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Short Communication

What Does The Time Factor Teach Us In Severe Pneumonia?

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Summery

1. Acute nonspecific inflammation of the lungs (ANSIL) is a prototype of such a nosology as acute pneumonia (AP), which has been known to medicine since ancient times [1]. Despite such a long period of its fame, AP remains an inflammatory disease that is difficult to treat and is one of the problems of global health, being among the leaders in mortality rates in recent years [2-4].

2. The development of microbiology in the late 19th and early 20th centuries contributed to the emergence of the so-called microbial theory of the development of AP [5], which, with the advent of antibiotics in clinical practice, not only strengthened, but also, despite numerous facts of contradictions and inconsistencies, completely took over professional ideas about the nature of the disease, turning into the dominant teaching. At present, the main cause of AP remains its pathogen, and the main means of hope for successful treatment are considered to be etiotropic drugs, among which, despite obvious changes in the etiology of the disease, antibiotics continue to play the main role.

3. With the advent of antibiotics in medical practice, it became known that their therapeutic capabilities are limited only by the antimicrobial effect, which in turn is selective in nature depending on the type of drug. There was and is no evidence that antibiotics can have a direct (!) effect on the mechanisms of the inflammatory process itself and its consequences so that this effect would immediately be reflected in clinical manifestations. Therefore, the action of antibiotics consists exclusively in the indirect fulfillment of their role. Neutralizing one of the integral factors of non-specific inflammation, they make it easier for the body to independently eliminate a sudden catastrophe, right?

4. In the era of antibiotics, there was a fairly long period when the principle of treating inflammatory processes "antibiotics alone", including AP, was quite satisfactory in its results. The gradual and natural decrease in the sensitivity of microbes to such drugs and the change in the list of AP pathogens increasingly required the use of additional and supportive therapy, which was a serious sign for a radical revision of the disease management strategy. However, medicine has been striving for many years to revive the former effectiveness of this therapy and, in particular, to achieve the earliest possible determination of the pathogen in order to prescribe targeted antimicrobial therapy. In this case, various methods were used to obtain material for early microbiological diagnostics, including even such traumatic and poorly substantiated options as transthoracic puncture of the lung [6] and even open organ biopsy [7].

5. It is noteworthy that attempts to achieve the possibility of differential diagnostics of AP by etiological sign have not been successful not only among bacterial inflammations, but also for distinguishing bacterial and viral forms of the disease in everyday practice [8-10]. A very indicative result of the failure of many years of attempts to determine the etiology of AP has been the recognition in recent years at the level of leading world forums on this problem of the empirical prescription of antibiotics as the main principle of antimicrobial therapy [11-12].

6. Attempts to master early diagnostics of AP pathogens have been going on for decades, without achieving the set goals and expected results. Moreover, in recent years, a clear increase in the proportion of viral forms of the disease and an increase in the number of negative results of microbiological diagnostics, exceeding half of the studies [13], make the previously stated goals even more distant and illusory. However, more and more new efforts in this direction continue to this day, striking in their obsession and blind faith in the decisive role of antibiotics [14-16]. At the same time, even after many decades, antibiotics continue to be unshakably considered a means of first and emergency aid for AP [15-18].

7. Today, continuing to rely on the effect of rapid empirical use of antibiotics in patients with AP, specialists know that the early terms of evaluation of the result are usually from 48 to 72 hours [11,12]. In the case of aggressive development of the inflammatory process, waiting for an indirect result of antimicrobial drugs for 2-3 days for many patients plays a tragic role in the further development of events. In this regard, it should be noted that the condition of many patients, which did not inspire concern at the time of hospitalization in general departments, already in the first two days after the start of treatment requires their urgent transfer to intensive care units (ICU)due to the observed deterioration of the condition [19]. Li Jianping et al. [20] note that many fatal cases occur in the first 48-72 hours after the start of treatment.

8. The antimicrobial strategy for treating AP began to form literally on the eve of the advent of antibiotics, when practical medicine was able to use sulfonamides and antipneumococcal antiserum [5]. Therefore, the psychological atmosphere was already prepared for the appearance of the first results of antibiotic therapy, and this therapy began to be perceived as the acquisition of a universal remedy for further success in the treatment of bacterial inflammatory processes. Over time, the leading role assigned to it in the treatment of AP looked increasingly dubious against the background

of the accumulation of contradictory facts. However, this point of view continued and continues to dominate, remaining a generally accepted practical guide. More than one generation of doctors has been brought up on the dominance of these principles, who are steadfastly guided by etiotropic approaches to the treatment of AP.

9. Over time, severe forms of AP that were poorly treatable with antimicrobial drugs and required additional and supportive therapy began to be observed more frequently, and the patients themselves were candidates for hospitalization in the intensive care unit. At the same time, the results of treatment of such patients were accompanied by severe complications and high mortality, and the examination data did not confirm the version of the presence of particularly virulent pathogens in them. This contingent began to be considered and analyzed separately in the hope of understanding the reasons for such an aggressive development of the disease [11,12,21-23]. However, the views of specialists, significantly tied to the important role of the pathogen, and not to the pathogenetic influence of the inflammation focus, turned out to be aimed mainly at finding prognostic signs [11,12,21-25]. The very principle of such studies reflects a wait-and-see attitude, demonstrating a certain stage-by-stage provision of assistance as the situation changes.

