

збільшують частоту хромосомних аберацій, а саме делецій, діцентриків, транслокацій, поодиноких та парних фрагментів, кільцевих хромосом і знижують мітотичну активність клітин червоного кісткового мозку. У 1/10 ДЛ50 ксенобіотики знижують кількість живих ембріонів та підвищують кількість місць резорбцій на тлі збільшення доімплантаційної, післяімплантаційної і загальної ембріональної загибелі. Прояв мутагенного ефекту на рівні загальнотоксичної їх дії дозволив виключити у даної групи сполучень наявність специфічної мутагенної дії.

Ключові слова: Лапроксида, ксенобіотики, хромосомні аберації, мітотична активність, мутації.

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chromosomal aberrations in the form of deletions, dicentric, translocations, single and paired fragments, ring chromosomes and reduce the mitotic activity of the cells of bone marrow. The 1/10 DL50 xenobiotics reduce the number of live embryos and increase the number of places resorption, with increased pre-implantation, post-implantation and general fetal death. Manifestation mutagenic effect at the level of general toxic action allowed to exclude them from this group of compounds the presence of **specific mutagenic action**

Key words: Laproxides, xenobiotics, chromosomal aberrations, mitotic activity, mutation.

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SUBMICROSCOPIC REORGANIZATION OF RESPIRATORY PULMONARY ALVEOLI AFTER EXPERIMENTAL THERMAL INJURY ALONG WITH COMBINED APPLICATION OF EXOGENOUS SURFACTANT AGENT AND FREEZE-DRIED XENOGRAFT SUBSTRATE

Submicroscopic state of components of aero-hematic barrier of respiratory portion of lungs after thermal injury has been studied during the experiment, involving white rats, in condition of early necrectomy and application of ground substrate of freeze-dried xenograft and administration of surfactant agent. It has been found that the combined use of such correction agents prevents the development of lesions in the aero-hematic barrier structures and has positive effect on the progress of regenerative processes and their normalization at the late stages of the experiment.

Keywords: aero-hematic barrier, ultrastructural changes, thermal injury, freeze-dried xenograft substrate.

The research paper has been made within the planned research scientific work, entitled "Identification of features of reparatory processes of burn wound and morphofunctional changes of the internal organs and clinicopathogenetic study of application of cryo freeze-dried fake tissues in burn injury" (National registration No. 0115U00153).

Burn injury is one of the most common types of injuries to date, and it permanently takes one of the leading places among the causes for disability. Complications, developing as a result of the extensive burns, require the development and implementation of the novel advanced methods of prevention and treatment. However, issues on methods of correction of the abovementioned pathology have not been fully elucidated in current publications [3, 4, 11].

In the pathogenesis of post-thermal injury lesions the burn-induced exo- and endogenous intoxication of the body takes the leading role. Ground substrate of freeze-dried xenograft is considered to be one of the novel and effective means for temporary burn wound closing. Its application onto wound, cleaned from the necrotic tissues, prevents from progressing intoxication from the lesion focus and the development of infections in wounds, reduces the manifestation of burn disease and promotes skin regeneration in the shorter term, which, in turn, has a positive effect on morphofunctional state of the burn body's organs [6, 7].

Burn injury, among other etiologic factors, causes the development of the acute respiratory distress syndrome (ARDS). Search for pulmoprotectors, which promote higher resistance of the lungs to the effects of pathological factors, is reasonable. Compensation deficiency of endogenous surfactant, promotes regeneration of damaged lung tissue in thermal injuries; therefore, special attention is given to various types of surfactants [2, 5, 8, 9, 10]. Consequently, the dynamic analysis of ultrastructural state of components of respiratory portion of lungs after thermal injury along with combined application of exogenous surfactant agent and freeze-dried xenograft substrate is crucial.

The purpose of the research was to identify the submicroscopic reorganization of rat aero-hematic barrier components of pulmonary alveoli of the respiratory portion in dynamics after thermal injury in application of ground substrate of freeze-dried xenograft and exogenous surfactant agent.

Methods and Materials. The experiments have been carried out on 20 senior male white rats. Third-degree burn was induced by placing of copperplates, heated in boiled water to 97-100 °C under ether anesthesia. The damaged area accounted for 18-20% of the epilating surface of the rats' body. Early necrectomy of damaged skin areas was carried out a day after burn induction. The originated wound was covered with ground substrate of freeze-dried xenografts. Ground substrate of freeze-dried xenografts, made from the porcine skin, is produced by the "Kombustilog" enterprise, approved for clinical use in

Ukraine. Single intratracheal instillation of 300 mg/kg CUROSURF® surfactant agent was performed simultaneously with application of xenograft substrate onto burn wound under general anesthesia. Animals were decapitated on day 7, 14 and 21. Small pieces of respiratory portion of lungs were analyzed in electron microscope, fixed in 2.5-3% solution of glutaraldehyde, postfixed in 1% solution of osmium tetroxide on the pH 7.2-7.4 phosphate buffer, dehydrated in alcohol and propylene oxide and embedded into mixture of epoxy resins with araldite. Ultrathin sections were contrasted with uraniacetate and lead citrate according to Reynolds and studied in the PAM – 125 k electron microscope [1].

