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MORPHOLOGICAL AND MORPHOMETRIC CHARACTERISTICS OF HYALINE MEMBRANE DISEASE AT BIRTH OF A CHILD

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Abstract: This scientific study shows the study of morphological and morphometric indicators of hyaline membrane disease in premature infants. The material was obtained based on the results of clinical and anamnestic analysis and lung tissue of premature infants aged 22-37 weeks. The results show that immaturity of the lung tissue, circulatory disorders and damage to the alveolar and bronchial epithelium play an important role in the development of hyaline membrane disease in the lungs of premature infants. The results of morphometric studies showed that only 1/3 of the lungs of infants born at the age of 22-27 weeks had air in the alveoli, the thickness of the alveolar interstitial tissue, the epithelium of the alveoli was relatively large, and as a result hyaline membranes were formed, which consisted of relatively thin fibers. In groups of children who died at 28-32 and 33-37 weeks, an expansion of the area occupied by airborne droplets in the infant's lungs, thinning of interstitial tissue and thickening of hyaline membranes were observed compared to the group of earlier terms.

Key words: infant, premature birth, lungs, alveoli, hyaline membrane, morphology

摘要：这项科学研究显示了早产儿透明膜病的形态学和形态学指标的研究。该材料是根据22-37周早产儿的临床和记忆分析结果以及肺组织获得的。结果表明，肺组织的不成熟、循环障碍以及肺泡和支气管上皮的损伤在早产儿肺部透明膜病的发展中起重要作用。形态计量学研究结果表明，22~27周出生婴儿的肺泡中只有1/3的肺泡内有空气，肺泡间质组织较厚，肺泡上皮较大，随着结果形成了由相对较细的纤维组成的透明膜。在28-32周和33-37周死亡的儿童组中，与早期组相比，观察到婴儿肺部空气飞沫占据的区域扩大、间质组织变薄和透明膜增厚。

关键词：婴儿, 早产, 肺, 肺泡, 透明膜, 形态

Relevance of the topic. According to the criteria adopted by the World Health Organization in 1970, the lower limit of live birth is 22 weeks of pregnancy, when the fetus weighs 500 grams and has a body length of 25 cm(3). As a result, the number of premature births has not decreased, despite the measures taken to

strengthen prenatal prevention to improve pregnancy (1,2). A new type of contingent has appeared in the neonatal intensive care unit - a group of infants with extremely low body weight. It is well known that the lower the body weight, the higher the incidence of diseases, including an increased incidence of hyaline membrane disease

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(BGM) (5). However, antenatal prevention of BGM has been developed, but morbidity and mortality remain high (6).

In addition, the results of modern technological measures, including: high-intensity artificial ventilation of the lungs, the use of exogenous surfactants, led to a change in the symptoms of BGM. To date, invasive and non-invasive methods are used in the treatment of BGM, including an increase in positive pressure in the respiratory tract, the introduction of endogenous surfactants (7.8). However, there are still no studies devoted to the morphological and morphometric study of the lungs of those who died from BGM.

The aim of the study was to determine the specifics of morphological changes developing as a result of BGM in the lungs of premature infants.

Materials and methods. The autopsy data of 52 premature newborns of varying severity and infants who died of pulmonary

insufficiency were obtained as a material. Initially, the medical histories of infants and the autopsy protocol were analyzed. Premature babies were divided into the following groups by weeks of gestation: Group 1 - 12 (23.1%) aged 22-27 weeks; group 2 - 18 people aged 28-32 weeks (34.6%); group 3 - 22 children born at the age of 33-37 weeks (42.3%) and died of pulmonary insufficiency (Table No. 1). Of these, group 1, i.e. infants born at the age of 22-27 weeks, who were deeply premature, had a very low body weight and died about 1 hour after birth, were taken as a control group. The aim was to identify the first morphological changes in the lungs of this group of infants, leading to the formation of BGM. The main cause of death in this group was postpartum asphyxia. In all cases, the presence of prenatal and intranatal risk factors in the mother, the presence of pathologies from the placenta and umbilical cord were revealed. The anthropometric indicators of the examined newborns are given in Table 1.

Table-1

Anthropometric indicators of premature babies, M±m

№	Group of premature babies	Quantity	Gestation time	Body weight, g	Height, cm
1	22-27-weeks	12	25,2±0,4	654±24,3	29,5±1,6
2	28-32-weeks	18	29,8±0,6*	1067±84,7*	38,4±4,6*
3	33-37-weeks	22	35,3±0,7**	1986±124,6**	43,2±8,5**

Note: * - $P \leq 0,05$ – The difference in gestation period, body weight and height in group 2 relative to group 1.

