COMPARATIVE DYNAMICS OF TUBERCULOSIS AND OTHER INFECTIOUS DISEASES OF THE LUNGS

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Savchenko Peter Pavlovich, Orcid ID 0000-0001-5850-8307, J-2658-2015, Head, Professor of the International Research Center of Medicine and Substances «Intersuccess», Kiev, Ukraine, Sc.D., Ph.D., Academician of the Ukrainian Academy of Sciences, Honorary Professor of the University «Lviv Stavropigion».

Savchenko P.P u-spp@i.ua

Annotation

The introduction of a dynamic approach, as the main scientific research method, including an interdisciplinary one, and the discovery of a new starting factor in the onset and development of the tuberculous process[1] made it possible to come close to the dynamics of lung specific and non-specific infectious diseases. As a result, it was possible to discover the characteristic features and differences in the development of inflammatory processes of specific and non-specific infectious lung diseases; identify a new bacterial pathology where bacteria live in a new environment and do not directly affect the respiratory tract. For the first time in a new aspect, the article shows the comparative dynamics of the development of tuberculosis and other infectious diseases.

Keywords: dynamic interdisciplinary research method, the starting factor for the emergence and development of tuberculosis – «the cellular process of irreversible defatting», the dynamics of surfactant in pulmonary pathologies, non-pathogenic bacteria of the respiratory tract and their irritating effect, the starting for

the onset of the formation of isolated tuberculous formations (tubercle, tuberculoma), COVID-19.

Background:

Specific and non-specific lung diseases are one of the important problems of modern medicine. This article presents the dynamics of diseases of an infectious lesion of the respiratory tract. Infectious diseases are diseases caused by pathogens such as bacteria, viruses, fungi or protozoa. Tuberculosis is usually, classified as a specific lung disease.

Non-specific lung diseases, however, like specific ones, occupy one of the leading places in the structure of human morbidity and mortality[2]. It should note that **there is no clear boundary between specific and nonspecific diseases**.

Currently, a new, unknown pathology called “COVID-19” has joined a very complex problem in the fight against lung diseases, where there are more questions than answers. Is it possible to sort out such new pathologies when there are not enough decisions regarding the old ones, and which continue to attack? The answer known.

That is why it becomes important to understand that until the old and painfully known pathologies reveal their secrets, no solutions for the new pathology cannot seen. At least in the history of science, it was not possible to prove otherwise.

There are various reasons for the occurrence of pathological conditions in the lungs. Therefore, their pathogenesis is different, which indicates many mechanisms leading to damage to the constituent components of the respiratory department of the lungs, the air-blood barrier[3].

Ignorance by researchers and clinicians of many unsolved issues in the etiopathogenesis of diseases leads to errors in the diagnosis and treatment of lung diseases.

For example, according to the National Institute of Phthisiology and Pulmonology. F.G. Yanovsky's, errors in the diagnosis of tuberculosis in feldsher-

obstetric centers are 96.6% - 99.5, the errors of doctors in rural outpatient clinics and district hospitals are 80.4% - 90.3%, errors of general practitioners in central district hospitals are 54.2% - 72.1%, errors of city and regional general practitioners are 42.2% - 51.7%, the errors of TB doctors are 3.2% - 4.7%. In general, in phthisiology, these data are similar.

According to scientists, this condition leads to the fact that patients are treated for a long time in general hospitals with the causes of non-specific pulmonary and extrapulmonary pathology, and then with advanced cases of tuberculosis they get to the TB specialist[4].

Very often, the tuberculosis process develops against the background of nonspecific pathological inflammatory changes in the respiratory system. The combined combination of infectious pathogens has a negative effect on the prognosis and the possibility of clinical recovery[5].

In the complex problems of lung diseases, the behavior is still a mystery of mycobacterium tuberculosis, which causes complex contradictions with the host organism, provokes incomprehensible protective immune responses, and is the only bacterium that behaves contrary to the behavior of other infectious bacteria.

If there are no particular difficulties with respect to major infections, then with respect to Koch's wand there is an incomprehensible complexity of the interaction between the host and the pathogen, which so far does not have a sufficient response. Because of this complexity, it becomes extremely difficult to identify the mechanisms involved in protecting the body[6, 7].

And the most basic problem into these contradictions is that in animal models during insemination it is not possible to develop necrotic foci, the precursors of cavities characteristic of advanced TB in humans[6]. These conflicting facts challenge to the researcher and confound him. Moreover, new studies reveal more conflicting results of the relationship of mycobacteria with the immune system and the host organism as a whole, and raise more and more unclear questions[1, 8, 9].