Results and Discussion. Pre-studied analysis of submicroscopic state of components of aero-hematic barrier of respiratory portion of lungs in experimental thermal injury found deep lesions of respiratory and secretory alveolocytes, endotheliocytes and basal membrane of hemocapillaries.

Electron microscopic analyses of respiratory portion of lungs of animals, who were applied with ground substrate of freeze-dried xenograft along with administration of surfactant agent after thermal injury showed that right on day 7 of the experiment lesions of component of aero-hematic barrier were less prominent than in group of animals, not provided with treatment.

Submicroscopically, the significant enhancement of organization of pulmonary components of aero-hematic barrier, as compared with group of animals, not provided with treatment, was noted on day 14 of the experiment in conditions of application of correction agents. Less degree of damage and active progress of regeneration processes with ultrastructure rejuvenescence of their components were found. The most pronounced positive effect of application of correction agents on the structural organization of aero-hematic barrier of lungs is observed especially on day 21 of the experiment.

During this periods of the experiment moderately dilated lumens with no signs of hypercoagulation and blood filling were specific for the majority of hemocapillaries. Single red blood cells, white blood cells were found in their lumens. Nuclei of endotheliocytes are oblonged with shallow invaginations of karyolemma. (Fig. 1).

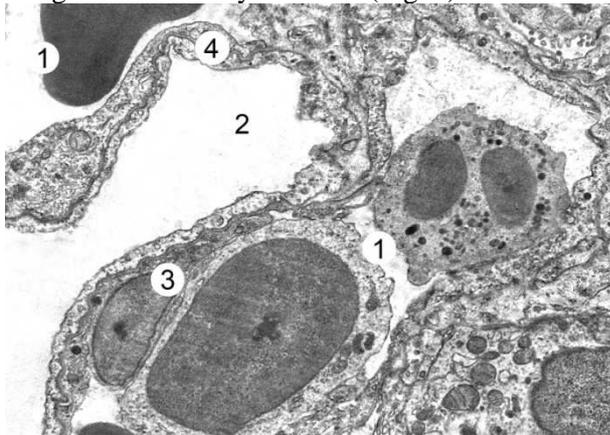


Fig. 1. Ultrastructural state of wall of pulmonary alveolus of respiratory portion on day 14 after thermal injury and application of correction agents. Capillary lumen with blood corpuscles (1), alveolus lumen (2), endotheliocyte (3), aero-hematic barrier (4). x 9 000.

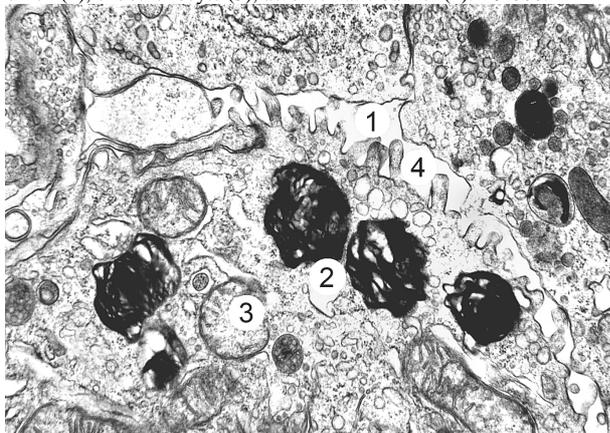


Fig. 3. Ultrastructure of fragment of secretory alveolocyte on day 21 after experimental thermal injury and application of correction agents. Alveolus lumen (1), lamellated corpuscles (2), mitochondrion (3), microvilli on the apical surface (4). x 25 000.

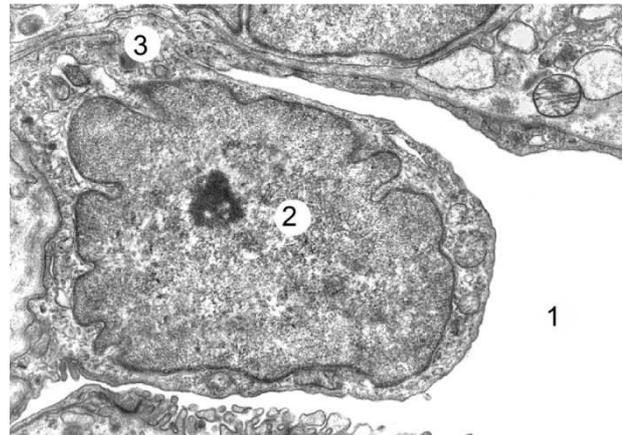


Fig. 2. Submicroscopic state of the respiratory alveolocyte on day 21 after experimental thermal injury and application of correction agents. Alveolus lumen (1), nucleus (2) and Type I alveolocyte cytoplasm (3). x 15 000.

