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Review Article

Why Antibiotics cannot be the Main Treatment for Acute Pneumonia

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Abstract

It has been known for almost two millennia that the inflammatory process of an organ disrupts its function, which determines the specificity of the clinical picture of the disease. Antibiotics can only have a selective antimicrobial effect but do not directly affect the mechanisms of the inflammatory process. The ability to suppress one of the initial factors of inflammation creates more favorable conditions for the body to fight inflammation. The first successes of antibiotics created the illusion of their decisive role in the treatment of inflammatory processes. Over time, under the influence of antibiotics, the etiology of pneumonia changed, and pathogens that are not included in the spectrum of action of antimicrobial drugs became leaders. This situation already now determines the urgent need for an urgent radical revision of the strategy in the treatment of pneumonia.

Abbreviations

AP: Acute Pneumonia; SARS-CoV-2 pandemic: Coronavirus Pandemic; COVID-19 pneumonia: Coronavirus Pneumonia; WHO: World Health Organization

Introduction

Modern medicine cannot imagine treating inflammatory processes without antibiotics, which have become the main method of treating most of these diseases. Long-term use of antibiotics in clinical practice has led to a transformation of professional ideas about the nature of such nosologies. For example, Acute Nonspecific Inflammation in the Lungs (ANIL) or Acute Pneumonia (AP), which throughout its history has never been considered a contagious process and still does not require special anti-epidemic measures, has been interpreted as an infectious disease in recent years. However, even more mysterious is the fact that antibiotics currently remain the main method of treating this serious disease. Drugs that, since their appearance in clinical practice, were known for their

ability to selectively affect only the bacterial factor, allowing the body to independently neutralize the mechanisms of inflammation and functional shifts, have served as the main, and sometimes the only, method of treating patients with AP for more than eight decades. Modern information examples show that the experience of the SARS-CoV-2 pandemic with a large number of viral pneumonia remained without radical conclusions. Therefore, the problem of treating OP requires a separate critical analysis and identification of the causes that prevent a reduction in the number of complications and mortality.

Discussion

Acute Pneumonia (AP) is one of the oldest nosologies known to medicine, the first description of which is attributed to Hippocrates [1]. This disease was characterized by severe inflammation and was distinguished by high mortality. In the absence of complete scientific knowledge and clear ideas about the features of this process, medicine was able to empirically find ways to help such patients, which were used by official

medicine throughout the entire observable history up until the middle of the last century. Having lost their positions in medical medicine, some of these methods remain in the arsenal of treatment and rehabilitation institutions, which serves as additional confirmation of their ability to bring certain results.

The principles of treating AP and, most importantly, the concepts of the nature of this disease began to change in the first half of the last century. This significant change was due to the development of microbiology, which was ahead of the studies of the physiology and pathophysiology of the lungs, as well as the appearance and first experience of clinical use of chemotherapy in patients with AP using drugs such as sulfonamides and the use of specific anti-pneumococcal antiserum [2]. The positive effect of these treatment methods laid the foundation for the etiotropic approach to providing medical care to this category of patients. Therefore, several years later, by the time antibiotics appeared in widespread medical practice and the first impressive results of their use, there were already favorable prerequisites for further intensive development of this direction and strengthening the etiotropic concept of the disease.

If the narrow views on the first experience of using antibiotics can still be explained by a certain euphoria that arose after receiving the first results and the non-standard nature of the observed effect, then the subsequent course of events in the coming years after the start of this therapy should have been subjected to a balanced analysis and professional assessment of the capabilities and place of these drugs in the general treatment of patients with AP. Firstly, it was initially known that these antimicrobial drugs are capable of exerting a neutralizing effect on certain types of pathogens of non-specific inflammatory processes, without directly affecting the mechanisms of development of the inflammation focus itself, which is the basis of the disease. The term "antibiotics" itself was proposed in 1947 by the American microbiologist Selman Waksman [3] and has since become quite widespread. Literally translated from Greek, this name means "against life", since it acts selectively on certain types of living biological objects, which are bacteria. The need for such a designation arose due to the fact that the number of antimicrobial drugs of similar origin began to grow rapidly, and the author of the term himself created streptomycin in 1944 - the second antibiotic after penicillin.

Secondly, even before the clinical use of penicillin, it was established and published in accessible professional literature that such drugs are relatively easily destroyed by bacteria, and the microorganisms themselves begin to acquire a strong resistance to this aggression [4-6]. The discoverer of penicillin and the founder of this type of therapy, Alexander Fleming, warned in his Nobel speech in 1945 [7] that the widespread use of antibiotics for other purposes carries the danger of accelerated spread of resistant strains.

