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What is the danger of the etiotropic marathon in acute pneumonia?

Abstract

The widespread use of antibiotics for over 80 years has created a heavy legacy of their side effects. Currently, the attention of specialists has begun to be attracted only by such a consequence as the continuing growth of microflora resistance. This side effect, observed throughout the era of antibiotics, has attracted more attention only due to the obvious loss of effectiveness of this therapy. A significant change in the list of AP pathogens, which affected the final results of treatment of these patients, is not yet among the topics for discussion. The current formation of plans for improving antimicrobial drugs without a detailed analysis of previous experience is a dangerous step towards further development of the root cause of the problem under discussion. The narrow etiotropic concept of the disease that has developed over the past decades does not take into account the classical canons of medical science and is the main obstacle to the successful solution of the tasks.

Keywords: acute pneumonia, antibiotics, side effects, etiology, pathogenesis, didactics, disease concept

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Abbreviations: AP - acute pneumonia; COVID-19 Pneumonia - coronavirus pneumonia; SARS-CoV-2 Pandemic - coronavirus pandemic since 2019; WHO - World Health Organization.

Introduction

Among the achievements of medicine in the 20th century, the discovery of antibiotics is rightfully considered one of the most outstanding. The practical use of these drugs saved millions of lives, and many previously hopeless patients were literally put on their feet. However, as we know, nothing in this world lasts forever, and the initial effect of this therapy has long since passed. Today, when we have crossed the threshold of the 21st century, it is becoming increasingly obvious with each passing year that the once successful direction of treatment over the long years of its use has turned into a heavy burden of its long-term consequences, which, unfortunately, have not yet found a well-founded scientific assessment and do not have clear plans for their correction.

Judging by the lively discussions on this topic, many specialists have not yet delved into the essence of the problem, which is the main obstacle to making optimal and worthy decisions. Literally in recent years, the attention of all specialists dealing with the problem of acute nonspecific inflammation in the lungs (ANSIL) has focused on the development of microbial resistance and solving problems to overcome it. At the same time, the relatively sudden concern about this phenomenon looks as if it arose quite recently. In addition, it is very important to note that antibiotics have now formed several remote side effects, among which, in my opinion, there are no less important and serious consequences. In order to understand the reasons for the discrepancy between modern professional ideas about the problem of the main nosology of ANSIL - acute pneumonia (AP) - and real facts and to determine the true place and role of antibiotic therapy in this complex process, albeit with a great delay, it is necessary to trace and remember many details of the formation of this type of care.

Discussion

In this context, it is necessary to highlight and recall those events and elements of the process of using antibiotics that can be confirmed at the present time. For example, even before the start of clinical trials of antibiotics, it was known that these drugs are capable of exerting only a selective neutralizing effect on certain strains of microorganisms, but do not have a direct effect on the mechanisms of the inflammatory process. Thus, this type of treatment was initially defined as etiotropic. In addition, at the pre-hospital stage of research, it was established that, on the one hand, microbes, acting for their own protection, can destroy the antibiotic, and on the other hand, they acquire properties of resistance to the action of this aggression.[1,2] To the noted facts, it is necessary to add the appeal of A. Fleming,[3] who in his Nobel speech in the first years of practical use of penicillin, discovered by him, warned about the danger of its wide and uncontrolled use in connection with the development of resistant microflora.

The above historical facts indicate that by the time antibiotics were widely used, it was well known that medical intervention at the level of the microbial supply of the body in its normal natural relationships was fraught with far-reaching consequences. In this regard, the sudden manifestation and increased concern about the development of microbial resistance after many years of antimicrobial therapy is an important characteristic of the principles and approaches to this type of therapy. This feature with the establishment of priority in achieving optimal results in the treatment of a severe category of patients with AP has its own reasons and explanations, which will be discussed below. But first, it is necessary to recall some more historical facts.

At the dawn of the development of pulmonary microbiology, it was established that AP could be caused by more than one pathogen, which excluded the specificity of this form of inflammation.[4] In addition, a report was soon published that the causative agent of AP could be opportunistic microflora present in the body.[5] These studies initially defined AP as a non-infectious and non-specific inflammation. At the same time, it was established that the most common causative agent of AP is pneumococcus, which received its name on the basis of this feature.[6] In this regard, it is very interesting to note that in the pre-antibiotic era, the etiology of AP remained stable over the foreseeable years. Thus, statistics for the period from 1917 to 1948, presented on the basis of materials from different regions, showed surprisingly stable results, according to which pneumococcus was the undisputed leader, accounting for 95 percent or more of its participation.[7-11]

Thus, by the time medicine mastered the new type of antimicrobial therapy, the main characteristics of both the etiology of AP and the features of these means of assistance were already known. In other words, all the necessary prerequisites were in place to apply this type of treatment. Firstly, antibiotics, in terms of their therapeutic capabilities, initially limited to neutralizing very specific types of pathogens, could only be considered as additional or auxiliary means of treatment. Secondly, information about the consequences of the influence of antibiotics on normal microflora should have become the basis for their use in accordance with special plans for regulation and control, the creation of which has only been discussed in recent years. Finally, there was information about a stable initial list of AP pathogens, changes in which during the use of antibiotics should have become an indicator of shifts in the etiology of the disease.

