

Lessons Not Learned in Antibiotic Therapy

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The beginning of the COVID-19 pandemic has put practical medicine in critical conditions, exposing the long-overdue problem of the lack of specific care for patients with acute pneumonia (AP). It is possible to foresee in advance that the mention of such concepts as a viral pandemic and AP in one bundle will be perceived by many readers as incorrect and contrary to modern scientific ideas in the section of lung diseases. However, the paradox and one of the main reasons for this situation is precisely the distortion of scientific concepts of AP, which differ from well-known facts and do not take in to account the fundamental materials of medical science. As a result, today practical medicine in patients with viral lung damage does not have effective means of providing assistance, being limited to symptomatic medications and auxiliary resuscitation methods.

Over the past decades, success in the treatment of patients with AP was considered only in terms of the priority of antibacterial therapy. There was even a certain form of treatment for this group of patients, which for many years appeared in the medical literature under the generally accepted term "antibiotics alone". No one paid attention to the fact that the same drug was considered the main treatment not only for AP, but also for diseases that were not comparable to it in their clinical criteria. In addition, the fact that antibiotics are exclusively antimicrobial and do not directly affect inflammatory and functional disorders did not cause alarm or discussion.

The biologically natural development of a stable microflora and the decrease in the effectiveness of antibiotics was compensated by the development of new, more advanced drugs that supported both the previous treatment principles and the narrow focus of the worldview on the problem. In the vast majority of patients with AP throughout the history of antibacterial therapy, drugs were prescribed empirically, and the true pathogens of the process remained unknown, but the assessment of the collective image of pathogens-microbes gradually transformed into the concept of the sole and main cause of the disease. This concentration of views eventually led to a re-evaluation of this nosology as an infectious disease, despite the lack of epidemic criteria and the risk of contact transmission of AP.

The modern concept of AP was formed around the dominant role of the microbial factor and considered its suppression as the main therapeutic goal. At the same time, such consequences as inflammatory tissue transformation and functional changes caused by it remained for the body itself to eliminate. When the process developed relatively slowly, and antibiotics gave a quick effect, the body was able to successfully overcome the disease. But over the years, the number of patients requiring additional care has steadily increased. And since the question was raised primarily about the suppression of infection, the methods were used by analogy and experience in the treatment of other infectious processes. The failures of such treatment were confidently explained by the lack of rapid microbiological diagnostics, the inability to use targeted antibacterial therapy, and the presence of particularly virulent strains.

The choice of additional methods of AP treatment is crucial for subsequent treatment results. The specificity of pulmonary inflammation and its treatment consists primarily in the complete functional contrast of the vessels of the small circle and blood flow in them in comparison with the systemic circulation. Therefore, treatment methods that bring the expected success in other localities of the inflammatory process, in the case of AP, are aimed at the opposite effect.

The totality of all representations and interpretations of the infectious nature of AP was mainly declarative and was based only on the potential success of antibiotics. But, if only the microbial factor determines both the occurrence of AP and the variants of its clinical course, then, sorry, but where are the undoubted arguments and objective evidence for such statements? After all, on the basis of these postulates, the rhetoric of training medical personnel has been built for many years, and the strategy of such representations has determined the tactics of treatment throughout the entire period of antibiotic use, isn't it? As is often the case in complex and difficult to explain situations, time proved to be the best tester and arbiter. While the effectiveness of AP treatment continued to decline, attempts to change the course of events and obtain objective evidence of the disease concept failed.

As a result, experts began to recognize that attempts to identify the causative agent of AP do not cancel the predominance of empirical choice of antibiotics and do not have a decisive influence on the final results of treatment [1,2]. However, such statements of long-established facts do not change the deep-rooted belief that only antibiotics can solve the problem of treating AP, and therefore such analytical publications ultimately retain their fundamental therapeutic role.

This brief overview of the recent history of AP treatment is necessary in order to understand the professional response of this branch of medicine to the sudden influx of a significant number of patients with viral lung lesions in COVID-19. Formed firm beliefs about the decisive role of the pathogen in the problem of AP do not allow us to look at coronavirus pneumonia on a full scale and evaluate the information received about them from other points of view. At the same time, this population of patients has lost the usual main remedy-antibiotics from the treatment list, without equivalent replacement options, and the future prospects and promises of antiviral drug development do not matter for patients who are already ill.

It should be noted that in patients with viral pneumonia, the morpho functional basis of the disease is comparable to bacterial forms. We continue to talk about AP with morphological inflammatory damage to the same organ structures as in bacterial inflammation [3,4]. This fact, combined with the clinical manifestation of this variant of AP, clearly indicates the identity of functional disorders in all forms of acute inflammation of the lung tissue. However, the subsequent direction of treatment efforts will depend entirely on the assessment of the causes of these disorders.