The above information and warnings have long been left without sufficient attention and a serious professional approach. The changes that have begun in the previously stable list of AP pathogens [2], the decrease in the effectiveness of

antibiotics, and the emergence of resistant strains have served as an incentive for the priority development and release of new drugs. The most active period of this work was observed until the 1970s when the largest number of types and forms of these drugs were created and released [8]. In parallel, it was established that antibiotics contribute to an increase in the mass of products in production processes in such industries as livestock, poultry, and even fisheries. Products of such enterprises containing antibiotics were distributed among the healthy population for many years, and waste accumulated in the environment. Despite widespread opposition to such practices and the introduction of certain regulations and prohibitions at the level of government agencies, it has not yet been possible to achieve a complete cessation of such stimulation [9].

Throughout the entire period of antibiotic use, their prescription was not characterized by strict adherence to the rules that reflected the actual need for these drugs. The use of these agents in the food industry led to the disposal of waste with the accumulation of such agents in nature. The formation of resistant strains in the external environment occurred even at low concentrations due to changes in the genetics of bacteria [10,11]. Among the reasons for the decrease in the activity of antimicrobial agents and the development of resistance in microflora, such phenomena as self-medication and the use of antibiotics not for treatment, but for prevention are noted [12-14]. Thus, for many decades, the main goal remained the restoration of the previous effectiveness of antimicrobial therapy, but, on the other hand, the use of antibiotics was arbitrary and unhindered without any particular concerns about the possible consequences of such prescriptions.

Thirdly, despite the initially known information about the narrow-specific antimicrobial action of antibiotics and the lack of ability of these drugs to directly influence the basis of the AP, the mechanisms of inflammation, and antibiotic therapy began to acquire an increasingly important primary significance. The main attention of specialists was paid to the preservation and maintenance of the effectiveness of this therapy, which was constantly declining due to the growth of microflora resistance and the dynamic change of leading pathogens. This trend in assessing the role of antibiotics naturally led to the fact that over time, relatively mild forms of the disease began to be treated according to the principle of "antibiotics alone". At the same time, no one asked the question, why one drug is used as the main, and often the only means of treating completely different and incomparable diseases? What kind of medicine is this, which is passed off as a panacea? In recent decades, with the increase in the number of aggressive forms of the disease and a noticeable loss of antibiotic effectiveness, the above principle has quietly disappeared from use.

The exaggerated assessment of the role of antibiotics in the treatment of AP presented pathogens as the leading cause of the disease and the main target of therapeutic efforts. However, numerous attempts to prove the leading role of this factor in the development of AP over many years have been refuted by the negative results of studying differential diagnostic signs

depending on the type of pathogen. The absence of such signs in bacterial forms of inflammation did not convince many specialists that this direction cannot provide the key to solving the problem. Therefore, the appearance of a large number of patients with viral forms of the disease led to the beginning of a new round of differentiation of bacterial and viral pneumonia. By now we already know that such attempts at differentiation were also unsuccessful [15-17].

Continuing to consider the basic essence of AP from the standpoint of the microbial theory of disease, such an important feature of all inflammatory processes as their classical signs of manifestation, and among them especially such as loss of function, was actually consigned to complete oblivion. Explanations of functional deviations in patients with AP by a violation of gas diffusion as a result of infiltration of the affected areas of the lung and attempts to correct this situation by supplying oxygen, given modern information on the physiology and pathophysiology of the next stage of gas exchange - the circulatory system, today look like a primitive and very superficial idea [18]. As the results of studies and the experience of applying pathogenetic principles to treating AP show, this section of professional ideas about the nature of the disease requires radical correction [19].

Finally, by now the concept of the disease has been formed and has become dominant in professional ideas about the essence of the problem of AP, in which the pathogen is considered as the main cause of the process that has arisen and etiotropic therapy is still considered the main hope for its successful resolution. Such a didactic transformation of ideas occurred as a result of many years of training of medical personnel in this area, the theoretical material of which was implemented and finally assimilated into everyday practice. The limitations of the professional worldview on the problem under discussion are now clearly manifested in reactions to current events.

The steady increase in viral forms of the disease over the past 3-4 decades has not affected the basic principles of treatment, but the emergence of the SARS-CoV-2 pandemic with the emergence of a large number of patients with COVID-19 pneumonia has become a serious test for modern medicine, exposing its vulnerabilities. Thus, in the latter category of patients, bacterial coinfection was detected in a small number of patients, usually not exceeding ten percent of the total contingent. At the same time, antibacterial therapy was carried out in 70-80 percent or more, despite the absence of such indications [20-22]. This information looks very curious against the background of active discussion and publication of various proposals and documents, including plans for the rational use of antimicrobial drugs to reduce the load of resistant microflora, which was carried out over the past few years literally on the eve of the disaster. Moreover, it was at this time that the WHO declared antibiotic-resistant forms of bacteria a global disaster [23], but all this did not affect the practical side of the issue.