However, the ideal use of antibiotics and actual treatment are two completely different events. The first results of the new therapy were clearly overestimated in terms of their potential use and were perceived as a universal remedy for the treatment of inflammatory diseases. It is unlikely that anyone considered the initial effect of antibiotics as a result of their impact on primitive microflora, which was not yet familiar with this type of aggression. Nevertheless, it was the possibility of achieving therapeutic success relatively easily and quickly that laid the foundation for further principles of using antimicrobial therapy. As is known, the primary effectiveness of antibiotics soon began to decline, and the number of other bacteria insensitive to penicillin began to grow among the pathogens. The desire to preserve and support the activity of this therapy was entirely focused on the results of treatment, which provided a powerful incentive for the development and release of new, more advanced drugs. The most productive time for the emergence of the overwhelming majority of new generations of antibiotics was the period before the early 1970s.[12]

As is known, the change in proportions between the AP pathogens began to be noted soon after the start of antibiotic use and continued throughout the entire period of this therapy, but this phenomenon was not assessed as a side effect of these drugs and did not have appropriate comments and explanations. Meanwhile, this circumstance had a serious impact on the tactics of using antimicrobial drugs. Gradual changes in proportional relationships between different pathogens, periodic changes in leading strains and the emergence of new previously unobserved AP pathogens forced a constant search for methods of verifying bacteriological factors and trying to select the most suitable drugs. Ultimately, as is known, the practical implementation of bacteriological diagnostics of AP did not bring reliable results and began to be recognized at representative forums of specialists as unsuccessful with recommendations for the empirical selection of antibiotics.[13]

A characteristic reflection of the long process of attempts at bacteriological diagnosis of AP and selection of antimicrobial drugs can be found in the sections of manuals and textbooks on this topic. The list of possible pathogens was periodically updated in the literature for training physicians and adjusted recommendations for the selection of necessary drugs were published, although it remained unclear how to achieve success in the early selection of targeted therapy. After a long period of persistent attempts to introduce an etiotropic approach to treatment, a moment came when it became absolutely clear that the usual treatment regimens ceased to bring even the effect that was observed several years ago. Given the fact that the entire strategy for solving the problem of AP is based on the effectiveness of antibiotics, widespread resistance of microflora was declared a logical reason for the loss of therapeutic success of the disease.[14] This statement was picked up in professional circles, which made it possible to refer to microbial resistance as a reason for the decrease in the effectiveness of treatment of patients with AP. However, by now we have sufficient materials that completely impartially show that the influence of resistant microflora on the results of treatment of this category of patients is clearly exaggerated. Studies on the spread of such strains give a completely different idea of their true place in the modern microbial landscape.

The results of numerous bacteriological studies indicate that resistant microflora is a natural change in many microorganisms under the influence of long-term exposure to antibiotics, and such microflora increases its presence, turning into habitual symbionts. It should be taken into account that in addition to medical purposes, antibiotics continue to be used in the food industry to increase production in such industries as livestock, poultry, and fisheries. This area of application of such drugs significantly increases their impact on the microbiota of healthy people and the microflora around us.

For example, the proportion of resistant pneumococcal strains in the microflora has already increased to 20%,[15,16] cephalosporin-resistant Escherichia coli and methicillin-resistant Staphylococcus aureus (MRSA) - to 42% and 35%, respectively.[17] The increase in the proportion of resistant bacterial strains has turned them into a common accompanying microflora of healthy people. Thus, in the general population, the habitual carriage of MRSA is 2-3%,[18,19] among medical personnel this figure increases to 4.1-6.4%,[20] and among farmers working with animals and receiving antibiotics, this pathogen is detected in 10%.[21,22] Moreover, in this case, we are talking about MRSA infection of healthy people who do not have any signs of the disease. Moreover, in this case, we are talking about MRSA infection of healthy people who do not have any signs of the disease. It should be noted that most of the above data were obtained over the past two decades and the current situation in this section may be even more impressive.

The tragedy and hopelessness of the current situation, when resistant microflora began to be considered as the cause of ineffective treatment of patients with AP, requires explanations that allow us to understand the selectivity, hyperbolization and excessive dramatization of the observed phenomena. Firstly, the resistance of microflora developed and grew over many decades, but during the entire long period of the antibiotic era, no serious and targeted measures were taken to reduce and overcome this phenomenon. The main efforts were aimed only at achieving the therapeutic effect of antimicrobial drugs, which acted as the main means. Such a long-term desire only contributed to the development of side effects of this therapy, which led to quite natural consequences.