** - $P \leq 0,05$ – The difference in gestation period, body weight and height in group 3 relative to group 1.

The results of clinical and anamnestic analysis showed that the shortest-lived and aggravated heart failure as a cause of death was observed in children of the first group, and relatively long-term - in the third group.

For histological examination, fragments were obtained from different areas of both lungs with pathological anatomy. The macroscopic appearance of the lung was evaluated by examining its appearance during autopsy. Lung

fragments were solidified in 10% neutralized formalin, passed through alcohols and infused in paraffin. Histological sections were stained with hematoxylin-eosin, CHIC reaction and Van Gieson methods. The following morphometric calculations were performed: 1) the percentage of the area of the alveoli where air enters, relative to the total area of the lung 2) measurement in the field of view of the alveoli having a glandular membrane. 3) measurement of the thickness of the hyaline membrane. 4) measurement of the height of the alveolar epithelium. 5) measurement of interstitial alveolar tissue thickness. Each indicator was calculated 10 times, and the average and the standard error were calculated. Statistical processing of quantitative indicators was carried out by methods of descriptive and variational statistics, the difference between the indicators was determined at the level of confidence $R \leq 0.05$.

Results and discussion.

The results of the study showed that the condition of the control group 1 newborns at

birth was very severe, with a profound lack of morphofunctional status, severe cardiac and respiratory insufficiency. The macroscopic condition of the lungs corresponded to the term of pregnancy. Histological examination showed that in most cases the epithelium of the alveolar tissue of this group of newborns was large, and their nuclei were stained with normochrome of a rounded shape. However, in some cases, the alveolar epithelium was damaged and the nucleus was deformed. In some areas of the lung, it was found that a small number of alveoli, expanded due to the intake of air, acquired a rounded shape, as a result of which the epithelium of alveocytes flattened and lengthened in shape. The remaining alveoli almost do not open, in the form of various holes and cracks, the wall of their interstitial is thick and has a multicellular structure due to the accumulation of tissue cells from the air (Fig. 1). The capillaries in the interstitial alveolar tissue are slightly expanded, filled with blood, in some places blood is detected without diapedesis (Fig. 2).

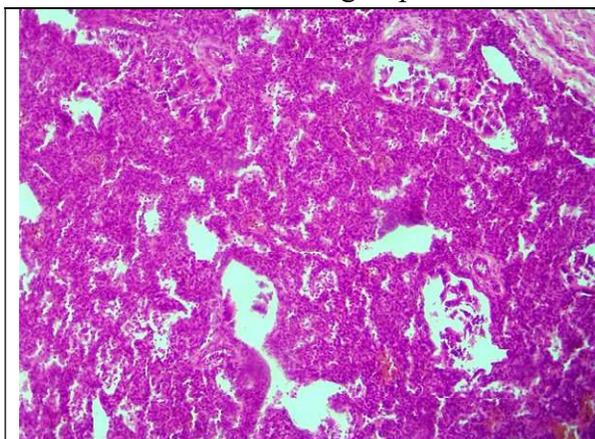


Fig-1. The baby was born at 25 weeks. Most of the alveoli do not open. Picture: G-E. Scale: 10x10.

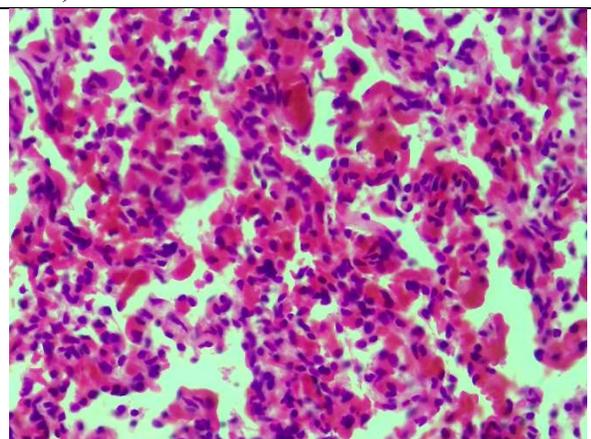


Fig-2. Fragment of Figure 1. Capillaries are full, there is bleeding. Picture: G-E. Scale: 10x40.

Morphometric measurements showed that the area of air-induced alveoli in group 1 was

$28.5 \pm 3.6\%$ of the total area. The average number of alveoli containing hyaline membranes

in the microscope cavity was 5.8 ± 1.4 . The height of alveocytes averaged 9.34 ± 3.4 microns, while the size of alveocytes ranged from 2.4 to 14.8 microns. In this group, the thickness of the alveolar interstitial barrier averaged 32.3 ± 5.2 microns, of which the thinnest was 9.6 microns, and the thickest was 54.2 microns. The presence of hyaline membranes was found in 22.8% of the lungs of the first group of young children. It was noticed that the fibers of the hyaline membrane of different thicknesses in some places spread out in the form of a lattice. Measurements of the thickness of the hyaline membrane showed an average of 9.6 ± 2.7 microns (Table 2) with a difference in thickness of 2.6 microns for the thinnest area and 16.8 microns for the thickest area. According to the results of clinical and anamnestic analysis in group 1, the presence of intranatal asphyxia, brain tumors and membranes, hemorrhages in most newborns were revealed as factors leading to hyaline membrane disease.