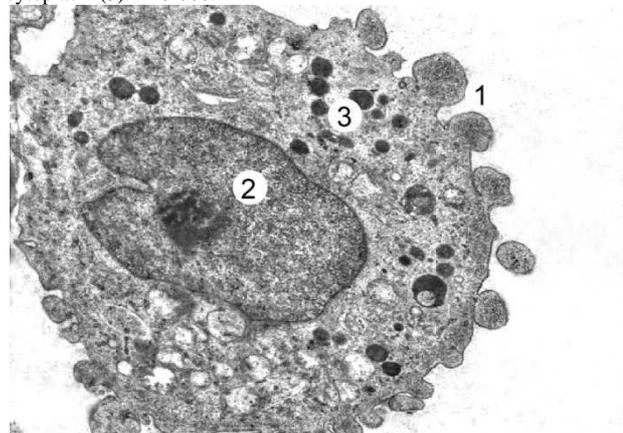


Fig. 4. Ultrastructural state of alveolar macrophage of pulmonary portion of lungs on day 14 after experimental thermal injury and application of correction agents. Cytoplasmic processes of plasmalemma (1), nucleus (2), lysosome (3). x 12 000.

Free ribosomes and polysomes are observed in the paranuclear area, as well as slightly dilated tubules of granular endoplasmic reticulum and cisterns of Golgi complex. Mitochondria of various shapes and sizes with matrix of the average optical density have been revealed and single mitochondria with cleared matrix and well structured cristae were partly noted. Numerous micropinocytic vesicles and small pits are found in the peripheral cytoplasmic areas of cells. Luminal surface of endotheliocytes contains single cytoplasmic evaginations in the form of microvilli. The junctions between endotheliocytes are not damaged. Basal membrane, as part of the aero-hematic barrier is relatively even and slightly thickened in some areas. Numerous microvesicles are noted in the peripheral parts of the respiratory alveolocytes and single microvilli and microprocesses are found in some cells. Nuclei of Type I alveolocytes are hypertrophied, oval-shaped with karyoplasms of moderate electron-optical density with evenly distributed fine-grained chromatin and small nucleoli (Fig. 2). Nuclei with cleared karyoplasms and marginal distribution of chromatin are also observed. Karyolemma has minor invaginations, clear boundaries of membranes, and moderately dilated perinuclear space.

The resulted submicroscopic analyses of secretory alveolocytes along with application of correction agents have revealed cells with normal functioning and alveolocytes in a state of heightened functional activity. Nuclei of such cells are oblonged with clear boundaries of karyolemma, predominantly containing euchromatin. Numerous hypertrophied mitochondria with clear cristae and moderate electron-dense matrix are found in the cytoplasm. Cisterns and vesicles of Golgi complex are observed in the perinuclear area. Slightly enlarged vacuoles and tubules of endoplasmic reticulum with ribosomes on the surface of their membranes are noted. Numerous free ribosomes and polysomes are also observed. In the cytoplasm of Type II alveolocytes numerous secretory multivesicular and osmiophilous lamellated corpuscles are found. The latter are characterized by their polymorphism according to sizes, structural organization and level of maturity (Figure 3).

The mature and young lamellated corpuscles of orbicular and oval shape with preserved structure of concentric or parallel osmiophilous lamellated corpuscles prevail in the secretory alveolocytes in conditions of application of correction agents at the late observation periods. Apical surface of the cells contains numerous microvilli. The output of the content of secretory corpuscles into the alveole lumen to form the membrane structures of surfactant is also observed.

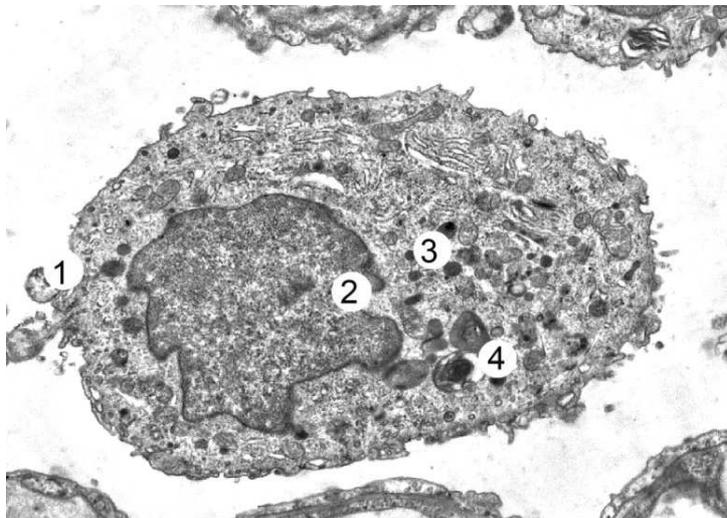


Fig. 5. Submicroscopic organization of alveolar macrophage on day 21 after experimental thermal injury and application of correction agents. Cytoplasmic processes of plasmalemma (1), nucleus with invaginations (2), lysosomes (3), single phagosomes (4). x 12 000.

