



Review Article

Modern Didactics of Acute Pneumonia as a Side Effect of the Antibiotic Era

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Abstract

The widespread and uncontrolled use of antibiotics for more than eighty years, including not only medicine but also the food industry, has had a significant impact on the usual relationships between representatives of the microbiosphere that accompanies our body. For a long time, the possibility of side effects remained without due attention, giving way to attempts to maintain the original antimicrobial effect of these drugs. Currently, evidence of the consequences of antibiotic therapy has received official recognition only in the form of resistant microflora. Phenomena such as the constant change of AP pathogens and the gradual loss of antibiotics for their purpose remain unstudied. The selective nature of specialists' attention to the side effects of antibiotics is due to a decrease in their effectiveness and the desire to restore the successes of previous therapy. The latter circumstance is a consequence of the negative didactic influence of antibiotics on professional views that determine the strategy for solving the problem and require, first of all, changes following the fundamental canons of medical science and numerous facts.

Introduction

The world around us, of which each of us is the smallest subject, is a complex but surprisingly balanced system, autonomously and according to its own rules and laws, maintaining its relative constancy at all levels. Human activity can have a very noticeable impact on natural phenomena, contributing to the development of various kinds of transformations and disasters. It is enough to mention such consequences of human activity as global warming, the shallowing of various rivers and reservoirs, or the catastrophic disappearance of many representatives of flora and fauna to understand how impressive and severe such consequences can be.

Medicine is a set of methods, artificial concerning nature, created by man to influence various deviations in the structures and functions of the body and aimed at returning them to their original state. The strategic foundations of medicine distribute emphasis between the causes and mechanisms of various pathological conditions and formulate tactics for

further action. Thus, the application of various therapeutic efforts and methods is determined by our understanding of the essence of the observed diseases and is entirely dependent on their ideology. In such situations, underestimating the natural reactions of nature to interference in its routine processes can significantly change the expected result and potentiate the side effects of such actions. A very striking and illustrative example of such consequences can be the principles of providing care to patients with Acute Nonspecific Inflammation in the Lungs (ANSIL), which were formed under the impression of antimicrobial approaches and had a strong influence on the formation of the ideology of these diseases in general, and Acute Pneumonia (AP) as their main nosology in particular.

Discussion

The positive effect of topical application of mold on inflammatory processes was known in ancient medicine [1], but the targeted development of this direction began only about a hundred years ago when Alexander Fleming published his revolutionary report on the antimicrobial action of penicillin



in 1929, which he managed to isolate from mold. [2]. Almost a decade and a half after this publication, by the time of the first clinical use of penicillin [3], which opened a new era in the treatment of inflammatory diseases, it was already known for certain that it is unstable to certain types of bacteria, as well as its ability to cause the development of resistance of those microflora which it has a detrimental effect [4,5]. Moreover, in 1945, when the use of penicillin had not yet reached the wide distribution in the world that was observed in subsequent years, A. Fleming in his Nobel speech especially emphasized the danger of unjustified use of such drugs, which is fraught with the development of resistant microflora [6].

The main medicinal quality and purpose of antibiotics were established at the preclinical stage, showing that these drugs are capable of acting only on certain types of microorganisms and do not have a direct effect on the mechanisms of the inflammatory process itself. Having all the above prerequisites on the eve of the widespread introduction and use of antibiotics, it would seem quite logical from the very beginning to determine their true role and place in the overall complex treatment of inflammatory diseases, strictly adhering to the indications for use. However, as the further course of events showed, the attitude towards the new type of treatment in official medicine was based more on enthusiasm about the first results of treatment than on a balanced and scientifically based approach. The ability to quickly achieve the desired result and the ease of use of this type of therapy have overshadowed the need for a rational and controlled approach to the administration of such drugs.

The belief that arose in the first years of antibiotic therapy that the success of treatment primarily depends on the antimicrobial result was not only not subject to logical revision even when side effects appeared, but, on the contrary, continued to strengthen, now becoming the dominant strategic dogma in the treatment of patients with AP. This shift in professional opinion can be traced throughout the history of antibiotic use, which now spans eight decades. This transformation of ideas became more and more large-scale and sustainable thanks to the training of more and more new generations of specialists on these principles.