The undisputed classic of medical science includes materials about the presence of its unique function in each tissue or organ of our body. Inflammatory transformation of tissues changes not only their structure, but also their function. Moreover, dysfunction is a mandatory feature of inflammatory processes, and this feature was first described by Galen several centuries ago, which actually determines the clinic of each such disease. Unfortunately, today this scientific and fundamental classic of medicine is replaced by assumptions about the decisive influence of the pathogen both on the development of AP and on the features of its course.

There is one significant difference between pneumonia in COVID-19 and common bacterial forms. The coronavirus pandemic has brought a tense epidemiological situation to our lives. The latter circumstance requires strict implementation of preventive and quarantine measures. But, even in these conditions, when there is only one (!) pathogen, the features of the occurrence and course of the disease have a huge range of differences. For example, observation and examination of large isolated groups in quarantine and the presence of coronavirus showed that in more than 80% of cases, infection and the presence of the virus in the body were asymptomatic [5-7]. At the same time, in those who had clinical signs, the disease manifested itself from barely noticeable symptoms to extremely severe conditions and fatal outcomes. In this situation, it is no longer possible to explain such sharp differences by the difference in virulence of the strains, is it?

Unfortunately, the authors who have observed and analyzed these closed human contacts on large cruise ships do not pay attention to this important fact from a scientific and clinical point of view, focusing, although quite rightly, only on the potential threat of the virus spreading by asymptomatic patients. The obvious individual features of the development of an inflammatory reaction were also not prop-

erly evaluated in bacterial forms of AP, so inattention to this factor is a continuation of the ideas about the absolute role of the pathogen of the process.

Another example of the persistent influence of this concept on the assessment of a new category of patients is the assumption of the development of viral sepsis in the case of severe blood flow disorders [8]. This interpretation ignores the violation of the regulatory function of the pulmonary vessels located in the main focus of the disease, and determines the control of hemodynamics and its therapeutic correction based on secondary changes in the systemic blood flow, the normal parameters of which have significant differences from the pulmonary one. Focusing on the indicators of peripheral blood circulation, the attending physician loses touch and understanding of the main cause of these disorders, which is localized in the pulmonary vessels and has a natural reflex effect on the systemic blood flow. However, the main thing in this situation is not so much a distortion of ideas about the mechanisms of development of the disease, but the subsequent correction of detected violations of peripheral, rather than pulmonary hemodynamics.

There is no point in discussing such an obvious fact as the inability of antibiotics to suppress viral aggression. Theoretically, the hopelessness of such treatment is known even outside the circle of professionals, but what does it look like in practice? For example, TM Rawson, *et al.* [9] reported that bacterial and fungal co-infection was detected in only 8% of patients with coronavirus, while 72% received antibiotics. Other reports also note automatic antibiotic prescribing in 71.0 - 82.9% of patients with COVID-19 [10,11]. Such reports only confirm the stability and inviolability of the treatment stereotypes that have developed under the hypnotic influence of antibiotics, which retain didactic authority when choosing treatment methods during a pandemic.

Currently, medical care for patients with COVID-19 pneumonia is not very effective and attempts to achieve better results follow from previous ideas about the leading role of the pathogen, which pursue the inevitable goal of suppressing it. The search for optimal treatment options for viral lung lesions continues, but at the moment the most realistic way to alleviate the condition of such patients is to supply oxygen or, in extreme cases, artificial ventilation. Meanwhile, such auxiliary methods are not necessary for all patients, but only for those whose compensatory capabilities of the body do not keep up with the speed of development of pathological disorders. Decompensation of vital functions is a very dangerous consequence of the rapid development of the disease. For example, obstruction of blood flow in the vessels of the small circle in patients with coronavirus pneumonia leads to the development of "Acute Cor Pulmonale" and death [12].

The infinite variety of individual variants of the development and course of infection by one identical pathogen is a kind of hint from nature about the most significant aspects of the disease and methods of first aid. The current situation shows that all infected people are spontaneously divided into certain groups. Most of these cases remain simply carriers of the virus, showing no further signs of the disease. This category of patients does not require any treatment and is subject to anti-epidemic measures.

Special attention should be paid to those who have the fact of infection accompanied by the appearance of symptoms of the disease, since it is from this category of observations that patients with signs of functional disorders and subsequent decompensation of vital functions begin to stand out. The very fact that the first signs of the disease appear is indirect evidence of the virus entering the cells and the beginning of an inflammatory reaction. Unfortunately, no one can predict the future course of events based on the first signs of the disease, but the more aggressive the beginning of the process, the more careful monitoring and early first aid should be.