Understanding the relationship between bacteria and the immune defense of the host organism using new resources and technologies, within the framework of old methods, remains for the time being within the limits of unrealizable hopes. New hypotheses that are put forward by researchers meet more and more contradictions in the experiment, and pose new questions. It becomes obvious that if you do not-unwind a tangled ball of ambiguities and contradictions to the first nodal incomprehensible moments for finding solutions, the continuation of research by generally accepted methods remains meaningless.

Until it is possible to answer the question, the main question, «Why, despite great efforts, the researchers still cannot create necrotic foci (precursors of caverns) characteristic of the spread of tuberculosis in humans in animal models?», until then, the full dynamics tuberculosis for humans will be closed. Which, in turn, will keep medicine in suspense, and not allow solving the problem of lung pathologies. At least the history of medicine does not yet know the opposite. The existing facts of a successful recovery do not yet have a sufficient explanation and often contradict the theory. Facts – in the manifest form, the thing is inexorable and not subject a man.

Objective:

Conducting a study using a new interdisciplinary dynamic method of histological and cytological pathological materials in order to: understand the difference in the dynamics of specific and non-specific lung diseases and reveal the starting factors of pathologies.

Materials and Methods:

In the study of the etiopathogenesis of specific and non-specific lung diseases, the personal interdisciplinary research method of Peter Savchenko, the philosophical approach (agreed scientific views) and the root cause method are used. In this procedure used of unique developments.

These methods are applied:

- in the analysis of histological and cytological pathological tissue materials after resection;

- in a comparative retrospective cross-assessment of their own material with basic histological and cytological materials (micrographs and descriptive parts), which were obtained in phthisiology from the 40s of the last century to this day[1]; including materials provided by researchers from the National Institute of Phthisiology and Pulmonology named after F.G. Yanovsky's[10].

Along with the starting factor of the onset and development of the tuberculosis process, which received experimental confirmation in the dynamics of changes recorded in cytological and histological preparations, similar confirmations discovered in the dynamics of non-specific infectious diseases, which presented in this article.

The article is the final material on the topic «Specific and nonspecific lung diseases» regarding pathologies of an infectious nature. The article in the form of short formulas presents fundamental discoveries, except for the elements of Know-How.

Results:

1. The dynamics of the tuberculosis process and infectious pathologies.

The dynamics of the tuberculosis process presented sufficiently in the materials of the study of the starting factor of the tuberculosis process[1]. In this case, the main changes should be noted:

- the appearance in the alveolocytes of the 2-type «cellular process of irreversible defatting» is the beginning of the tuberculosis process;
- a decrease in the synthesis of surfactant in the cellular structures of alveolocytes 2-type, including in the final «osmiophil lamellar bodies», develops in the direction: from the zone of extra-tuberculous formation to the center of the focus, due to the lack of starting materials for the synthesis of surfactant in the absence of irreplaceable substances;

- in the area of the pathological tuberculous focus, the alveolar system (alveolar passages and walls of the alveoli) is disrupted and does not participate properly in gas exchange;

- alveolocytes type-2 produce radical surfactant, that **is the root cause for isolating the body's own cells into individual tuberculosis formations**;

- the surface of intact alveoli is covered with a radical surfactant, which is synthesized by alveolocytes type-2, causing damage to the epithelium.

Own micro-shooting of infectious materials and filming from phthisiology and pulmonology materials in the fundamental elements are completely identical, no significant differences were found. The descriptive dynamics, which presented above in their own samples and from other sources of phthisiology almost identical in appearance. The general picture of the TB lesion described above presented in *Fig. 1*.

In **the initial stage of infectious pathologies**, the following main dynamic changes were recorded, which are directly related to the discoveries presented below:

- The alveolar system in the focus for other infectious diseases, in contrast to the tuberculous focus of inflammation, partially damaged, and at the same time performs its functions.

- An inflammatory exudate observed inside the alveoli, which complicates, but does not exclude, gas exchange in the lungs; gas exchange does not occur in the tuberculous focus;

- On the surface of the walls of the alveoli is a surfactant of a radical nature arising from damage by infections, and exposure to a radical surfactant leads to damage to the epithelium;

- The walls of the alveoli are thickened, and one of the reasons is an increase in the synthesis of surfactant to compensate for the destroyed complex.

