

Causes, pathogenesis, clinical and anamnestic analysis and morphometric examination of respiratory distress syndrome and atelectasis in infants.

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Abstract

This article, compiled on the basis of an analysis of scientific literature, is devoted to the problem of respiratory distress syndrome and atelectasis in infants. Respiratory disorders are in 2nd place among diseases of infants, their overall incidence is 1% of all infants, and in premature infants it is up to 14%. The most common form of respiratory distress syndrome is atelectasis, the main causes of which are: weakness and slowing of the respiratory center, underdevelopment of the respiratory system, hypoxia or asphyxia, brain or spinal cord injury. Externally, the focus of atelectasis is fleshy, swollen, dark gray, microscopically the walls of the alveoli are tightly packed, the alveolocytes are displaced, and cells and hyaline membranes are found in the space.

Keywords: infant, lung, breath, respiration, atelectasis, hyaline membrane, surfactant.

Urgency. Respiratory system diseases in infants are one of the most urgent problems. Among the diseases of infants, respiratory disorders are in second place - 8.9% and most often occur in premature infants, due to the morphofunctional characteristics of the respiratory system. In particular, respiratory distress syndrome in infants is 7-12.5% in general, 1-1.8% in premature infants, and 0.4-0.5% in very low birth weight infants. The main cause of the development of this disease is the lack of endogenous surfactant in the lungs of infants, weakness of the respiratory muscles and the inability to breathe independently. In foreign scientific literature, the terms “respiratory distress syndrome” and “hyaline membrane disease” are synonyms. Primary atelectasis often develops in the lungs of infants as a separate nosological unit. Clinical differential diagnosis of these lung diseases in infants is very difficult. Pathological examinations reveal atelectasis, edematous-hemorrhagic changes, and hyaline membranes as direct causes of infant death. Respiratory disorders in infants are mainly related to the gestational age of pregnancy. The shorter the gestation, the higher the degree of disease development, and the longer the gestation, the less frequent the disease.

Infant respiratory distress syndrome (IRDS) is a non-infectious process that develops in the first days after birth, manifested by acute respiratory failure, surfactant deficiency, underdevelopment of pulmonary tissues, and dysfunction of other systems. Respiratory distress syndrome is an important cause of morbidity and mortality in both premature and term infants.

Risk factors for the development of respiratory distress syndrome include: birth at a gestational age of less than 35 weeks, birth with morphofunctional immaturity, acute and chronic hypoxia, maternal diabetes mellitus, hypothyroidism and other endocrine diseases, twin pregnancy, cesarean section, premature placental abruption, the presence of congenital and genetic diseases, birth with head injury. Local causes include: respiratory center deficiency, bronchial stenosis, surfactant deficiency, intercostal muscle insufficiency, low lung tissue elasticity, respiratory rate, bradypnea.

Infantile pulmonary atelectasis is a failure to open or re-close the alveoli of the lungs within 2 days after birth, due to the specific structure and central control of the bronchoalveolar tissue. The literal translation of atelectasis is “incomplete collapse,” and it refers to the anatomical condition of the lung. Atelectasis of the lungs in infants is a respiratory distress syndrome and occurs in 1% of all infants and 14% of premature infants. The relevance of the problem of pulmonary atelectasis for the pediatrics field is due to the fact that there are many reasons why alveolar tissue in the lungs collapses in infants under one month of age. In pulmonary atelectasis, a diffuse reduction of the respiratory surface of the alveolar tissue and the part of it that participates in breathing is observed. As is known, there are more than 300 million alveoli in the lung tissue, and they

enrich the blood with oxygen during breathing. Atelectasis is a manifestation of respiratory distress syndrome, the main cause of respiratory failure in the neonatal period, and its incidence is higher with gestational age and body weight. It occurs in an average of 65% of infants born at 30 weeks of gestation, 35% if prophylaxis is carried out with steroid hormones, 25% in those born at 34 weeks of gestation, and 10% with prophylaxis. All conditions leading to surfactant deficiency are risk factors for respiratory distress syndrome. These include underdevelopment of the lungs, fetal asphyxia, morphofunctional insufficiency, impaired pulmonary-cardiac coordination, pulmonary hypertension, metabolic disorders, including: acidosis, hypoproteinemia, hypofermentation, electrolyte disorders.

When a baby is born, air first enters the lungs. In this case, the diaphragm creates negative pressure in the chest, surfactant increases the tension on the surface of the alveoli, preventing them from collapsing. However, at birth, the amount of surfactant in the lungs is very low.

According to the international classification, depending on the significance of this pathology and taking into account its prevalence, focal, total and subtotal atelectasis are distinguished. There are also: congenital and acquired atelectasis. The congenital form is observed in premature babies when the lungs are not fully developed, and the airways are blocked by mucus and cerebrospinal fluid. The mechanism of the development of congenital atelectasis is that in fact, in the fetus, the lungs are in a collapsed state without air and are waiting for the first breath. Sometimes atelectasis can develop physiologically in normal-born babies, but it quickly opens.