The above-mentioned predictions of A. Fleming [6] began to come true soon after the launch and widespread introduction of this therapy. The emergence and spread of resistant strains and the decrease in the initial effectiveness of antibiotics in AP have constantly stimulated the search for restoring the effectiveness of this therapy, becoming a "chronic" topic of scientific discussions. This lengthy search process pursued the main goal, first of all, to achieve treatment success, so the consequences of the use of antibiotics for a long time did not receive due attention and critical analysis. The primary interest of researchers and practitioners has been in developing new, more effective drugs, most of which were introduced and released in the first three decades of the antibiotic era [7].

When treating patients with AP, close attention began to be paid to early diagnosis of the etiology of the disease for the targeted use of antimicrobial therapy, which was seen

as a prospect for improving results. The current state of this problem is a convincing confirmation of the fiasco of these electoral trends, which, unfortunately, actively continue to this day. At the same time, another side effect of antibiotics, which arose as a result of suppression of microflora, was observed in parallel with the emergence of resistant strains and caused difficulties in choosing antimicrobial drugs, and has not yet been properly assessed by specialists. It should be noted that it was precisely this phenomenon, in my deep conviction, that finally, after long indifferent observations, forced us to declare the stability of microflora a worldwide catastrophe [8]. In this case, we are talking about a manifestation that did not have similar signs in the pre-antibiotic period and was caused by a constant change in AP pathogens.

Statistics on the etiology of AP in the pre-antibiotic period convincingly demonstrate its enviable stability over 30 years. Thus, statistical data from 1917 to 1948, including intermediate results with an interval of several years, show that the undisputed leader among the causative agents of AP was pneumococcus, which demonstrated its absolute superiority, the incidence rate of which did not fall below 95% [9-13]. Subsequently, after the widespread use of antibiotics began, such statistics among pathogens became a thing of the past, and pneumococcus lost its leading position, having low and periodically changing indicators, which, as a rule, did not go beyond half of the observations. Among the causative agents of AP, other representatives of the microflora began to appear, which had not previously shown their high activity or were not detected in this disease. At the same time, the list of AP pathogens changed periodically, acquiring other leaders at different periods.

In this context, we are talking about the general phenomenon of a constant change in pathogens of AP, which arose and is observed throughout the entire period of use of antibiotics. Individual details and circumstances, which can be found in the literature if desired, in this aspect do not have serious significance when discussing strategic provisions. At the same time, the observed changes in the etiology of diseases are very significant consequences of antibiotic therapy, but, unfortunately, the significance of these phenomena for understanding the entire problem of AP and its solution remains insufficiently understood and taken into account.

Firstly, the growing diversity of the etiology of AP during the use of antibiotics and the resulting unpredictability of the selective participation of an increased number of microflora representatives in inflammation of the lung tissue over a long period is the reason for the development of new methods for their early detection. Such persistent efforts to achieve success in this diagnosis are due to the deep conviction that only targeted exposure to antimicrobial drugs can bring the long-awaited result. However, as noted above, such unsuccessful attempts, despite the contradiction of real facts, continue with the same result to this day.

Secondly, today the attention of specialists of all profiles, to one degree or another concerning the problem of treating patients with AP, is focused only on the side effects of antibiotics



in the form of microflora resistance. The lively discussion of the dangers of antibiotic-resistant microorganisms exaggerates their real threat. The constant increase in the proportion of such strains of pneumococcus in the microflora has already reached 20% [14,15], cephalosporin-resistant *Escherichia coli* and Methicillin-resistant *Staphylococcus Aureus* [MRSA] – 42% and 35%, respectively [16]. The latter circumstance has turned resistant strains of bacteria into familiar representatives of the microbiota of healthy people. For example, in the normal population the carriage rate of MRSA is 2% – 3% [17,18], among healthcare personnel this figure increases to 4.1% – 6.4% [19], and among farmers who work with livestock receiving antibiotics, this pathogen is detected in 10% [20,21]. All these data refer to healthy people colonized with MRSA without any evidence of disease.

Third, in addition to medicine, antibiotics continue to be widely used to increase production in areas such as livestock, poultry, and fisheries [22]. Long-term use of such initiatives in the food industry not only has the potential to spread antibiotic exposure to the general population but also leads to uncontrolled environmental pollution [23,24] with subsequent changes in bacterial genetics and antimicrobial resistance [25,26]. The presence and influence of such a trend in our daily lives, judging by the results of ongoing research, can have much greater consequences than it seems. However, the problem of resistant microflora is assessed mainly by taking into account the therapeutic use of antimicrobial drugs, with a fair indication of the negative role of self-medication and prophylactic administration of this therapy [27–29]. Widespread environmental and food exposure to antibiotics remains in the early stages of study [30].