Numerous fascicles, interstitial macrophages, fibroblasts, plasmocytes and lymphocytes are found in the intersticium. On day 14 of the experiment the alveolar macrophagocytes with signs of heightened functional activity were found in the alveoli lumen. Their plasmolemma forms numerous, thickened cytoplasmic evaginations and invaginations. The nuclei are orbicular with moderate osmiophilous karyoplasm and invaginations of karyolemma membranes. Synthetic apparatus of macrophages is represented by numerous free ribosomes and polysomes, moderately dilated tubules of endoplasmic reticulum and hypertrophied dictyosome of Golgi complex (Fig. 4).

Submicroscopically, on day 21 well- pronounced lysosomal apparatus, represented by small osmiophilous lysosomes and single big phagosomes, containing osmiophilous lamellated fragments, in particular, was found in alveolar macrophages. Their plasmolemma forms small cytoplasmic processes (Fig. 5).

Conclusions

The results of submicroscopic analyses give evidence to the fact that early removal of necrotic skin areas after thermal injury and wound closing with ground substrate of freeze-dried xenograft along with administration of surfactant prevents the action of pathogenic factor on the lungs and reduces the extent of the damage to the structures of the respiratory portion. Combined use of agents contributes to

active flow of regenerative processes in components of aero-hematic barrier, providing gradual improvement of their ultrastructure. Consequently, a relative normalization of the structural components of the walls of the alveoli and hemocapillaries occurs at the end of the experiment.

Perspectives of further experimental research will encompass the study of structural reorganization of pulmonary components in thermal injury using correction agents of other types.

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Реферати

СУБМИКРОСКОПІЧНА ОРГАНІЗАЦІЯ АЛЬВЕОЛ РЕСПІРАТОРНОГО ВІДДІЛУ ЛЕГЕНЬ ПІСЛЯ ЕКСПЕРИМЕНТАЛЬНОЇ ОПІКОВОЇ ТРАВМИ В УМОВАХ СПІЛЬНОГО ЗАСТОСУВАННЯ ЕКЗОГЕННОГО ПРЕПАРАТУ СУРФАКТАНТІ СУБСТРАТУ ЛІОФІЛІЗОВАНОЇ КСЕНОШКІРИ
Небесна З. М.

В експерименті на білих щурах проведено вивчення субмікроскопічної стану компонентів аерогематичного бар'єру респіраторного відділу легень після термічної травми в умовах проведення ранньої некрэктомії і застосуванні подрібненого субстрату ліофілізованої ксеношкіри і введення препарату сурфактанту. Встановлено, що спільне застосування даних коригувальних засобів запобігає розвитку деструктивних змін у структурах аерогематичного бар'єру і позитивно впливає на перебіг регенераторних процесів та їх нормалізацію в пізні терміни експерименту.

Ключові слова: аерогематичний бар'єр, ультраструктурні зміни, термічна травма, субстрат ліофілізованої ксеношкіри, сурфактант

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СУБМИКРОСКОПИЧЕСКАЯ РЕОРГАНИЗАЦИЯ АЛЬВЕОЛ РЕСПИРАТОРНОГО ОТДЕЛА ЛЕГКИХ ПОСЛЕ ЭКСПЕРИМЕНТАЛЬНОЙ ОЖГОВОЙ ТРАВМЫ В УСЛОВИЯХ СОВМЕСТНОГО ПРИМЕНЕНИЯ ЭКЗОГЕННОГО ПРЕПАРАТА СУРФАКТАНТА И СУБСТРАТА ЛИОФИЛИЗИРОВАННОЙ КСЕНОКОЖИ
Небесная З. М.

В эксперименте на белых крысах проведено изучение субмикроскопического состояния компонентов аерогематического барьера респираторного отдела легких после термической травмы в условиях проведения ранней некрэктомии и применении измельченного субстрата лиофилизированной ксенокожи и введение препарата сурфактанта. Установлено, что совместное применение данных корректирующих средств предотвращает развитие деструктивных изменений в структурах аерогематического барьера и положительно влияет на течение регенераторных процессов и их нормализацию в поздние сроки эксперимента.

Ключевые слова: аерогематический барьер, ультраструктурные изменения, термическая травма, субстрат лиофилизированной ксенокожи, сурфактант.

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