The causes of primary atelectasis in newborns are: weakness and slowing of the respiratory center, underdevelopment of the respiratory system, previous hypoxia or asphyxia, damage to the head or spinal cord. In addition, ascites aspiration syndrome is also a cause of primary atelectasis. This syndrome is observed mainly when the child is born late or prematurely, and hypoxia, hypercapnia, acidosis develop in the child's body, which stimulates the respiratory center, the act of breathing begins in the fetus, intestinal peristalsis increases, meconium enters the cerebrospinal fluid and aspirates the respiratory tract. The respiratory tract, i.e. the trachea, bronchi, and lung parenchyma, becomes obstructed and inflamed, causing atelectasis.

2) moderate - due to impaired blood circulation in the lungs, pulmonary edema; 3) severe atelectasis - covering the lungs with pathological tissues, i.e. pneumosclerosis, bronchial retention cyst, bronchiectasis. Depending on the prevalence of the pathological process: atelectasis of the entire lung, segmental atelectasis, segmental, subsegmental atelectasis.

Depending on which lung develops atelectasis, it proceeds in different morphological and functional forms. Atelectasis of the lower lobe of the left lung develops when the bronchiole of the lung segment is obstructed, as a result of which it involves and stretches the organs of the lower part of the thoracic cavity, including: the heart, esophagus and thymus. Atelectasis of the upper lobe of the right lung involves the organs located in the upper part of the thoracic cavity. In this case, the middle lobe of the right lung, the lower part of the upper lobe, is subject to compensatory emphysema, and some ruptures are complicated by the development of pneumothorax. Ring or disc atelectasis is manifested by the collapse of the parenchyma of neighboring segments in diffuse pathologies of the bronchial tree. The causes of this are pneumonitis, fibrosing alveolitis, sarcoidosis. Another type of atelectasis is middle lobe syndrome. In this case, the lymph nodes of the middle lobe of the right lung, as a result of inflammatory diseases or tuberculosis, compress the bronchus and it becomes obturated, as a result of which atelectasis develops.

The Pathogenesis of Obstructive Atelectasis

The pathogenesis of obstructive atelectasis occurs when the bronchial lumen is blocked by a tumor, foreign body, vomit, sputum, or blood, leading to a focus of dyselectasis in the alveolar tissue. In this case, air is absorbed into the blood vessels of the lung tissue through the bronchial wall, provoking impaired lymphatic and blood circulation, such as engorgement. If the obstruction is not removed within three days, it can lead to serious complications.

Purpose of the Study

In Uzbekistan, several scientific studies are being conducted on the role and significance of pathological-anatomical indicators in diagnosing and effectively treating undiagnosed and complicated neonatal deaths due to respiratory failure. However, the incidence rate, risk factors, and pathological anatomy of pulmonary atelectasis in infants have not yet been fully investigated.

The main objective of the study is to analyze the risk factors for pulmonary atelectasis in infants, improve the assessment of pathomorphological changes developing in the focus of atelectasis depending on gestational age and postnatal life, and assess its diagnostic significance in respiratory distress syndrome.

Materials and Methods

A clinical and anamnestic analysis was conducted on mothers and the birth process of infants born with primary atelectasis. Archival material from the Republican Center for Pathological Anatomy was used as the basis for analysis for the years 2017–2022.

The study and analysis of medical documents from a total of 448 infants who died of respiratory distress syndrome of varying degrees revealed that the risk factors for developing primary atelectasis in newborns included maternal conditions such as preeclampsia, infectious diseases, endocrine pathology, and various extragenital diseases, as well as complications related to the birth process.

Risk factors also included maternal age under 20 or over 35, preeclampsia, infectious diseases, complicated labor, head and brain injuries, and a high incidence of congenital malformations. Primary atelectasis of the lung was most common in premature infants, with risk factors also being significantly high (see Figure 1). The second group of risk factors contributing to the development of atelectasis in full-term infants is outlined in Figure 2.