Thus, a comparative analysis of the dynamics of the inflammatory process has established that;

- in tuberculosis, the synthesis of surfactant by its own cells leads to the appearance of a radical surfactant, which from alveolocytes type-2 stands out on the surface of the alveoli and damages the epithelium (adherence effect);

- in tuberculosis, the alveoli with tuberculous cells are isolated into a separate formation in which the isolated masses turn into a caseous conglomerate (*Fig. 1*), and they lose their respiratory function;

- in case of tuberculosis in alveolocytes type-2 outside the focus that retain their function, the synthesis of surfactant is increased to ensure the lungs functional activity instead of alveolocytes type-2 that have gone out of the process and become tuberculous;

- in infectious pathologies, the surfactant that covers the surfaces of the alveoli is destroyed by the infection and becomes radical, and the epithelium is damaged by the damaged surfactant (adherence effect);

- in case of infectious diseases, the alveoli retain their working architecture, where the walls of the alveoli thicken (*Fig. 2*) due to the increased synthesis of surfactant to ensure the functional activity of the lungs, since the surfactant on the surface of the alveoli is destroyed by the infection and becomes radical, damaging the epithelium.

2. Surfactant.

A study of the dynamics of pathological processes in the lungs raises the question of surfactant, its occurrence and movement from the cell to the surface of the alveoli, and the state of the surfactant in the air space of the alveoli. Therefore, questions are discussed about the structure of surfactant related to the topic.

Many surfactant functions been identified to researchers. But the changing dynamics of surfactant synthesis is still not clear enough.

In general, Surfactant is a mixture of dipalmatoilphosphatidylcholine (40%), other phospholipids (40%), surfactant associated proteins (5%) and other minor compounds like cholesterol (5%)[11]. Surfactant separates the surface of the alveoli from the air in the alveoli.

It’s believed that the relative amount of surfactant in the lungs of an adult healthy person is only 5-15 mg / kg of body weight and this value is lower than in healthy newborns[12].

It should be noted that in the body there is a constant and ongoing process: substances for the synthesis of surfactant enter the body from the outside, then they enter the cellular structures where the synthesis of surfactant takes place, which after synthesis is released on the surface of the alveoli. The surfactant fulfills its operational requirements, and the trachea and the esophagus it comes for the disposal of the digestive system. Thus, in order to maintain the work of the sufactant complex, it is necessary to constantly supply, irreplaceable substances to the body.

Only at first glance does the question of maintaining the work of the surfactant complex seem simple, and it cannot solved by replenishing the artificially selected surfactant from the outside.

It should be specially noted that over the past two decades a large amount of very conflicting data has been published on the effectiveness of the use of exogenous surfactant in patients with lung pathology[12, 13, 14, 15]. Here need to study.

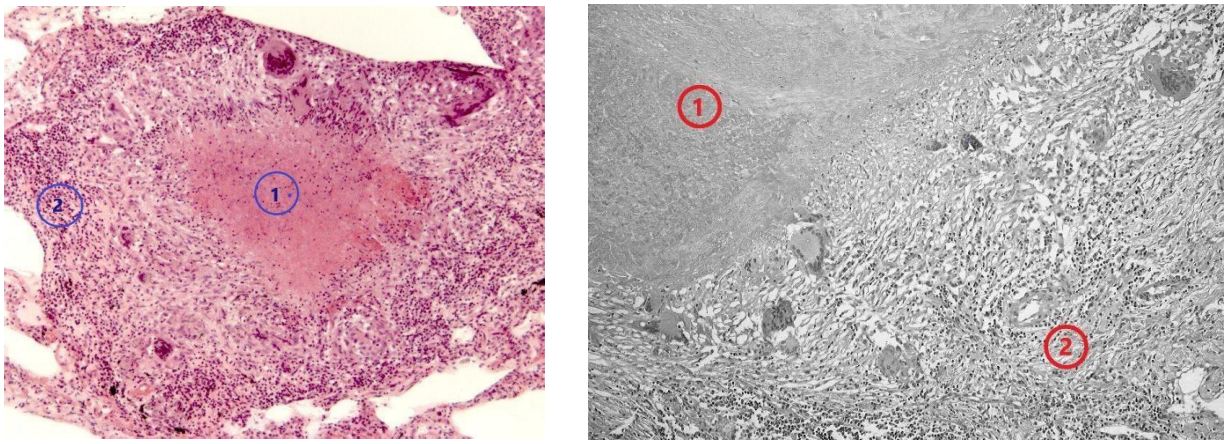

Fig. 1. *Tuberculous lesion with isolated formation.* On the left and right figures: 1 – the center of caseous necrosis, 2 – epithelial shaft of an isolated tuberculosis formation.