10. Identification of patients with severe course of the disease at the initial stages of development of AP using prognostic tests does not give the expected results, having quite real grounds. The meaning of such stratification is to identify patients with AP for hospitalization in the intensive care unit, based on the characteristics of treatment in such units. However, the general principles of basic treatment, which are currently applied to all inflammatory processes, regardless of their localization and mechanisms of development, are completely incompatible with the specifics of the pathogenesis of AP. Intensification of such therapy in a more severe category of patients with ANSIL is, in my opinion, one of the main reasons for such a significant difference in mortality rates among hospitalized patients, which in general departments is 5-10%, and in intensive care units reaches 50% or more [26-28].

11. The fact that the arterial pressure in the pulmonary vessels is approximately 8 times lower than in the systemic circulation is known to every specialist [29,30]. It is also known that the two circulations are closely and inextricably linked, maintaining a constant parity of the cardiac output of the two heart ventricles with such opposite indicators and supporting the vital need for synchronous heart function. The mechanisms of such adaptation act automatically, independently of our consciousness, literally ensuring our salvation in the most critical situations. However, in this regard, the logic of modern medical actions in patients with severe AP defies explanation.

12. On the one hand, the inflammatory transformation of tissues is based on a vascular reaction with a pronounced impairment of blood flow and a sharp increase in vascular permeability [31]. On the other hand, unlike all known inflammatory diseases localized in the systemic circulation, only OP is the only nosology that occurs in the vessels of the pulmonary circulation. The pulmonary vessels, through which all circulating blood passes, are equipped with baroreceptors that respond to the slightest fluctuations in arterial pressure and play a critical role in regulating the general blood flow, which was established almost a century ago [32]. It is this mechanism that allows maintaining synchronicity in the work of the two halves of the heart, ensuring unloading of the right chambers of the heart and equalizing proportions with its left half. Unfortunately, this compensatory reaction was only rarely considered in previous years in such extreme situations as, for example, pulmonary embolism or attracted the attention of pathophysiologists [33-36]. In recent years, research on the problem under discussion has been aimed exclusively at studying micromechanisms, rather than integral manifestations of the process.

13. With aggressive development of the inflammatory process in the lung, the body is limited in time for smooth adaptation to new functional conditions. Rapid development of the focus is accompanied by an extreme protective reaction, which is manifested by a generalized spasm of small-diameter pulmonary vessels [37,38], creating a state of relative excess of venous return and overload of the right heart. In such situations in modern medicine, instead of the logically necessary elimination of the pathological mechanism that has arisen, which is the cause of respiratory and circulatory disorders, patients undergo etiotropic therapy, and while waiting for its results, bolus infusions are administered [11,12,15,16,18]. Such medical care is explained by the septic condition of patients, although in reality, the observed disorders are not infectious, but pulmonogenic in nature and can be quickly eliminated [39].

14. Infusion therapy, which in similar situations with other inflammatory processes has a pathogenetically conditioned direction, has a directly opposite effect in AP, stimulating both local and general disorders [39]. The earliest changes in general circulation, when there are no deviations in blood flow indicators, are manifested by signs of microcirculation disorders [40-42]. In this case, widespread disruption of the blood supply to tissue structures is accompanied by a change in metabolism and an increase in the level of various substances. Many of these microfactors are currently used as markers for predicting possible variants of disease development, but, ultimately, these processes manifest themselves in the most vulnerable localizations. Therefore, it is quite natural that the first to show their functional insufficiency are organs that have already been subjected to previous damage and diseases.

15. The most frequent complication in the treatment of AP remains acute respiratory distress syndrome (ARDS), the cause of which should be considered primarily a disturbance of microcirculation in the pulmonary circulation, accompanying severe forms of the disease. Persistent disturbance of the blood supply to the alveolar parts of the lungs is not particularly amenable to currently accepted treatment (etiotropic therapy, intravenous infusions, vasopressors) and, if it persists over time, can only worsen against the background of such therapy, having classic prerequisites for the development of this syndrome. From my point of view, it is easy to understand that the development of ARDS in severe patients with AP is a reflection of the lost time waiting for the effect of antimicrobial therapy and efforts directed against adaptive mechanisms.

16. The occurrence of ARDS syndrome with pronounced disturbances of blood flow in the pulmonary circulation, through which all the blood circulating in the body passes, inevitably leads to profound disturbances of blood circulation in the systemic circulation. In such cases, modern attempts to influence individual links of the neglected process, undertaken today at the cellular and molecular level, are palliative in nature. As the results of such actions show, miracles do not happen and the next stage in most observations is predictably multiple organ failure [21-23,42-44]. If we initially consider the timing of intubation of such patients as strategic (!?) measures [45] and begin to discuss the important role of oxygen delivery methods [46-48] or the urgent need to issue additional artificial lung ventilation devices [49-51], then we must forget about the possibility of achieving success in solving the problem under discussion. The choice of these directions reflects the recognition of the inevitability of the expected results and is devoid of the search for the main causes.