**Figure 1. Risk factors for primary atelectasis in premature infants: Morpho-functional insufficiency, Hypoxia
 Amniotic fluid aspiration
 Placental abruption
 Brain injury
 Congenital malformations**



**Figure 2. Risk factors for primary atelectasis in full-term infants: Diabetes mellitus
 Maternal infection
 Amniotic fluid aspiration
 Placental abruption
 Brain injury
 Congenital malformations**

In addition, morphometric examination of the structural units of the lung tissue was carried out using the “point counting” method of G.G. Avtandilov. Three forms of primary atelectasis of the lungs of infants were selected: acinar atelectasis; segmental atelectasis; fragmentary atelectasis. To compare the quantitative indicators of these forms of atelectasis, the lung tissue structures of children who died from extrapulmonary head injuries were counted as a control group. In the images taken from histological sections prepared from lung tissue of these groups with atelectasis stained with hematoxylin and eosin, the points corresponding to the following structural units were counted: alveolar space, blood vessels, foci of hemorrhage, foci of atelectasis, alveolar wall. Based on the available quantitative data, the following coefficient can be calculated: the ratio of the area of the alveolar space to the area occupied by the alveolar wall or foci of atelectasis - the alveolar space activity coefficient (ASAC). Using the morphometric method of G.G. Avtandilov, the “point

counting-test system”, 3 forms of primary atelectasis of the lungs of infants were selected: 1) acinar atelectasis, 2) segmental atelectasis, 3) fragmentary atelectasis. To compare the quantitative indicators of these forms of atelectasis, the lung tissue structures of children who died from extrapulmonary head injuries were counted as a control group. These groups were counted as points corresponding to the following structural units in histological sections prepared from atelectasis lung tissue stained with hematoxylin and eosin. An average of 10 points were counted in each group:

- Alveolar space – Rab;
- Blood vessels – Rqt;
- Hemorrhage sites – Rqq;
- Atelectasis sites – Raw;
- Alveolar wall – Rad.
- The points counted in 10 images for each structural unit were added up and the average was calculated, and the area occupied by the structural unit (V) was calculated from it based on the following formula, for example: the area occupied by the alveolar space - $V_{ab} = Rab/R \times 100$. In this way, the areas occupied by all structural units of the lung tissue were calculated: V_{ab} , V_{qt} , V_{qq} , V_{aw} .

Based on the quantitative data obtained on these indicators, the following coefficients can be calculated:

The coefficient of the ratio of the alveolar space area to the area occupied by the alveolar wall or foci of atelectasis is the alveolar space activity coefficient (ABFC);

Table 1

Control group

Number of microphotos	Number of points				Total number of points
	Rab	Rqt	Rqq	Rau	
1	96	34	8	61	200
2	102	30	7	60	
3	104	28	5	63	
4	94	36	9	61	
5	98	35	8	59	
6	101	29	10	60	
7	103	28	7	62	
8	95	35	8	62	
9	103	31	6	60	
10	99	33	8	60	
Σ	995	321	76	608	2000
M±m %	49,7±2,23	16,1±1,64	3,8±0,85	30,4±2,08	

CONCLUSION

1. Among the risk factors for the development of primary atelectasis in babies, it has been proven that the mother's endocrine, infectious, preeclampsia diseases, complicated childbirth, early placental migration, birth defects and premature birth are more significant.

2. The shorter the gestation period, the more severe and diffuse atelectasis due to the underdevelopment of the lungs. If the gestational months are relatively long, the atelectasis appears as a large focus, the development of acinar atelectasis with small foci in full-term infants, and the development of secondary changes such as inflammation and sclerosis in the lungs depending on the length of time the babies live.

3. It was confirmed that primary atelectasis occurs in most cases in segments I, II, IX, X of both lungs, and in segments IV and V of the left lung, of which small-focal atelectasis develops in the upper segments I, II of the lungs, and large-focal and diffuse atelectasis develops in the lower segments IX, X, and histologically, the lung tissue in these segments is underdeveloped.

4. It was confirmed that, depending on the forms of primary atelectasis, the alveolar space decreases sharply, the area it occupies decreases by 2.4 times in acinar atelectasis, 3.6 times in segmental atelectasis, and 5.3 times in segmental atelectasis, while, on the contrary, the area of atelectasis increases, the alveolar space activity coefficient, indicating the level of respiration in the lung tissue, is 1.63 in the control group, this indicator decreases by 3.5 times in acinar atelectasis, 6.5 times in segmental atelectasis, and 10 times in segmental atelectasis.

References:

1. E. *Lungs of Newborns* / Edited by R. Polin; Translated from English under the editorship of D.Yu. Ovsyannikov. Moscow, 2015. 672 pages.
2. Belousova Natalya Alexandrovna. *Morphological Characteristics of the Lungs in Fetuses and Newborns with Extremely Low Birth Weight in Respiratory Distress Syndrome: Dissertation for the Degree of Candidate of Medical Sciences: 14.00.15* / Belousova Natalya Alexandrovna; Military Medical Academy. - Saint Petersburg, 2006. - 120 pages.
3. Wauer R. *Surfactant in Neonatology. Prevention and Treatment of Respiratory Distress Syndrome in Newborns*. Moscow, 2011. 96 pages.
4. Garstukova L.G., Kuznetsov S.L., Derevyanko V.G. *Visual Histology (General and Special)*. Moscow: Medical Information Agency, 2008. 204 pages.
5. Gelfand B.R. *Acute Respiratory Distress Syndrome*. M. Littera, 2007. – 232 pages.
6. Novikov N.Yu., Birkun A.A. (first author), Nesterov E.N. *Problems of Diagnosing Acute Respiratory Distress Syndrome. Ukrainian Pulmonology Journal*, 2012, No. 3, pp. 47-52.
7. Ovsyannikov D.Yu. *European Consensus on Neonatal Respiratory Distress Syndrome, Revised in 2013*. Peoples' Friendship University of Russia, Moscow, 2014.
8. Ovsyannikov D.Yu., Kravchuk D.A., Nikolaeva D.Yu. *Clinical Pathophysiology of the Respiratory Organs of Premature Infants*, Vol. 6, No. 3, 2018.
9. Orynbasarov Serik Orynbasarovich. *Pathomorphological Characteristics of the Lungs, Placenta, and Their Chemical Composition in Fetuses and Newborns During the Perinatal Period in the Aral Sea Region: Abstract of the Dissertation for the Degree of Candidate of Medical Sciences: 14.03.02* / S.O. Orynbasarov; Novosibirsk State Medical University. - Novosibirsk, 2015. - 24 pages.
10. Serikbay M.K., Alsherieva U.A., Anayatova B.Zh. *Primary Atelectasis of the Lungs in Premature Newborns. Scientific Outlook into the Future: Institute of Marine Economy and Entrepreneurship (Odessa)*. – 2017. – Vol. 2, No. 7. – pp. 94-99.
11. Spirin A.V. *Pathomorphology of Adult Respiratory Distress Syndrome Associated with Pregnancy [Text]: Abstract of the Dissertation for the Degree of Candidate of Med*
12. Simon A., Amman R.A., Wilkesmann A. et al. Respiratory syncytial virus infection in 406 hospitalised infants premature infants: results from a prospective German multi center database // Eur. J. Pediatr. 2007. Vol. 166. P. 1273–1283.
13. Checchia P.A., Nalysnyk L., Fernandes A.W. et al. Mortality and morbidity among infants at high risk for severe respiratory syncytial virus infection receiving prophylaxis with palivizumab: systematic literature review and metaanalysis // Pediatr. Crit. Care Med. 2011. Vol. 12, N 5. P. 580–588.

14. Carbonell-Estrany X., Quero J., Bustos G. et al. Rehospitalisation because of respiratory syncytial virus infection in premature infants younger than 33 weeks of gestation: a prospective study // *Pediatr. Infect. Dis. J.* 2000. Vol. 19. P. 592–597.
15. Stevens T.P., Sinkin R.A., Hall C.B. et al. Respiratory syncytial virus and premature infants born at 32 weeks' gestation or earlier: hospitalization and economic implications of prophylaxis // *Arch. Pediatr. Adolesc. Med.* 2000. Vol. 154. P. 55–61.
16. Resch B., Resch E., Muller W. Should respiratory care in preterm infants include prophylaxis against respiratory syncytial virus infection? The case in favor // *Paediatr. Respir. Rev.* 2013. Vol. 14. P. 130–136.
17. Huang L., Chen Q., Zhao Y., Wang W. et al. Is elective cesarean section associated with a higher risk of asthma? A meta-analysis // *J. Asthma*, 2015. Vol. 52, N 1. P. 16–25.
18. Algert C.S., Bowen J.R., Lain S.L., Allen H.D. et al. Pregnancy exposures and risk of childhood asthma admission in a population birth cohort // *Pediatr. Allergy Immunol.* 2011. Vol. 22. P. 836–842.
19. Brehm J.M., Acosta-Perez E., Klei L., Roeder K. et al. Vitamin D insufficiency and severe asthma exacerbations in Puerto Rican children // *Am. J. Respir. Crit. Care Med.* 2012. Vol. 186. P. 140–146.
20. Civelek E., Cakir B., Orhan F., Yuksel H. et al. Risk factors for current wheezing and its phenotypes among elementary school children // *Pediatr. Pulmonol.* 2011. Vol. 46. P. 166–174.
21. Collier C.H., Risnes K., Norwitz E.R., Bracken M.B. et al. Maternal infection in pregnancy and risk of asthma in offspring // *Matern. Child Health J.* 2013. Vol. 17. P. 1940–1950.
22. Getahun D., Strickland D., Zeiger R.S., Fassett M.J. et al. Effect of chorioamnionitis on early childhood asthma // *Arch. Pediatr. Adolesc. Med.* 2010. Vol. 164. P. 187–192.
23. Goyal N.K., Fiks A.G., Lorch S.A. Association of late-preterm birth with asthma in young children: practice-based study // *Pediatrics.* 2011. Vol. 128. P. 830–838.