

OPINION

Acute Inflammation of the Lung Tissue in the Light of our Views and Real Facts

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Acute pneumonia [AP] is one of the oldest nosologies known to medicine, which for many centuries belonged to the category of severe diseases with high mortality, but was not included in the category of contagious and did not pose a danger to others. The search for ways to help patients with AP has been conducted empirically for most of its history.

Understanding of the nature of the disease began to expand with the development of microbiology, which discovered bacterial pathogens of AP. Despite the results of bacteriological studies initiated about a century and a half ago and testifying to the role of microflora in the development of this disease, they have not changed the interpretation of the process as inflammatory, not infectious.

Cardinal changes in the views on the essence of acute inflammation of the lung tissue began to form after the discovery and widespread use of antibiotics. During this period, a gradual transformation of ideas about the nature of AP began to be observed, which contradicted the facts of the observed reality and the laws of medical science. To date, the widespread doctrine of the AP continues to consider the solution of the entire problem in isolation from the existing contradictions.

The unexpected phenomenal results of the first applications of antibiotics marked the beginning of an exaggerated assessment of their therapeutic effect and purpose. An important role was played by reducing the burden on medical personnel, when the introduction of antibacterial drugs gave a fairly rapid effect and eliminated the need for additional therapeutic efforts. Of course, this option of medical care greatly facilitated the maintenance of a large flow of patients and bribed with its simplicity.

The subsequent course of events showed that attempts to preserve the previous effect of this type of treatment at any cost were dictated by desire, and not by a balanced assessment and long-term prognosis. Despite the growing side effects and the decrease in therapeutic efficacy, antibiotics have become the main, and often the only help for AP. The gradual transformation of antibiotics into the main means of treating AP occurred contrary to existing facts and ideas about their curative ability.

Firstly, as is known, antibiotics can only act on bacteria, and selectively, but do not directly affect the inflammatory process caused by the latter. In this regard, the principle of treatment “antibiotics alone”, which has been used for a long time in the treatment of AP, should be considered as a narrowly focused etiotropic, and not a special “anti-pneumonic” remedy. Under these conditions, a very familiar situation has become quite typical, when one type of antibiotic began to be defined as the main means for the treatment of completely incomparable diseases.

Secondly, even with the rapid action of antibiotics, which was observed in the initial period of their use, the final elimination of the inflammatory reaction and its consequences remains the task of the body itself. By helping to eliminate one of the important factors of the disease, the effective action of antibiotics has greatly facilitated this task. However, in the case of aggressive development of an inflammatory reaction, the time of the disease before reaching the critical stages is significantly reduced and antibacterial therapy does not have time to bring the expected result. Over time, similar situations began to be observed due to a decrease in the activity of antibiotics.

Thirdly, unlike the bulk of drugs that affect the substances and mechanisms of the macroorganism, antibiotics are directed at other biological objects that accompany or enter the patient's body. Being separate living objects, bacteria have the ability to adapt. These circumstances have generated a grandiose process of side effects of antibacterial therapy and initiated a complex of permanent changes in the microflora, which is observed throughout the entire period of clinical use of antibiotics.

The slow but inevitable decline in the effectiveness of the drugs used, the constant need to develop and release new, more advanced antimicrobial forms, the emergence and expansion of the list of antibiotic-resistant strains accompany this type of therapy throughout its relatively short history. The ability of bacteria to resist external aggression factors, as well as to consolidate, develop and reproduce acquired qualities does not allow to return the original effectiveness of antibiotics, despite the development and introduction of more advanced drugs. Changes in bacteria as living objects under the influence of external factors are a convincing confirmation of the inevitability of biological laws.

Fourth, the active use of antibacterial therapy has led to the emergence of a new phenomenon that was not observed in the pre-antibiotic era. We are talking about a periodic and fairly obvious change of leaders among the agents of the AP. So, if before the use of antibiotics, pneumococcus was the causative agent of AP in 90-95% of cases [1-3], in recent years its participation in this disease has been confirmed only in 33-50% of positive bacteriological studies [4]. But, among the entire contingent of patients with AP, among whom in recent years it has not been possible to identify the causative agent in half or more cases, the role of pneumococcus in the etiology of the disease is confirmed only in 10.9% - 22.5% of cases [5].