17. If we follow the stages of treatment and analyze the timing of the appearance of the first signs, and sometimes the development of complications themselves in patients with severe forms of AP, then the most significant and fateful period is the first 2-3 days. During this time, the inflammatory process in severe forms of the disease can in some cases progress literally by the hour, and further success will depend on the speed of assistance, and most importantly, on its direction and nature [39]. Stubbornly concentrating on etiotropic approaches to the treatment of AP,

modern medicine completely ignores many of its own studies, the results of which show that the etiology of the process does not determine its manifestations and severity, which depend on the functional characteristics of the affected organ [39].

18. The atmosphere of delight and positivity after the first results of antibiotic therapy, which seemed endless to many, has long since evaporated, but incredible attempts to revive this medical direction continue with unabated efforts. All these studies rely only on the latest developments, delving into the molecular-cellular world, through the prism of which doctors try to understand what is happening to the patient. The thousand-year experience of ancient medicine, obtained empirically and continuing to be used in health and rehabilitation complexes, was declared untenable and even quackery by official medicine [52,53]. However, having discarded the previous experience without serious research and having started a new stage virtually from scratch, official medicine has reached a dead end in the problem under discussion, but few specialists are aware of this yet.

19. Contrary to the widespread negative opinion about ancient methods of treatment, modern medicine resorts to some of them in clinical situations. For example, cooling the body of patients is used for some diseases, demonstrating its positive properties [54], but the FDA has not yet approved this type of therapy, requiring more serious evidence [55]. In our previous work, in the treatment of severe forms of AP, we used such a modern method of emergency care as cervical novocaine vagosympathetic blockade (CVSB), as well as such ancient methods as short-term general body cooling of patients (GBC) and cupping therapy (CPT). Modern studies, as a rule, do not provide for an assessment of the direct effect of the studied treatment methods. As a rule, the treatment results are compared between the main and control groups, and it is sometimes difficult to understand what role the tested method played. In contrast to such approaches, we used the registration of comparative rheopulmonograms before and immediately after the procedure, obtaining objective evidence of the real effectiveness of these methods in a short period of time [39].

20. At present, the main hopes for success in the treatment of AP continue to be placed on antibacterial therapy, the assessment of the result of which is usually expected in 2-3 days. At this time, the supply of oxygen to seriously ill patients, as is known, does not make any decisive changes in the dynamics of the process, performing a supporting and auxiliary function. Emergency infusions in such patients give the opposite effect. The question naturally arises - what first and emergency aid for the most seriously ill patients can quickly and noticeably alleviate their condition? It remains to be noted that today in the arsenal of medicine there are no options for such emergency aid, capable of invariably and immediately making significant positive changes in the condition of patients with AP in the initial period of the disease.

21. In the 1930s, antipneumococcal antiserum was successfully used in the treatment of patients with AP, the effect of which was viewed in terms of its emergency administration after results confirming the pneumococcal etiology of the inflammation [5]. To optimize this care, a large network of microbiological diagnostic laboratories was created in the United States, operating around the clock, and the urgency of the clinical situation for pneumonia was compared with the need for emergency care for acute appendicitis [5]. The organization of this system of care for patients with AP was dismantled after the advent of antibiotics, the early results of which created the illusion of faith in their exceptional curative power. This belief system continues to dominate professional thinking despite the changes that have occurred over more than eight decades.

22. As a result of the above analysis of data on the modern complex of medical care for patients with AP, one can note the clearly protracted, but not capable of having a real impact on the dynamics of the inflammatory process, dominance of a narrowly focused etiotropic approach. Attempts by a number of specialists to explain the "undoubted effectiveness" of antibacterial therapy in the majority of patients with AP, "successfully treated" in outpatient settings [4], is a purely statistical declaration. Compare these data with the results of observations of patients with inflammatory processes of coronavirus etiology during the SARS-CoV-2 pandemic, when patients found themselves without specific etiotropic therapy, and you will not see a significant statistical difference between the groups of patients - those who fell ill but recovered on an outpatient basis, and those hospitalized [56,57]. This suggests that similar processes of the same localization develop according to a single scenario, differing only in the rate of their spread and the level of adaptability for the host organism.

23. The absence of pathogenetically substantiated first and emergency care for patients with AP is the reason for the loss of precious time in the initial period of the disease, which allows the neglected mechanisms to progress. Without changing the basic principles of treatment of this category of patients and without trying to radically revise existing ideas, modern medicine is trying to improve etiotropic methods of treatment, while simultaneously searching for tests that allow predicting the likelihood of complications of the process and fatal outcomes. The latter trend reflects the absence of signs of a new ideology in modern research on the problem under discussion and the actual capitulation to the current circumstances. It is easy to understand that all these misconceptions are based on the mental legacy of many years of veneration of antibiotics, which is the first and inevitable factor that requires elimination.

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