In the second group, 3 premature babies died within the first 6 hours after birth, 6 (33.3%) between 12 and 24 hours, 5 (27.7%) after 72 hours and another 4 (22.2%) 120 hours after birth. Hyaline membranes with a homogeneous structure are found in some areas of the lungs in 3 infants who died within 6 hours after birth. It was noticed that the alveoli with a hyaline membrane in the cavity are located mainly in the peribronchial region. It was found that hyaline membranes have an annular structure and the alveoli fit snugly to the inner surface. In addition to hyaline membranes, fragments of amniotic fluid, meconium corpuscles and maternal erythrocytes were found in the alveolar cavity. In infants who died between 12 and 24 hours after birth, hyaline membranes were found in most

areas of lung tissue and a relatively small alveolar cavity. It was noticed that most of the alveoli are dilated, hyaline membranes in the form of dark purple sandy-sandy color are present in their cavities. Non-wrinkled alveoli lack hyaline membranes. In the wall of the alveoli, the reaction to hyaline membranes was not sufficiently developed.

The alveoli of the lungs of infants who die within 72 hours of birth have different sizes, and some of them have hyaline membranes. At the same time, the shape of the alveoli is triangular, elongated, stellate, in their cavities, in addition to hyaline membranes, amniotic epithelium, fibrin-like mass and segmented nuclear leukocytes are revealed. There is the appearance of foci of distalectase around blood vessels and bronchioles, blood vessels dilate, interstitial tissue and alveolar cavity become serous.

In infants who died within 120 hours after birth, most of the areas of the alveolar lung tissue were filled with air, enlarged emphysematous foci appeared in some areas, and hyaline membranes in the alveolar cavity were torn and fragmented. In this group, there is a strong reaction of interstitial tissue to hyaline membranes, i.e. lymphohistiocytic infiltration. Small foci of atelectasis and distelectasis are found in the peribronchial and perivascular areas.

Morphometric measurements of the lungs of the second group of newborns showed that the area of air-induced alveoli was $48.7 \pm 6.2\%$ of the total area. The average number of alveoli with hyaline membranes in the cavity of the field of view of the microscope was 7.8 ± 1.4 . The height of the alveocytes averaged 7.18 ± 3.6 microns, while the size of the alveocytes ranged from 3.4 to 12.8 microns (Table 2). In this group, the thickness of the alveolar interstitial barrier averaged 25.3 ± 3.2 microns, of which the

thinnest was 6.6 microns, and the thickest was 42.4 microns. Hyaline membranes were found in 27.8% of the lungs in the second group of infants. It was noticed that the fibers of the hyaline membrane of different thicknesses in some places spread out in the form of a lattice.

Measurements of the thickness of the hyaline membrane showed an average of 11.6 ± 2.8 microns, and the difference in thickness was 3.6 microns for the thinnest area and 21.8 microns for the thickest area.

Table - 2

Morphometric indicators of hyaline membrane disease (M±m)

№	Surveyed indicators	Group -1	Group -2	Group-3
1	The area of the alveoli where the air enters (relative to the total area) in%.	28,5±3,6	48,7±6,2*	78,4±8,5**
2	Height of the alveolar epithelium, microns	9,34±3,4	7,18±3,6*	6,15±2,4**
3	The distance between the alveoli. Fabric thickness, microns	32,3±5,2	25,3±3,2*	18,3±2,3**
4	Number of alveoli with hyaline membrane	5,8±1,4	7,8±1,4*	6,9±1,3**
5	Hyaline membrane thickness, microns	9,6±2,7	11,6±2,8*	12,7±3,6**

Note: * - $P \leq 0,01$ – the degree of reliability of the indicators of the second group relative to the first group.