It is also necessary to recall that in the 60-70s of the last century, that is, in the interval between the periods of the statistics presented above, a "staphylococcal catastrophe" suddenly arose, in which pneumococcus actually disappeared from the list of pathogens of AP, and staphylococcus had almost total influence. In the future, there was an equally "spontaneous" decrease in the proportion of staphylococcus with an increase in other microorganisms in the etiology of the disease and a gradual return of pneumococcus. Scientific explanations for such unusual ethological oddities of AP and discussion of these features of the disease have not been found in modern literature. It is strange that these facts relating to the most studied section of AP, etiology, are of no interest to modern researchers.

Fifth, experts have been paying attention to the growing role of viruses in the development of AP for quite some time. So, according to statistics, about two decades ago, 200 million cases of viral pneumonia were registered annually in the world, which at the time of analysis was almost half of all cases of AP [6-8]. It is quite acceptable to assume that the above-mentioned figures of negative etiology studies in bacterial forms of AP [5] were caused by viruses, but timely virological diagnosis was not carried out in these cases.

The sudden and unexpected occurrence of the SARS-CoV-2 pandemic, as this phenomenon is presented not only in the media, but also often in professional publications, actually had not only the prerequisites noted above. The expectation of such an event was indicated by the increase in the incidence of viral pneumonia, the transformation of influenza epidemics into an annual "tradition" and, of course, at least two severe coronavirus epidemics that became a prelude to a pandemic [9].

Is it possible in this situation to deny the effect of antibiotics on the long-term growth of viral lung diseases? From my point of view, there are enough facts and patterns that may be the result of years of suppression of the bacterial segment of the microbiome and the growing role of viruses. Currently, this statement does not have sufficient objective arguments to be absolutely proven. At

the same time, the information already available does not allow us to reject this point of view. Therefore, at this stage, such an interpretation of the reasons for the growing viral expansion can be used as a postulate, which can be further confirmed as new information accumulates.

If we summarize the dynamics of the etiology of AP noted above for a relatively short period coinciding with the use of antibiotics, then the inevitable solution in this situation should be, first of all, a critical assessment of the role of this therapy in the overall treatment package, right? At the same time, as the statistics of the disease show, the development of principles of medical care for viral lesions, which have been seriously competing with bacterial forms for many years, is on the agenda. Unfortunately, reality shows that the growth of viral pneumonia in recent years has not led to natural changes in treatment approaches. Even during the SARS-CoV-2 pandemic, significant efforts are being made to preserve the leading role of antibiotics in the treatment of AP.

For many years, the decrease in the effectiveness of antibiotics and the growth of microflora resistance have been trying to compensate for various attempts at early recognition of AP pathogens. Such efforts have been undertaken in the hope of accelerating targeted antimicrobial therapy and improving outcomes. It took a long time to be convinced of the futility of these attempts and to recognize the absence of their impact on the final results of treatment [10,11].

It is symbolic that such confessions began to appear on the eve of the SARS-CoV-2 pandemic, but this did not change the previous strategic line. Not only a narrow etiologic approach to solving the problem of AP in general and COVID-19 pneumonia in particular has been preserved, but also the leading role of antibiotics in this process. During the pandemic, more than 70% of patients with viral lung lesions continued to receive antibiotics, although indications for their use in the form of bacterial coinfection often did not exceed 10% [12-16]. Moreover, a number of reports noted the complete preservation of previous approaches to the treatment of pneumonia caused by COVID-19, and strongly recommended the continued use of antibiotics [17,18].

Thus, during the period of the predominance of bacterial forms of AP, one of the ways to improve the empirical choice of antibiotics was considered to be the separation of patients according to the place and conditions of the disease. This classification of AP, which distinguishes groups of patients with community-acquired, hospital-acquired, ventilator-associated pneumonia, continues to be used to this day [19], despite the fact that its introduction did not affect the overall results, and its justification is based on assumptions [20].

