does not exceed 0,07 in all observation groups.

Discussion. Numerous of a pathological reactions appearing in salivary glands, for example lymphoepithelial sialadenitis, characterize by benign lymphocytic infiltrate with parenchymal atrophy and foci of ductal hyperplasia with lymphocytic epitheliotropism [2]. The hyperplastic epithelium predominantly ductal basal cells that lack immunohistochemical markers specific to myoepithelium [2]. The majority of lymphocytes are reactive with T–cells markers while the lymphocytes in and around the lymphoepithelial lesions are mostly reactive with B – cells markers. Foci of epithelial hyperplasia are reactive for cytokeratin but are unreactive for myoepithelial specific markers [3]. The study of malignant transformation of pleomorphic adenoma show that the immunohistochemical analysis of COX-2 and Ki-67 proliferation index, significant increase was observed in Ca ex-PA, especially with adenocarcinoma, compared to pleomorphic adenoma and sialadenitis [4].

Earlier studies of the antigenic antenatal influences to throat, gums epithelium and pancreas morphogenesis [11] supplied the findings that the antigenic action caused reactive changes in epithelial cells differentiation and proliferation in early postnatal period. Thus, at the study of salivary glands epithelial cells component, we indicated the statistically significantly lymphocytes quantity increase in antigenpremium group from the first to fourteenth day of postnatal life, in comparison intact group. The number of epithelial cells in a mitotic activity condition significant increase per thousand cells of salivary gland parenchymal zone in antigen-influenced group. Dynamics of the intraepithelial lymphocytes content during observed terms has an undulatory character and is dependent from indicators of mitotic activity epithelial cells content. These findings confirm the indicators changes of the epithelial – lymphocytic coefficient.

CONCLUSIONS

1. Newborn animals, after intrauterine antigen action determined the increased content of major salivary glands' epitheliocytes with mitosis figures, compared intact group.

2. Quantity of mitotic activity epithelial cells is directly proportional to lymphocyte number and these indicators in antigenpremium animals significantly exceed the same parameters in intact group. Furthermore, observed changes remain during two weeks after birth, gradually decreasing to the 45th day of postnatal formation.

Further researches prospects. In our further researches, we will study the the dynamic of fibroblasts mitotic activity in the connective tissue structures of rat's major salivary glands after intrauterine antigen action depending on the lymphocytes quantity.

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Динаміка мітотичної активності епітеліальних клітин великих слинних залоз щурів після внутрішньоутробної антигенної дії в залежності від кількості лімфоцитів

З метою визначення динаміки мітотичної активності епітеліальних клітин великих слинних залоз щурів після внутрішньоутробної антигенної дії в залежності від кількості лімфоцитів вивчено 224 підщелепні слинні залози білих лабораторних щурів з використанням гістологічного та статистичного методів дослідження. У новонароджених тварин, після внутрішньоутробної дії антигену, встановлено більший вміст епітеліоцитів великих слинних залоз з фігурами мітозу, порівняно з інтактною групою. Кількість мітотичноактивних

епітеліальних клітин прямо пропорційна вмісту лімфоцитів та цей показник у антигенпреміюваних тварин перевищує такий самий параметр в інтактній групі. Виявлені зміни залишаються до 14 – ї доби з поступовим зменшенням проявів до 45-ї доби післянатального розвитку.

Ключові слова: слинні залози, лімфоцити, епітеліальні клітини, мітоз, щури.

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Динамика митотической активности эпителиальных клеток больших слюнных желез крыс после внутриутробного антигенного действия в зависимости от количества лимфоцитов

С целью определения динамики митотической активности эпителиальных клеток больших слюнных желез крыс после внутриутробного антигенного действия в зависимости от количества лимфоцитов изучено 224 подчелюстных слюнных железы белых лабораторных крыс, с использованием гистологического и статистического методов исследования. У новорожденных животных, после внутриутробного действия антигена, установлено большее содержание эпителиоцитов больших слюнных желез с фигурами митоза, по сравнению с контрольной группой. Количество митотически активных эпителиальных клеток прямо пропорционально содержанию лимфоцитов и данный показатель у антигенпремированных животных превышает аналогичный параметр в интактной группе. Выявленные изменения остаются до 14 –х суток с постепенным уменьшением проявлений до 45 – х суток постнатального формирования.

Ключевые слова: слюнные железы, лимфоциты, эпителиальные клетки, митоз, крысы.

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DYNAMICS MITOTIC ACTIVITY OF EPITHELIAL CELLS OF SALIVARY GLAND OF RATS FOLLOWING INTRAUTERINE ANTIGENIC ACTION DEPENDING ON THE NUMBER OF LYMPHOCYTES

С to determine the dynamics of the mitotic activity of epithelial cells of large salivary glands of rats after intrauterine antigenic action, depending on the number of lymphocytes was studied 224 submandibular gland white laboratory rats using histological and statistical methods.

Newborn animals after prenatal action antigen, found a higher content epitheliotsitov large salivary glands with figures motoza, compared with the control group.

Number of mitotically active epithelial cells is directly proportional to the content of lymphocytes and the figure at the antigenpremirovannyh animals exceeds the similar parameter in the intact Grupe.

The detected changes remain up to 14 days -x with a gradual decrease in symptoms and 45 - th day of postnatal formation.

Key words: salivary glands, lymphocytes, epithelial cells, mitosis, rats.

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ВИКОРИСТАННЯ ІНТЕРАКТИВНИХ МЕТОДИК В НАВЧАЛЬНОМУ ПРОЦЕСІ НА КАФЕДРІ ГІСТОЛОГІЇ, ЦИТОЛОГІЇ ТА ЕМБРІОЛОГІЇ

Анотація: В роботі проведено комплексний аналіз інтерактивних методів організації навчального процесу, які використовуються на кафедрі гістології, цитології та ембріології ЗДМУ протягом останніх десяти років. Проведено систематизацію основних методик, і на підставі власного досвіду використання даних методик визначено області застосування та сформульовано рекомендації щодо їх використання в курсі гістології, цитології та ембріології. Інноваційні технології демонструють високу ефективність засвоєння знань студентами, а також, новий рівень взаємодії між викладачем і студентом. Оптимізація навчального процесу потребує комплексного підходу з позиції вдосконалення методів навчання, розробки нових принципів побудови навчальних програм і посібників, які об'єднують кращі досягнення традиційних та інноваційних моделей, індивідуалізації процесів навчання.

Ключові слова: інноваційні технології, інтерактивні методики, вища медична освіта, навчальний процес.

Вступ: Вхідження України в єдиний Європейський освітній простір ставить серйозні проблеми перед вітчизняною медичною освітою [1]. В останні десятиліття сума знань у суспільстві зростає вдвічі кожні 2 роки. Змінюється і структура знань: частка традиційних знань зменшується з 70% до 40%, прагматичних - з 15% до 10%, але зростає частка нових знань - з 5% до 15% і знань, спрямованих на розвиток творчих здібностей особистості - з 3% до 25%. На даний момент освіта є підтримуючою, перспективна освіта має стати в сучасному інформаційному суспільстві випереджаючою. В зв'язку з цим актуальним завданням сучасної медичної освіти є розробка, апробація та впровадження нових методів і форм навчання з урахуванням основних положень закону України «Про вищу освіту» в редакції 2014р., в якому передбачено синтез освіти, науки та інноваційної діяльності [2]. В рамках реалізації даного завдання на кафедрі гістології, цитології та ембріології ЗДМУ проводиться робота з розробки та впровадження нових освітніх технологій, що дозволяє формувати у студентів професійні компетенції, забезпечують їх