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Opinion

Unaccounted Side Effects of Antibiotics and their Role in Solving the Problem of Acute Pneumonia

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Abstract

Acute pneumonia (AP) is characterized by unpredictable clinical manifestations and; in severe cases; persistent progression of the inflammatory process despite intensive therapy. Treatment principles for this category of patients are based on the AP ideology; which for nearly a century has viewed nonspecific inflammatory pathogens as the primary cause of the disease; and antibiotics as the primary; and often only; treatment method. The most significant biological side effect of the long-term use of these etiotropic drugs has been the constant shift in the spectrum of AP pathogens; leading to the gradual predominance of etiologic agents outside the range of antibiotic activity. Maintaining the previous understanding of the disease and ignoring the contradictions between obvious facts and the canons of medical science; amid declining antibiotic effectiveness; has led to an exaggeration of the danger of resistant strains. However; a balanced and critical analysis of available materials on this topic convinces us that the main consequence of antibiotic use is its negative didactic effect; the elimination of which requires a fundamental revision of the AP doctrine.

Keywords: Acute pneumonia; Etiology; Antibiotics; Change in the etiology of pneumonia; Resistant microflora; Concept of acute pneumonia; Didactic effect of antibiotics

Abbreviations: AP: acute pneumonia; CAP: community-acquired pneumonia; COVID-19: coronavirus disease 2019; HAP: hospital-acquired pneumonia; ICU: intensive care unit; ICUAP: intensive care unit-associated pneumonia; MRSA: methylenepenicillin-resistant Staphylococcus aureus; SARS-CoV-2: coronavirus pandemic; VAP: ventilator-associated pneumonia; WHO: World Health Organization

Introduction

The era of antibiotics has lasted for over eight decades. During this long period of widespread use; these drugs have not only brought enormous benefits and successfully treated millions of patients; but also caused side effects; which have become increasingly noticeable in recent years and impact the quality of medical care. Unfortunately; as an analysis of the current professional understanding of the role and significance of this therapy in treating patients with inflammatory processes shows; many consequences of antibiotic use remain unnamed; and their impact on methodological aspects and practical medicine is not adequately assessed or taken into account. This situation is most illustrative in the case of patients with acute pneumonia (AP).

Discussion

The first; less significant side effect of antibiotics concerns the aforementioned AP and associated terminology. AP is a single disease; regardless of its etiology. The etiology of AP is nonspecific and universal; and despite being caused by different pathogens; the clinical picture remains the same in all patients. Modern medicine persistently strives to restore the initial effectiveness of antibacterial therapy through the early; targeted use of antibiotics; considering them the primary treatment method. However; achieving this goal is hampered by the inability to obtain samples from the site of inflammation for bacteriological examination in the early stages of the disease. Even if this problem is resolved; the wait for results will be excessively long; leading to the loss of precious time during the acute stage of inflammation. To expedite and improve the reliability of drug selection; it was proposed to classify pneumonia types by site of origin; citing the usefulness of this classification for distinguishing identifiable pathogens. This led to the emergence of community-acquired pneumonia (CAP); hospital-acquired pneumonia (HAP); and ventilator-associated pneumonia (VAP). Simply put; this terminology arose as a way to roughly "bacteriologically diagnose" the disease in the hopes of improving the outcome of antibacterial therapy. Although it is now clear that this approach did not achieve the expected success; its basic idea remains in use today [1,2]; and the classification continues to expand; pursuing the same original goals. For example; this is how intensive care unit-associated pneumonia (ICUAP) emerged [3-5].

However; the key indicator of AP development—not the site of onset; but the patient's initial condition—has been relegated to the background. Meanwhile; it is precisely these conditions that play a decisive role in its development. While CAP develops in apparently healthy individuals; all other variants of the disease are observed in hospitalized patients with varying degrees of severity of various pathologies. An intubated patient connected to a ventilator has a significantly higher risk of developing an inflammatory process in the lungs than a person outside the hospital leading a normal life; isn't that true? At the same time; attempts to differentiate AP by the nature of the pathogen have proven ineffective; even when distinguishing between bacterial and viral forms of inflammation [6-8]. Given the well-known negative results of such long-term efforts; reflecting the "infantile" role of pathogens in the development and progression of the disease; the logic of searching for targeted antimicrobial therapy; at first glance; becomes unclear. Further analysis of the materials on the problem under discussion reveals that the roots of this phenomenon run much deeper than initially appears.