The lack of success of such medical care was accompanied by an unprecedented appearance of a whole series of

publications, representing a kind of confession of specialists who participated in the treatment of such patients, up to the expression of disappointment in the chosen profession [24-27]. However, apart from a kind of auto-da-fé with a feeling of hopelessness and despair, such reports do not contain not only radical proposals but also any initiatives to get out of the current situation. The latter circumstance, from my point of view, testifies to the persistent and unwavering acceptance of those narrow standards at the level of "antibiotic vs. microbe", which more than one generation of doctors has been trained in for many decades.

Additional evidence of deep didactic distortions in the existing ideas about the nature of AP is the excessive reverence for resistant bacterial strains, which have recently been actively attributed to the main causes of treatment failure. However, the latter point of view contradicts the real state of affairs. On the one hand, such strains have long been common representatives of the microbiota of healthy people, and their presence does not necessarily threaten the development of the disease [28-32]. On the other hand, they can be dangerous in case of disease only if etiotropic therapy continues to be considered the main method of salvation. The use of pathogenetic principles of treatment can radically change the results and show that the fear of such microflora is exaggerated [19]. At present, it should be taken into account that in recent years, most studies have noted the lack of identification of the pathogen in half or more cases [33]. At the same time, among patients with AP, in whom the etiology of the process was established, the number of cases with a resistant pathogen was insignificant [34], which does not allow us to consider this factor as influencing the results today.

In the modern period, there is a very curious trend in the presentation and interpretation of the etiology of AP. It would seem that the experience of the recent SARS-CoV-2 pandemic clearly demonstrated the shortcomings of providing care to patients with COVID-19 pneumonia and the depressing results of such practice, which should have become a serious reason for a radical revision of the entire system of views and approaches to solving the problem of AP. However, the materials reflecting today's views in this section indicate that the strategy for solving the problem has remained the same. The persistence of a large number of viral pneumonia and the lack of information about the causative agent in most cases is a natural result of many years of antibiotic use. These data are simply recorded today but do not entail natural discussions and radical changes. In addition, the predominance of such indicators in the modern etiology of AP indicates protective reactions of nature in response to interference in its harmony and balance.

Currently, the side effects of antibiotics are certainly associated only with the formation and spread of resistant microflora, which is the main cause of concern for specialists and the main goal of sought-after solutions. During the period of antibiotic use, many circumstances in the development of AP have changed, a consistent interpretation of which can help in understanding the essence and nature of the disease. Unfortunately, it must be noted that most side transformations that occurred under the influence of antibiotics do not attract

the interest of researchers and clinicians at all, remaining in the category of some unidentified phenomena. The omission and neglect of such consequences can only be explained by the fact that antibiotics in professional thinking continue to play a major role in the treatment of AP.

Thus, when describing modern studies, the main attention is paid to the virulence features of resistant strains, but the authors try not to emphasize the share of such cases among the total number of observed patients, which usually constitutes an insignificant group [35–37]. Publishing their recommendations for the choice of antimicrobial drugs in such reports, none of the authors pay attention to such an obvious result of the antibiotic era as the emergence and pattern of transformation of the etiology of AP. This stable and ongoing phenomenon has led to the fact that the need to prescribe antibiotics has significantly decreased. In other words, there has been a gradual and peculiar self-elimination of antibiotics from the general treatment complex. The reason for this situation is a significant increase in the share of viral pneumonia among the total number of this disease. According to some studies, the size of such a share of viruses in the development of AP already exceeds half of all observations [38,39].

If we try to evaluate the results of long-term use of antibiotics, we can understand that, despite the general desire and efforts to maintain the therapeutic effectiveness of these drugs, this goal has not been achieved. Long-term interference in natural connections has quite reasonably forced the biosphere to take counter-protective measures. Such changes are characterized by a significant transformation of the proportions and qualitative composition of the microworld around us, the state of which has been monitored for many decades, which has made it possible to note the differences that have arisen during this period. Further continuation of the system of measures aimed at preserving and maintaining the therapeutic potential of antibiotics carries the risk of developing deeper and more severe consequences of this therapy. Unfortunately and extremely surprisingly, representatives of modern therapy are not active in a detailed analysis of many hitherto untouched facts about the unique features of the development of AP and understanding the limitations of the existing system of views on this problem.

The current research and trials create the impression that no major changes have occurred in the conditions for the development of AP, except for the emergence of a large group of resistant strains, and that it is entirely justified to apply the same principles and options for solving the tasks set as in previous years. However, the previous concept of the disease has begun to acquire even more stable positions. Thus, the leading role of the AP pathogen is now additionally emphasized by including this disease in the category of infectious diseases, to which it has never belonged and, according to the available facts, still does not belong [19]. Only now has AP become the leading cause of death among all infectious diseases in the world [40,41]. Among the studies aimed at achieving a relatively rapid result from the targeted use of antimicrobial agents, one can encounter a return to the previous evaluation

criteria, when the effect of the use of these drugs is tried to be determined using the time factor after their administration [42].