Fourthly, the constantly growing latent carriage of resistant strains does not correspond to the alarming and frightening assessments that characterize the problem of resistant microflora today. The likelihood of a long-term and harmless presence of such potential pathogens in the body can develop into a serious problem only if an inflammatory process develops. However, for such a situation to arise, additional factors are required, not just the presence of the corresponding microbe, right? Moreover, this option can only be seriously considered if antimicrobial therapy remains the mainstay of treatment, in which case its success becomes problematic. In light of modern views on the problem, it is the latter circumstance that serves as a cause for concern and fear of resistant strains.

Finally, the constant change in the microbiological factors of AP, which arose with the beginning of the widespread use of antibiotics, but has not received proper assessment, has gradually led to the fact that the justified need for prescribing these drugs is becoming increasingly unnecessary. The rise of viral forms of the disease, which accounted for nearly half of all cases two decades ago [31,32], has increased significantly during the SARS-CoV-2 pandemic, further complicating the already challenging task of caring for these patients. This is especially true during aggressive developments. While maintaining previous conceptual traditions, modern medicine, despite numerous facts and scientific materials, continues to preserve and even promote the widespread use

of antibiotics, while forgetting its thesis about the danger of further deepening microbial resistance. For example, when the presence of bacterial coinfection was limited to as little as ten percent, patients with COVID-19 pneumonia continued to receive antimicrobial therapy in 70% to 80% or more of hospitalizations [33–35]. It is not difficult to understand that by resorting to such measures of assistance, the illusion of etiotropic therapy is created and self-deception continues.

The presented data summarizes the causes of erroneous ideas formed in professional ideas about the role and place of antimicrobial therapy in the modern complex of treatment. The false belief in the indispensable role of antibiotics in the treatment of AP, which continues to dominate in solving the problem of these diseases, does not have serious counterarguments in its defense in the light of the stated facts. At the same time, the persistence of these views and the actions resulting from them, which persist even in conditions where the need for antibiotics has been completely exhausted, serves as a reason for a serious assessment of the interpretation of the nature of the disease.

Meanwhile, in addition to the increasing viral expansion over the decades, in recent years there have been increasing reports of an increase in the number of patients with fungal infections of the lung tissue [36,37]. Against the background of the widespread use of antibiotic therapy with its destructive effect on the bacterial sector of the microflora, the increasing role of fungal infection also seems to be a completely natural consequence. However, factors such as global warming, environmental damage, and an increase in the number of people with weakened immune systems are considered among the causes of the latter phenomenon, rather than antibiotics, the role of which has not even been noted [37].

In light of all the facts stated above, it is very interesting and instructive to pay attention to the attitude of official medicine towards the only discussed side effect of antibiotics – microflora resistance. This quality of the new therapy was known before its widespread use from preliminary trials [4–6], and the first signs of such effects began to appear in the early years of this treatment. Resistance of microorganisms accompanied antibiotic therapy throughout the subsequent period, continuing to increase and involve new strains. During this transformation, the main goal pursued by medicine was the creation and use of more advanced and effective drugs. Over the past period, despite the growing problem of bacterial resistance, manifested in a decrease in the effectiveness of antibiotics and the search for new ones, there have been no global efforts to reduce this burden.

Against the background of the already familiar hope for the use of antibiotics for AP, attention was suddenly drawn to a long-existing dilemma in the treatment of this category of patients. Without removing the leading role of antibiotics in the treatment of inflammatory processes from the agenda, the World Health Organization [WHO] declared antibiotic-resistant microorganisms a global disaster [8]. In my opinion, it is no coincidence that the timing of this announcement coincided with the height of the SARS-CoV-2 pandemic. The



coronavirus invasion has created a clear situation where a large flow of patients with viral inflammation of the lung tissue found themselves without the usual etiologic treatment. The WHO statement appeared only as a result of the global spread of this pathogen, as if there had not been two major epidemics, SARS and MERS, and the coronavirus did not continue to figure in the etiology of AP until the pandemic [38,39]. It may seem strange that there is a connection between the declaration of antibiotic-resistant microflora as a global disaster and the coronavirus pandemic, which these drugs have nothing to do with neutralizing.