The introduction of such a gradation of the disease was due only to the desire to apply targeted antimicrobial therapy as early as possible, the effectiveness of which continued to decline. In this situation, it is not entirely correct to compare the initial condition of healthy people who have fallen ill with AP in a normal situation with the condition of patients admitted to the hospital with other diseases or, moreover, who were on artificial ventilation. It was this principle of separation of patients with AP that formed the basis of this classification, and inflammation of the lung tissue began to be interpreted as the result of bacterial infection, in which the alleged participation of various pathogens depended on the circumstances of the beginning of the process.

If, in bacterial forms of AP, attempts to use such a gradation of patients were explained by the permissibility of the participation of various pathogens and the desire to improve the choice of etiologic drugs, then in the conditions of the SARS-CoV-2 pandemic, the question of the possible diversity of pathogens disappeared. However, this trend continues to work automatically as a stable stereotype in an attempt to find an explanation for the varying severity of COVID-19 pneumonia, depending on the place and conditions of its occurrence [21].

Continuing to be guided by the concept of the leading role of the pathogen in the development of AP, modern medicine is trying to find differential diagnostic criteria between bacterial and viral forms of lesion during the current SARS-CoV-2 pandemic. Attempts to solve this problem and reduce the inappropriate use of antibiotics were unsuccessful, which again showed the absence of dependence of clinical symptoms and severity of the disease on the etiology of the process [22-24].

In the latter connection, the classical signs of inflammation help answer the question of why, with the same etiology of inflammation, the symptoms and condition of patients will differ depending on the localization of the focus. For example, it is almost impossible to confuse pneumococcal pneumonia and pneumococcal meningitis, although we are talking about inflammatory diseases of the same etiology, isn't it? A comparison of these two diseases indicates that the specificity of the clinical picture in each case is due to a violation of the function of the organ affected by the inflammatory process, and therefore the picture of lung inflammation will differ from the clinic of inflammation of the meninges. At the same time, each of these diseases can have an infinite range of clinical manifestations due to the individual reaction of the body to the aggression of one type of pathogen.

Determining the causative agent of AP on the basis of clinical symptoms and indirect signs leads the study of the whole problem away from assessing the actual causes. Such long-term efforts did not affect the results of treatment and, as the experience of etiological diagnosis of bacterial forms of the disease showed, did not make practical sense.

The danger of AP disease is greatly exaggerated even by the example of the current SARS-CoV-2 pandemic, despite the rapid spread of the coronavirus. Infection of the population during a pandemic gives the same results in different parts of the globe. Current statistics show that 80% of infected people tolerate contact with coronavirus relatively safely on an outpatient basis, despite the lack of specific treatment. At the same time, up to 20% of them learn about their infection based on tests, since there are no clinical symptoms. Only 20% of those infected need hospitalization, and 5% of them are in intensive care units [25-27].

It is possible to evaluate the effectiveness of professional medical care for coronavirus infection [excluding vaccination as a preventive measure] only in a hospital setting. The progressive severity of the condition of patients admitted to hospitals is due to the development of COVID-19 pneumonia, and in this situation, maximum mobilization of the capabilities of practical medicine is required. Unfavorable results of such care traditionally relate to the most severe patients in intensive care units, where mortality reaches 30-50% [28-31].

The results show that every second or third patient with coronavirus pneumonia sent to intensive care units loses the battle with the disease. This situation creates an atmosphere of anxiety and fear, which is not only supported by media reports on morbidity and mortality, but is also described by professional doctors as a feeling of powerlessness in the treatment of such patients [32-34].

However, if we compare the presented mortality figures from coronavirus pneumonia with similar indicators for the so-called community-acquired pneumonia in recent years, it turns out that these data have remained at the same level of 30-50% and there is no reason to talk about their sharp deterioration [35-39]. In other words, even the most critical indicators of the results of medical care for patients with AP have not changed since the beginning of the pandemic, and the reason for negative assessments and stressful conditions recently is a change in some circumstances.