By the time functional disorders appear, the priority of medical care should already be shifted from the pathogen to the consequences of its aggression, which are manifested by a violation of the function of the lung tissue as a result of its inflammatory transformation. At this stage of the disease, elimination of the pathogen can not bring rapid relief to the patient, since such drugs do not have a direct functional effect. Therefore, emergency assistance to the body, which cannot independently cope with the compensation of functional disorders, should be primarily aimed at eliminating the causes that prevent the work of the pulmonary-cardiac apparatus. In order for such assistance to be targeted and effective, it must be formed in accordance with the unique mechanism of development of the pulmonary inflammatory process.

AP is known to medicine as a disease with many pathogens. Although viruses as pathogens of AP appear in the literature for a long time, such references were more informational than practical. Cases of viral lesions did not have a high frequency, and the lack of means of suppressing pathogens (unlike bacterial ones) did not cause much concern and discussion. However, it should be emphasized that in this context we are talking about a single nosologically form of the disease. The viral variant of AP development has its own pathoanatomic features, which, despite the unity of the pathogen (in COVID-19), differ in individual diversity. At the same time, the pathogenetic mechanisms and clinical signs of the disease, regardless of its etiology, are determined by the localization of the process with a violation of the function of similar structures and have a constant sequence.

A brief review of only the most significant and well-known facts clearly indicates the need for a radical revision, first of all, of existing views on the nature of AP, since ideas about the nature of the disease determine the direction of medical care. This need becomes even more obvious when we consider that the main work in this direction has already been carried out and successfully tested in clinical settings. The circumstances and features of this work, which was completed more than 30 years ago, as well as the reasons why its further continuation was interrupted, are described in detail in the recently published monograph: Igor Klepikov "Acute pneumonia. New doctrine and first treatment results" - ISBN (978-620-2-67917-6) > {<https://www.cheapesttextbooks.com/IM/?keyval=ISBN+%28978-620-2-67917-6%29>}.

This was a period when the bacteriological forms of AP were absolutely predominant, and the success of treatment was explained only by the action of antibiotics. However, the results of the study proved that the effect of treating the most difficult situations with aggressive forms of AP depends on pathogenetic methods of treatment, and antibiotics are an auxiliary method and can be used in short courses. Moreover, the results obtained allowed us to speak about the guarantee of prevention of complications of the disease, if the necessary assistance is provided in a timely manner.

PS: And the last thing that is absolutely necessary to note. The main goal and task of each of us is professional and high-quality performance of our duties in accordance with the chosen specialty. This is the key to progress and prosperity. Farmers create an abundance of agricultural products for us. Employees of municipal services ensure the convenience of our life... Doctors should use the maximum of modern opportunities to save patients' lives, and in the event of adverse trends in treatment results, carefully and comprehensively analyze their causes and look for a way out of this situation. Such actions are especially expected and necessary from specialists who take leading positions in the discussion of the problem.

I was born and lived most of my life in a country where science, especially its biomedical branches, was often used for political purposes, distorting facts and even denying scientific arguments. The consequences of such steps in the future required time and a lot of effort to eliminate them. In this regard, attempts to shift all responsibility for the consequences of the current pandemic to the state administration and ignore their own professional short-sightedness are surprising and perplexing [13]. If the pages of the same influential journal discuss such proposals as careful monitoring of patients with coronavirus in order to select the appropriate time for their intubation [14], and for further support, it is recommended to increase the production of artificial ventilation devices [15], then what success in treatment can be achieved with this "strategy"?

In connection with the appearance and replication of accusations against state leaders who are not directly related to the strategy of providing medical care, it is quite acceptable to ask the question: is the administration to blame for the inefficiency of modern approaches to the treatment of AP and the lack of necessary and timely care for patients with viral pneumonia? Maybe the country's leadership insists on teaching us the concept of views on AP, the principles of its treatment, and continues to monitor the quality of medical care for patients with coronavirus? Could it be that the administration failed to save the deceased patients? Then, excuse me, but what is the role of medicine in this issue and for what purposes does such an expensive health care system exist? Searching on the side of those who are responsible for the negative results of our work is inherently unconstructive and even destructive. The review process should start with ourselves and our own professional ideas and "preferences".

A long period of antibiotic use led not only to an increase in microflora resistance and a distortion of ideas about the features of AP, but also contributed to an increase in the role of viruses in the etiology of this disease. This trend is clearly visible in the last couple of decades, indicating the beginning of the viral era of diseases.

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