Antibiotics, which for many decades were considered the mainstay of treatment for AP and were often considered to help these patients in the status of “antibiotics alone,” suddenly became ineffective for a large number of seriously ill patients. Professional help for this disease was limited to auxiliary and symptomatic methods and means, since in the conditions of the new leader in the etiology of AP, no rational solutions were found. A situation arose when medicine was unprepared and unable to provide adequate care to a severe group of patients, and the measures taken during hospitalization did not prevent the inhibition of the process, which in many cases continued to progress despite therapy. After many decades of passive observation of microbial resistance, its recognition as another global problem during the coronavirus catastrophe could not influence the course of events and change the results of treatment, but such a document made it possible to indirectly preserve the “honor of the uniform” by explaining the reason for the difficulties in treatment.

On the one hand, the WHO, on the eve of this statement, published other documents with proposals for the development of a system of measures to strengthen control over the prescription and use of antibiotics [40,41], although such ideas, when expressed and implemented, were many decades late. At the same time, on the other hand, a large number of proposals have appeared, including from WHO experts [8], on the need to further improve antimicrobial drugs that can act against resistant strains [8,16,42,43]. Such proposals aimed at solving the problem of resistant microflora create a new platform for reviving the cause that caused the changes being discussed. Another paradox? It seems to me that this goes beyond simple misconceptions.

For example, among proposals of this kind, possible plans to create new antimicrobial drugs using biogenic and nanotechnologies at the microstructural level deserve attention [42]. If proposals of this kind begin to be implemented, the consequences of such profound structural changes will ultimately lead to even more dire consequences than those we already have. One can only imagine the catastrophic consequences of such interference in natural mechanisms, which have already been significantly transformed under the influence of “conventional” antibiotics. The desire to solve a problem without a comprehensive analysis and conceptual revision of its foundations by reinforcing previous trends only to continue the same therapy is, from my point of view, a reflection of a kind of ideological obsession. At the heart of

this desire is a strong commitment to the dominant concept of AP and confidence in its infallibility, although numerous facts have long pointed to the need for its radical revision.

The SARS-CoV-2 pandemic taught medicine a completely frank lesson, creating a situation with a sudden increase in the number of severe viral cases of pneumonia, the treatment of which was very demonstrative without the usual means of assistance. Uncertainty about the success of treatment should the disease occur has led to public fear and anxiety about the spread of the coronavirus. However, according to various sources, 20% - 40% of those infected with coronavirus had no signs of the disease at all and learned about it only based on diagnostic tests [44-46]. By now it is already known that during the pandemic, preventive measures, including vaccination, were not a complete guarantee against the disease, and the completeness of their implementation cannot serve as an indicator of the quality and effectiveness of medical care. For example, Sweden has clearly shown that the abandonment of anti-epidemiological measures does not lead to an extreme deterioration of the situation, which continues to follow the general scenario [47].

At the same time, treatment of patients with AP remained the main hope for a favorable outcome of the disease, but, as the practice has shown, it turned out to be powerless to influence the negative dynamics of the process. It is the results of patient treatment that have become the main criterion for the effectiveness of medical care during the pandemic. Thus, on public information sites demonstrating the results of the development of the pandemic in different countries, as a rule, two indicators appeared - the number of infected and the number of deaths. If the first figure gave an idea of the spread of coronavirus and made it possible to indirectly judge not only preventive measures but also the coverage of the population with diagnostic testing, then the mortality rate served as an objective result of the work of medical institutions in providing medical care to the population.

Unfortunately, the materials of the pandemic were not properly assessed, so its didactic signals did not influence professional ideas about the nature of AP. A significant example in this regard is the opinion of the editors of one of the leading journals, *The New England Journal of Medicine*, who stated in their pages that one of the compelling reasons for the high incidence in the United States during the pandemic was the wrong government strategy [48]. This view has received strong support from some experts [49]. At the same time, summing up the results of medical care during the pandemic, the editors of the same journal rather unexpectedly highly appreciate this work, noting the special role of vaccination of the population in this [50]. However, the main results - the treatment of patients with AP, indicating the failures of medicine in this section during the pandemic, are not even mentioned, being replaced by the standard emphasis on the aggressiveness of the new pathogen as the cause of the severe development of the disease.