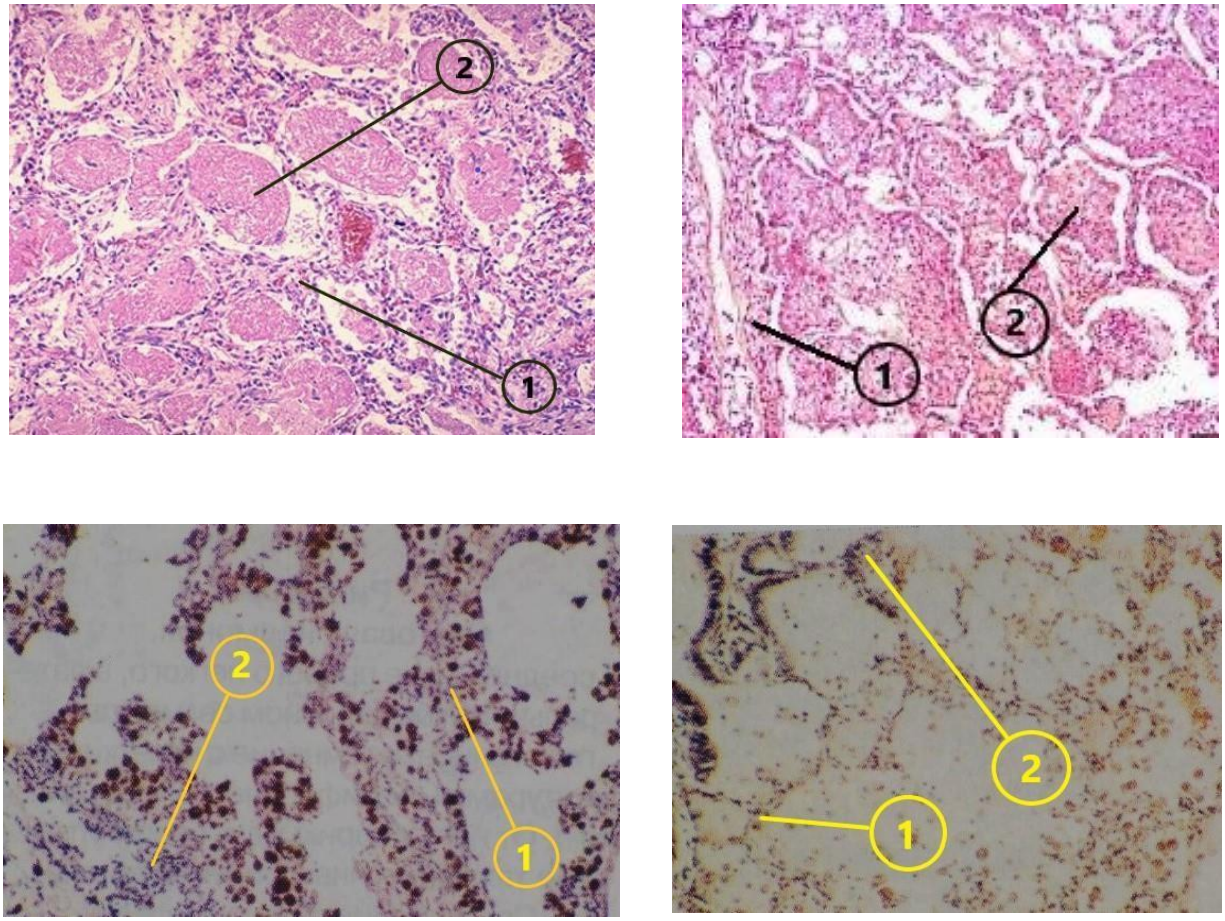

Fig. 2. *Infectious pathologies*. On 4 samples indicated: 1 – thickened walls of the alveoli, 2 – inflammatory exudate.

Given the results of research, it is necessary to note the following:

- with tuberculosis, the surfactant turns into a radical pathological tool due to a violation of the synthesis of surfactant in view of the arising cellular process of irreversible degreasing;
- in other infectious diseases, the surfactant turns into a radical pathological tool not in the cell, but on the surface of the alveoli in view of damage to the surfactant from bacteria.