Secondly, resistant microorganisms play the same role in the etiology of the disease as bacteria that have not undergone such a transformation. As the examination of healthy people shows, the presence of one bacterial factor is not enough for the development of the disease. Other conditions are necessary for this. The idea of a greater danger of resistant microflora in the case of a disease can have only one explanation - if we continue to consider antimicrobial therapy as the main and only means of specific treatment. In such a confluence of circumstances, antibiotics, as the main hope for success, may encounter resistance on the part of the pathogen.

Thirdly, in recent years, in more than half of the cases of AP, the causative agent of inflammation remains unidentified, which is explained, in particular, by the growing proportion of viruses in the etiology of the disease.[23,24] Bacterial forms of inflammation are diagnosed only in a small proportion of these patients. Among them, the number of patients with AP in whom resistant strains of pathogens

are detected is a very small percentage of the total number of patients.[25] Such statistics show that references to resistant microflora as the cause of increasing treatment inefficiency are incorrect and cannot serve as an explanation for treatment failures.

Fourthly, multiple attempts to conduct differential diagnostics based on the etiological sign have not only failed to produce results in bacterial forms of AP, but have also shown the futility of attempts to separate bacterial and viral forms of inflammation.[26-28] The results of such studies convincingly indicate that the type of pathogen, which is one of the triggers of the inflammatory process, does not have a noticeable effect on the picture of the disease. At the same time, the persistent uniqueness and constancy of symptoms, regardless of the etiology, are due to a classic sign of inflammation - dysfunction of the affected organ. Unfortunately, at present this reason continues to be explained from the standpoint of the role of the pathogen, which ultimately leads to a distortion of ideas.

Finally, in light of the above data on the significant growth of viral inflammations of the lung tissue and a significant reduction in bacterial forms of the disease, when the number of patients in whom one can hope for the successful use of antibiotics has noticeably decreased, intensive research continues in various directions with the aim of restoring the action of these drugs. Along with the development and testing of new systems of accelerated bacteriological diagnostics, which have not yet yielded the expected results,[29,30] the beginning of the development of a new generation of antimicrobial drugs is declared.[31-33]

The latest initiative, which is supposed to be implemented by creating new forms of antibiotics using biogenic, nanotechnologies and other modern methods of formation at the molecular level, should, at the very least, cause extreme caution. Such attempts to revive antibiotic therapy are striking, first of all, by their approach. The experience and consequences of many years of using this therapy have not received a comprehensive critical analysis and reasoned conclusions. The problems facing medicine in this section of assistance have arisen as a result of the long-term impact of antimicrobial drugs, as evidenced by comparative conditions before the beginning of the era of antibiotics and at present. But what is striking in this process is not the consequences of antibiotics that are obvious and which are the goal of the planned initiatives, but the main principle of their solution. Without burdening itself with a very important and necessary analysis of the factual material of the 80-year history of antibiotic use and without giving a full report on the causes of the development of a number of side effects of this therapy, modern official medicine, starting with WHO experts, proposes to continue and further improve the cause that gave rise to the problems under discussion. It is difficult to imagine what new consequences the practical implementation of this seemingly more fundamental and complex project might lead to.

Conclusion

If we generalize all of the above and draw a conclusion from such a brief analysis, it should become absolutely clear that the most important and difficult to overcome consequence of the long-term use of antibiotics was their powerful didactic influence on the formation of professional ideas about the nature of AP. This gradual education of generations of doctors took place under the auspices of the exceptional role and indispensability of these drugs as the main means of treating inflammatory diseases. By now, the evolution of a narrow, one-sided view of the problem has reached such a degree that many obvious facts and inconsistencies do not attract the attention of specialists at all and do not receive due and adequate correction.[34]

During the training of medical personnel and subsequent practical consolidation of the obtained information, the main attention was paid to the leading role of the pathogen in the development of AP and the exclusive only possibility of achieving success in treatment due to the choice of antimicrobial drugs. The professional view on the essence of the problem of this disease that was formed during this time ceased to take into account the peculiarity of its pathogenesis, diametrically opposed to the pathogenesis of any other localizations of inflammation both in the mechanisms of its development and in the indicators of the measured parameters. Auxiliary therapy measures carried out without taking into account these differences give directly opposite results in patients with AP, being one of the leading causes of the progression of the process, despite treatment.[34] Attempts to study the mechanisms of pathogenesis at the cellular and molecular level depending on the type of pathogen, carried out over many years, do not give the expected clinical results, since they do not reflect the causes of the integral manifestations of the disease and do not indicate adequate ways to eliminate them.

Today, guided only by the etiotropic system of views on the problem of AP, it is impossible to plan and expect success in its solution, and the continuation of further implementation of this strategy is fraught with the danger of even greater deepening of those serious changes that are currently observed. It is absolutely obvious that a successful solution to the discussed problem is impossible without a radical revision of the concept of the disease and bringing it into line with the classical canons of medical science. It is this step that must precede any other initiatives.

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Conflict of interest

The author states that he has no conflict of interest.

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