The above examples can serve as further evidence that the long-term exaltation of antibiotics as the main, and often the only, means of treating AP has led to a persistent distortion of



professional ideas about the nature of the disease. As a result, a stable opinion was formed about the dominant role of the pathogen and its properties in the development of the disease. The actual loss of antimicrobial therapy during the pandemic turned out to be an unexpected dead end for many specialists, although the process of antibiotics losing their positions as a result of the growth of viral forms of AP has been observed for several decades. Instead of a balanced and comprehensive analysis of the observed facts with a search for rational solutions, one could observe attempts to translate the medical problem into a political plane [48,49].

The desire to present vaccination as a factor in the success of medicine against coronavirus infection requires, first of all, reasoned justification, since the real situation allows such a statement to be made in the subjunctive mood, and the above-mentioned "Swedish experiment" generally raises great doubts about this. At the same time, the understatement regarding the treatment of sick people is not entirely understandable, since specialists occupying such key positions in the medical hierarchy are accustomed to highlighting not only achievements but also important problems of medicine. However, if we recall the statistics of the pandemic, the mortality rate from COVID-19 pneumonia in the United States is known to be the highest in the world. Such indicators in the conditions of one of the most developed healthcare systems require comprehensive analysis and reasoned conclusions, which have not been given by anyone, and as long as etiologic concepts dominate in the concept of AP, in my opinion, there will be no scientific justification for these failures. So far, attempts to answer the cause of the pandemic have not progressed beyond fatal and standard observations about the virulence of the pathogen and suspicions of deliberate infection, which have not been confirmed [51].

Currently, experts are only concerned about the development and spread of resistant strains, which is motivated by the difficulty of effectively using antimicrobial drugs. However, analysis of the side effects resulting from long-term, readily available, and widespread use of antibiotics allows us to draw attention to several such consequences. The idea that the pathogen plays a leading role in the disease AP, which arose and strengthened due to the use of antibiotics, determines not only the strategy for solving this problem but also approaches to assessing the phenomena occurring. Therefore, the main hopes and attention to the early diagnosis of the etiology of the disease and the search for effective antimicrobial drugs have led to ignoring and underestimating such important changes as the radical transformation of the list of pathogens of AP compared to the pre-antibiotic period [9-13] and the increasing loss of antibiotics from their original purpose.

The above is confirmed by the results of determining the causative agent of AP in recent years, which reflect the real state of etiological diagnosis and the continued empirical prescription of antibiotics. Negative microbiological results of examination of patients with AP account for more than 60% of observations, which is explained, in particular, by viral infection [52,53]. During periods of viral epidemics and pandemics, the number of such cases can be even more

impressive. Operating with such facts, practical medicine is trying to find a justification for the use of previous standards of antimicrobial therapy, not paying attention to the fact that the conditions for such implementation have long since changed dramatically. The reason for such aspirations can only be the negative didactic impact of antibiotic therapy on the professional worldview.

The last of these antibiotic side effects is the main reason for the confusion that currently exists in ANSIL's interpretation of the nature of the problem. In this regard, it should be noted that the ideology of ideas about the essence of the tasks being solved determines our choice of the necessary means and actions to achieve the goals, isn't it? Therefore, before further improvement of antimicrobial therapy, which is currently on the agenda [8,16,42,43], as the cause of the problem of resistant microflora, a radical change in the system of ideas about the essence of the ongoing transformations is necessary. Without such a revision, further efforts will have the same results that accompany the treatment of this category of patients at this stage. A more detailed analysis of common misconceptions regarding the nature of AP and the principles of its treatment is presented in the author's recently published monograph [54].

Conclusion

Antibiotics were one of the outstanding medical advances of the last century, saving many millions of lives. However, after decades of presence in our environment, their side effects as a result of exposure to living representatives of the microcosm every year more and more demonstrate the process of their self-elimination from the category of active antimicrobial therapeutic agents. The reason for this phenomenon is such consequences as microflora resistance, the emergence of variability in the etiology of AP, a change in leaders among the pathogens of the disease, and the gradual replacement of bacteria by other components of the microflora. The only side effect that worries specialists is the resistance of the microflora, which is due to a decrease in the therapeutic effect of the drugs. The selectivity of this approach to the long-term results of antibiotic therapy lies in its negative didactic impact on the professional worldview, which represents the main obstacle to understanding and successfully solving the problems that have arisen.

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