3. Alien non-pathological infection – false pathology.

During the study of specific and non-specific lung pathologies, diagnostic material and analysis of the course of diseases in patients, us had to come across amazing facts. The course of the disease was observed in 5 patients.

The observed pathology has no descriptions in any of the known pulmonary pathologies. These studies require the increased participation of scientists and new methodologies. Therefore, this article covers only preliminary actual results. Our center is ready to conduct joint research if someone shows interest in this pathology.

So, a cough is a protective mechanism designed to remove a foreign body, sputum from the respiratory tract. Coughing occurs with irritation of the corresponding reflexogenic zones lined with ciliary epithelium in the respiratory tracts.

Inflammatory, mechanical, chemical, and temperature factors can provoke a cough. Receptor irritation can occur not only upon contact with a foreign body, mucus, etc., but also due to inflammation in the mucous membrane of the larynx, trachea, and bronchi. With the constant irritating effect of the ciliary epithelium, a cough effect occurs, with which the irritant removed.

A cough observed in a false pathology and continuing during the vegetative period of bacteria does not bring benefits, does not evacuate a partially foreign body (foreign bacteria), moreover, it can injure the larynx by sharp coughing.

At this stage, it was possible to establish:

- prolonged sharp cough is caused by non-pathogenic bacteria at the time of the vegetative period of life after reproduction by mechanical action on reflexogenic zones;
- in normal mode, these bacteria live in the hairline of the skin of domestic animals (cats, dogs and others), and due to atmospheric pollution, the bacteria move to more favorable conditions for themselves, in the human respiratory tract.
- the habitat zone of non-pathogenic bacteria in the human body is located in the vallecular of epiglottis region, where during the vegetative period of bacterial life their chaotic movement occurs, leading to irritation of the reflexogenic zone in this region (in *Fig. 3*);
- **the use of antibiotics in this pathology is unacceptable**.

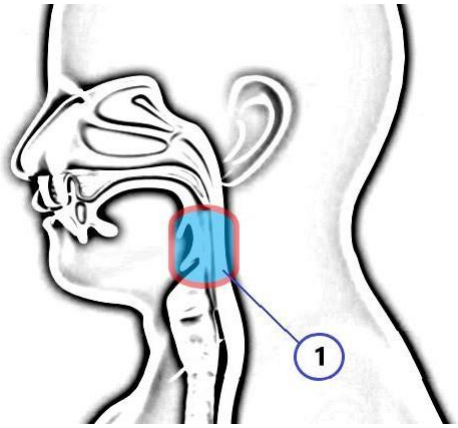

Fig. 3. *Epiglottis Vallecula Area,* depicted by the number 1.

This pathology is at the stage of further research and study. At the preliminary stage, certain impact techniques been created that improve the course of the pathological process, which still need to be confirmed properly. We invite researchers to participate in these works.

Conclusion:

As a result of a comparative analysis of the dynamic component of the pathological processes of the lungs with tuberculosis and other infectious diseases, the following facts were established:

- radical surfactant, which damages the alveolar epithelial surface under the influence of adhesion, is secreted in alveolocytes type-2, in the form of a radically damaging agent of endogenous etiology, as a result of a lack of substances for the synthesis of the complex, and in this form it leaves the cells to the surface of the alveoli (tuberculous process);
- radical surfactant, which damages the alveolar epithelial surface under the influence of adhesion, turns into a state of a radially damaging agent of exogenous etiology from a normal surfactant under the influence of infections inside the air space of the alveoli (non-tuberculous process);
- in tuberculosis, a damaging surfactant of endogenous origin accumulates on the surface of the alveoli, and with other infectious diseases – of exogenous origin;

- for the first time, a clear boundary has been established between a specific disease (tuberculosis) and other infectious diseases in the form of «a radical surfactant of various etiologies, in the first case – of an endogenous nature, in the second – of an exogenous»;

- the appearance in the 2-type alveolocytes of the «cellular process of irreversible defatting», and as a result, the appearance of radically damaging surfactant from these cells on the surface of the alveoli, is the initial signal to the body's defenses for the formation of an isolated tuberculosis formation (tubercle, tuberculoma);

- the need for essential substances coming from the outside for the synthesis of surfactant varies between 5-15 mg / kg of body weight;

- revealed the nature of a new pathology of non-infectious damage that occurs as a result of penetration into the human body into the area of «*the vallecula of epiglottis*» of bacteria that live in the hair of domestic animals (cats, dogs and the like); and which cause a subsequent irritant effect in the vegetative period of bacterial life, which causes a prolonged and often a sharp cough, which can lead to mechanical damage to the respiratory tract.