So far we have discussed only the obvious features of the problem of AP, which are currently considered as tasks on the agenda and requiring an inevitable solution. However, the problem of AP includes another very important subject of discussion, which in recent years has begun to be presented as a separate independent nosology. In this case, we are talking about the so-called septic complications of AP, which are incorrectly interpreted and overdiagnosed. At the same time, AP, which over the past decades has been considered the leader among the causes of generalized infection, accounts for more than half of all sources of sepsis [38,43,44].

Modern medicine today considers sepsis from the standpoint of generalization of the infectious factor and approaches the treatment of such patients in a standard manner regardless of the primary cause of these conditions. The latter circumstance conceals a gross error since the features of the pathogenesis of AP are directly opposite to all other localizations of inflammatory processes. A sudden powerful irritant effect (inflammation) on the vessels of the pulmonary circulation is accompanied by an inevitable reflex reaction with an adaptive change in peripheral blood flow, which is difficult to distinguish from septic shock conditions by clinical symptoms. In such cases, the so-called pulmonogenic shock, which naturally develops in patients with AP, especially in cases of aggressive development of the process, is accepted and treated as septic. Such an interpretation leads to a false increase in the contingent of septic patients, the number of which has almost doubled in recent years, and their treatment based on general therapeutic principles has increased the number of fatal outcomes by the same amount [45–47].

It should not be assumed that the allocation of sepsis as a separate nosology and the generalization of the results of treatment of such patients was undertaken purposefully to improve the statistical indicators of AP and to identify another complex reason explaining the ineffectiveness of treatment. However, as they say, the fact is obvious. Most of the so-called septic complications occur in patients with AP and are a reflection of the pathogenetic mechanisms of this disease. In previous years, when great importance was attached to the results of bacteriological blood tests, it was patients with AP who raised doubts about the septic nature of complications, distinguished by a low percentage of positive tests in them compared to other nosologies [48,49]. The study, research, diagnosis, and most importantly, treatment of so-called sepsis in isolation from its original source is, in my opinion, another gross error leading us astray from the right path in solving the problem of AP.

Taking the inflammatory agent as the main cause of the disease and considering its virulence as a factor affecting the vital systems of the body, sepsis is currently diagnosed by scoring several indicators [50,51]. But at the same time, for

example, the respiratory rate is taken into account. Unlike other diseases, AP is initially characterized by shortness of breath, while with other localizations of inflammation, this symptom can really be a manifestation of sepsis, right? A decrease in systemic arterial pressure in patients with AP is secondary and indicates an increase in pressure in the pulmonary circulation. However, no one monitors the pressure in the pulmonary artery in patients with AP, and a decrease in systemic pressure in this disease is accompanied by a set of the same measures as in other inflammatory processes. As a result, many clinicians, being frank, note the deterioration of the condition of many patients with AP during treatment [52,53] and even the development of septic shock, which was not there at the time of hospitalization [54].

Thus, the information presented above allows us to look at the problem of AP from a different angle and understand why the results of treatment of this pathology cause deep concern among specialists. Unfortunately, serious concern about solving the problem of AP will not bring the desired results until all the consequences of long-term use of antibiotics are taken into account and analyzed and their role and place in the treatment process are completely revised. Today, an absolutely obvious situation has arisen in which antibiotics can no longer be the main means of treating AP and bring the same effect as in the first decades of their appearance. This is due not only to a noticeable reduction in the number of AP observations, in which the indications for prescribing these drugs remain. First of all, we must remember the limited exclusively antimicrobial capabilities of these drugs. The changes that occurred in the era of antibiotics revealed gaps in the therapy of these patients, which for a long time did not attract the attention of professionals. Today, when the observed contradictions and inconsistencies in the interpretation of the problem and attempts to solve it have become more obvious, another, more important side effect of antibiotics is revealed.

Conclusion

At present, specialists do not see the existing misconceptions and the obvious need to bring professional views on the problem of AP in line with the canons of medical science. Learned models of treatment, in which antibiotics remain the main means of treatment, are becoming the main obstacle to changing the existing circumstances. Such a situation, as a result of a detailed analysis of the accumulated facts, no longer raises doubts and does not require new evidence. It is enough to recall that the lively discussion of the fight against resistant microflora by creating new generations of antibiotics, which we are witnessing today, is actively supported by WHO experts and leading specialists. In other words, the solution to the problem of one of the side effects of antibiotics, which has found itself in the spotlight, is proposed by developing those areas that have already led to the emergence of the problem under discussion. I am convinced that further development of this area should also be carefully weighed and be under strict control of responsible organizations, since the solution proposed today does not have convincing arguments about its real capabilities, and its implementation can bring unpredictable consequences.

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