** - $P \leq 0,01$ – the degree of reliability of the indicators of the third group relative to the first group

In the third group, it was found that 8 (36.3%) premature babies died within 12-24 hours after birth, 6 (27.3%) within 72 hours and another 8 (36.3%) within 120 hours. In infants who died between 12 and 24 hours after birth, hyaline membranes were found in most areas of lung tissue and they filled a relatively enlarged alveolar cavity (Fig. 3). In the cavity of most alveoli, the presence of migrating alveocytes, segmented leukocytes, cell fragments, bronchial epithelium and lymphocytes is detected. The lung alveoli of infants who died within 72 hours of birth have different sizes, and some of them have hyaline membranes. The alveolar interstitial

tissue is thickened, in which fibroblasts and lymphoid cells proliferate (Fig. 4). The bronchial cavity is expanded and contains a mass of leukocytes, migrated epithelium and erythrocytes. In infants who died within 120 hours after birth, most of the areas of the alveolar lung tissue were filled with air, enlarged emphysematous foci appeared in some areas, and hyaline membranes in the alveolar cavity were torn and fragmented. In this group, there is also a strong reaction of interstitial tissue to hyaline membranes, that is, lymphohistiocytic infiltration.

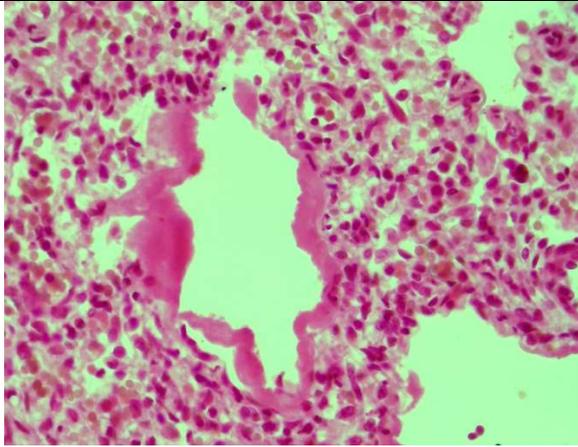


Fig. 3. The baby was born at 34 weeks. Thick hyaline membrane in dilated alveoli. Picture: G-E. Scale: 10x40.

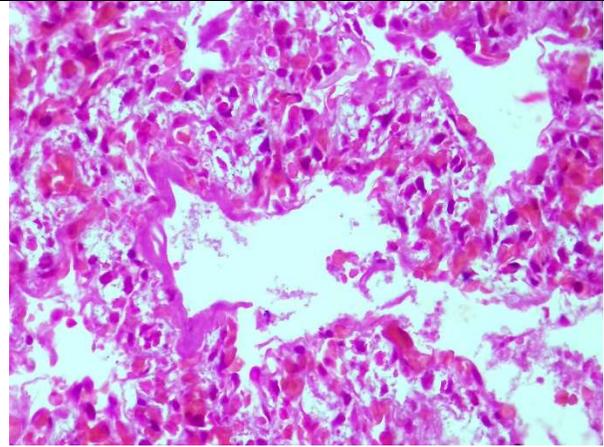


Fig. 4. The baby was born at 36 weeks. Alveoli are enlarged, fibroblasts grow in interstitial tissue. Picture: G-E. Scale: 10x40.

Morphometric measurements of the lungs of the third group of newborns showed that the area of air-induced alveoli is 78.4 ± 8.5 of the total area. The average number of alveoli with hyaline membranes in one cavity of the microscope was 6.9 ± 1.3 . In this group, the thickness of the alveolar interstitial barrier averaged 18.3 ± 2.3 microns, of which the thinnest was 4.7 microns, and the thickest was 38.4 microns. Measurements of the thickness of the hyaline membrane showed an average of 12.7 ± 3.6 microns, and the difference in thickness was 5.6 microns for the thinnest area and 27.6 microns for the thickest area. The average height of alveocytes was 6.15 ± 2.4 microns, the size of alveocytes ranged from 5.2 to 14.8 microns (Table 2).

Conclusion

Lung tissue damage, circulatory disorders and damage to the alveolar and bronchial epithelium play an important role in the development of hyaline membrane disease in the lungs of premature infants. Of great importance is the accumulation of amniotic epithelium, meconium bodies, maternal erythrocytes in the alveolar cavity due to intranatal hypoxia and

aspiration of amniotic fluid in premature infants due to damage to the alveolar epithelium. Morphometric studies showed that only 1/3 of the lungs of infants born at the age of 22-27 weeks contained air in the alveoli, the interstitial tissue of the alveoli was thicker than in the subsequent groups, the alveolar epithelium was relatively large, and the resulting hyaline membranes were relatively large. In the second group of infants who died at 28-32 weeks, the area occupied by alveoli in the lungs doubled, interstitial tissue became thinner (25.3 ± 3.2), the number of alveocytes decreased, and the formed hyaline membranes thickened compared to the previous group. In the third group of infants who died at 33-37 weeks, it was noted that the area of the respiratory alveoli in the lungs increased sharply and amounted to $78.4 \pm 8.5\%$ of the total lung area. It was found that interstitial tissue is also thinner, alveocytes are smaller, and the hyaline membrane formed in the alveolar cavity is thicker than in other groups.

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