The revealed facts, as a result of studies and repeatedly confirmed from the moment of the main discoveries in the years 80-90 and up to the present, allow us to answer many questions and contradictions that occur in pulmonology and phthisiology, to significantly review the existing methods and protocols of treatment, to proceed developing a new generation of drugs.

Targeted diagnosis of the surfactant complex will allow a more accurate diagnosis of lung disease, including on the problem of COVID-19, and, accordingly, a complete selection of treatment methods and drugs.

Literature

1. Savchenko P.P., Savchenko L.L., A new starting factor for the emergence and development of the tuberculous process. // Popular science journal of the Ukrainian Academy of Sciences, «Inventor and innovator» №2 -2017, p. 25-27, Kiev, http://vir.uan.ua/archives/2017/2-2017.pdf.

2. Putov N.V., Fedoseev G.B. Pulmonology manual. // The medicine, 1984, p. 456.

3. Erokhin V.V., Functional morphology of the lungs», // The medicine, 1988, стр. 204.

4. Feschenko Yu.I., Melnik V.M., Cherenko S.A., Matusevich V.G., Zhurilo A.A., Novozhilova I.A., Linnik N.I., Current trends in the study of tuberculosis problems // http://www.ifp.kiev.ua/doc/staff/naukday2013.pdf**.**

5. Spiridonova L.G., Ten MB, Labutin I.V., Mezhebovskiy V.R., Detection of non-specific microflora and its drug resistance in patients with pulmonary tuberculosis // журнал «Эффективная фармакотерапия». 2019. Том *15.* № 7, Пульмонология и оториноларингология.

6. Stefan H.E. Kaufmann, Stewart T. Cole, Valerie Mizrahi, Eric Rubin, and Carl Nathan, Mycobacterium tuberculosis and the host response, // 2006, DOI: 10.1084/jem.20050842/ Published June 6, 2005, electronic source – http://jem.rupress.org/content/201/11/1693.

7. Alamelu Raja, Immunology of tuberculosis. // Indian J Med Res 120, October 2004, pp 213-232.

8. Divangahi, M., Mostowy, S., Coulombe, F., Kozak, R., Guillot, L., Veyrier, F., Kobayashi, K. S., Flavell, R. A., Gros, P., Behr, M. A., NOD2-Deficient Mice Have Impaired Resistance to Mycobacterium tuberculosis Infection through Defective Innate and Adaptive Immunity. // (2008), J. Immunol. 181: 7157-7165. http://www.jimmunol.org/cgi/content/abstract/181/10/7157

9. Kursar M., Koch M., Mittrucker H.-W., Nouailles G., Bonhagen K., Kamradt T., Kaufmann S. H. E., Cutting Edge: Regulatory T Cells Prevent Efficient Clearance of Mycobacterium tuberculosis. // (2007). J. Immunol. 178: 2661-2665. electronic source – http://www.jimmunol.org/cgi/content/abstract/178/5/2661.

10. Feshchenko Yu.I., Suslov E.I., Melnik V.M., Galakhin K.A., Podgaevskaya T.P., Atlas of Lung Diseases. // Kiev, Health, 2001.

11. Chanaka Kahathuduwa, Surfactant – Lowering Pulmonary Surface Tension, // July 28, 2013, https://owlcation.com/stem/Surfactant-Lowering-Pulmonary-Surface-Tension.

12. MacIntyre N.R., Aerosolized medications for altering lung surface active properties. // Respir Care 2000; 45(6):676–683.

13. Gunther A, Schmidt R, Harodt J, Schmehl T, Walmrath D, Ruppert C, Grimminger F, Seeger W., Bronchoscopic administration of bovine natural surfactant in ARDS and septic shock: impact on biophysical and biochemical surfactant properties. // Eur Respir J. 2002 May; 19(5):797-804.

14. B Spragg RG, Lewis JF, Wurst W, Hafner D, Baughman RP, Wewers MD, Marsh JJ. Treatment of acute respiratory distress syndrome with recombinant surfactant protein C surfactant. // Am J Respir Crit Care Med. 2003 Jun; 167(11):1562-6.

15. Spragg R.G., *Surfactant replacement therapy*. // Clin Chest Med. 2000 Sep;21(3):531-41.