First of all, with the beginning of the pandemic, the epidemiological situation has changed. If in the old days there was no need to isolate patients with AP and observe the rules of personal protection when contacting them, now the rapid spread of coronavirus forces the use of the maximum possible set of anti-epidemic measures. It is only necessary to clarify that we are talking about the spread of the causative agent of infection, and not about the expansion of its consequences, which pose a real threat to the health and life of the population, but, fortunately, according to statistics, are observed only in a small percentage of observations [see above].

In addition, the spread of the virus has destroyed the belief in the irreplaceable role of antibiotics in the treatment of inflammatory processes. Although with the onset of the pandemic, the final results of AP treatment in patients have not changed [see above], but the previous belief in the curative capabilities of medicine has been replaced by an anxious sense of insecurity.

Finally, the epidemiological situation forced the concentration of patients with COVID-19 pneumonia in specialized departments, creating a kind of extreme stress ranges for working staff. When patients with AP were admitted to the hospital in previous years, they were among the most severe by the nature and dynamics of their disease, but they were among patients of a different profile.

The organization of special purpose departments for patients with lung damage caused by coronavirus has excessively increased both the physical and psychological burden on medical personnel [32-34].

Unfortunately, the circumstances and facts listed above do not attract due attention to their assessment for reforming the ideology of the AP. In the current situation, the etiotropic strategy of the problem continues to dominate, under the flag of which the search for drugs capable of neutralizing the viral pathogen is being conducted. However, the prospect of success in these studies is very doubtful due to the peculiarities of the development of inflammation of viral etiology.

As you know, the presence of the virus in the body does not give any external signs. In order for the inflammatory process to begin with an appropriate clinical picture, the virus must enter the cell. In this regard, current research is conducted in two main directions. A significant amount of work performed today is devoted to the search for means of protecting cells from the penetration of pathogens. That is, we are talking about the prevention of viral pneumonia, and not about helping those who are already ill, which is what we are talking about in this case.

Virus neutralization is demonstrated in laboratory studies when the tested drug is in direct contact with the pathogen [40-42].

However, such attempts in the real conditions of the emerging disease cannot repeat the previous effect. In such a situation, drugs that can affect the virus in the laboratory are not always able to follow the pathogen into the cell, but when they have this ability, they can increase the toxic effect on cellular structures [40].

In addition, attention has already been drawn to the fact that the suppression of the pathogen during the growing cascade of severe functional disorders is a belated measure. In emergency situations, with the aggressive development of the process, even an effective effect on the pathogen does not leave the patient enough chances and time to successfully adapt to the emerging violations of the function of the affected organ. In such conditions, it is necessary to help the body to correct the mechanisms of the disease, focusing on the sequence of its pathogenesis. Currently, pathogenetic methods of assistance are more declarative, since the pathogenesis of AP is considered through the prism of pathogenic properties of the pathogen.

As evidenced by the above information about the AP problem, current trends in its solution focus on the fundamental role of the pathogen, considering the latter as a leading factor that also determines the pathogenesis of the disease. In this regard, the localization features of the process and the important role of the dysfunction of the affected organ are lost. The unique mechanisms of the development of inflammation in the lungs pass into the category of unclaimed knowledge, while AP in its etiology and treatment methods is equated to completely incomparable diseases. The reason for such a deformation of ideas about the specifics of the disease is associated with a long and excessive attachment of medicine to antibiotics, which had a strong didactic influence on the professional worldview.

The effectiveness of antibiotics in the initial period of their use formed an idea of the universal therapeutic effect of this therapy.

This initial impression continued to prevail and persisted throughout the subsequent time. The increased side effects of this therapy and the decrease in its activity did not entail a logical revision of its role and place in the overall complex of AP treatment. The natural result of the preservation of such orthodox views was the gradual transformation of the original idea of antibiotics into a so-called *destructive meme* with its spread through an *information cascade* [43,44].

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To date, the main obstacle to the successful solution of the problem of AP is not so much the microbiology of inflammatory processes of the lungs, on which all attention is focused, as the distortion of professional ideas about the causes and nature of these diseases. Eliminating these psychological factors is a very difficult task, but without its implementation, further progress in this area is impossible.

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