This example of applying disease classification to such an unusual goal as "bacteriological" diagnostics; although a rather paradoxical and imprecise method; nevertheless reflects the didactic influence of antibiotics on professional consciousness. Having taken root in medical literature but not yielding the expected results; this terminology continues to be used to search for the optimal choice of antimicrobial agents [1,2]. The latter testifies to the firm professional conviction that the development of AP is based on a bacterial factor; and antibiotics are the primary method of treating inflammatory (!) diseases; primarily those of non-specific etiology. Such diseases typically develop and progress with the participation of symbiotic microflora; including opportunistic bacteria. Even in the early stages of studying the etiology of AP; when most of its pathogens had not yet been discovered; the participation of symbiotic bacteria in this inflammatory process was proven [9,10]. These results revealed the reason for the non-contagious nature of this disease.

This debate; which requires detailed analysis; would not be a topic for discussion if the currently used approaches and treatment methods for patients with AP were producing the expected results. However; the effectiveness of treatment for this category of patients continues to decline; the incidence of septic complications is increasing [11,12]; and the principles of medical care for this disease remain unchanged; stubbornly maintaining their stability. Blind adherence to old treatment models requires; at a minimum; an explanation for why the efforts and resources expended are not producing the stated and expected results. And now a "new" bogeyman appears in the form of resistant microflora.

The rapid emergence of antibiotic resistance in microflora was demonstrated even during preclinical studies of these drugs [13,14]. Official documentation of resistant microflora began in 1961 with the discovery of methylenepenicillin-resistant Staphylococcus aureus (MRSA) [15,16]. This strain of staphylococcus attracted particular attention because it demonstrated protective properties against synthetic penicillin; although resistance to the natural drug had been observed before this event. No large-scale measures to curb or reduce the growing burden of antibiotic therapy were taken either before or after this event. More active discussion of this topic and the emergence of guidelines and recommendations from the World Health Organization (WHO) have only begun to occur with increasing intensity in the last couple of decades.

The long-standing; virtually indifferent attitude toward resistant microflora was explained; on the one hand; by the lack of clear manifestations of its hyper aggressiveness. As is known; no one has discovered or presented evidence of increased virulence of microorganisms as a result of their acquisition of antibiotic resistance. In other words; individual bacterial strains acquired resistance to antibiotics; but their other properties remained unchanged. On the other hand; for most of the history of antibiotic use; the etiology of pneumonia remained bacterial; consistent with the spectrum of antibacterial drugs used. However; in the last two to three decades; there has been a significant increase in viral pneumonias [17,18]; which has led to a decrease in the effectiveness of traditional treatment.

Maintaining an ideological commitment to the microbial factor as the primary cause of AP and ignoring other motivators and stimuli of the inflammatory process; medicine naturally turned its attention to resistant strains; seeing them as the basis for treatment failure. Thus; for many years of pursuit of rapid antimicrobial efficacy; the development of resistant microflora remained a mere known phenomenon; without targeted efforts to reduce this burden. In recent years; the prevailing circumstances have forced medicine not only to acknowledge these changes but also to declare them the cause of a total catastrophe [19,20]. Notably; this assertion arose at the height of the SARS-CoV-2 pandemic; when a flood of patients with COVID-19 pneumonia overwhelmed many hospitals; and the quality of care for these patients was reduced to supportive and auxiliary measures.

Modern literature on the significance of resistant strains focuses primarily on just one characteristic feature of such pathogens: the difficulty of neutralizing them with traditional antibacterial drugs. This narrow focus is a natural consequence of the established professional understanding of the nature of AP; which emphasizes the pathogen itself and the importance of etiotropic treatment. Therefore; most publications on this topic contain declarative statements about the extreme danger of resistant microflora without any objective evidence of such a threat.

The situation with actual resistance of strains in acute pneumonia is quite different. The few reports on the incidence of antibiotic-resistant strains indicate that such observations do not exceed 1–2% [21-23]. These figures are not only lower than the prevalence of some resistant microflora as latent carriers in the general population (2–3%); but also several times lower than; for example; the prevalence of MRSA as a commensal pathogen (up to 6–10%) among individuals in certain professions [24-26]. For an objective and well-founded understanding of the problem under discussion; it is important to understand that all these data require not only comparison but also a reasoned explanation.

Today; physicians show little interest in the incidence and causes of the spread of resistant microflora among healthy individuals. Therefore; these statistics are not used to compare clinical studies. Instead of explaining the causes of this phenomenon; conclusions

are drawn about the need to develop and release new generations of antimicrobial drugs [20,27,28]. Thus; relying on the foundations of old ideology and without properly assessing the consequences of long-term antibiotic therapy; representatives of modern medicine propose further improvements to the potential of drugs that have led to the side effects discussed. No one predicts the deeper and more serious consequences that will inevitably arise from the implementation of such plans. To do this; it is first necessary to understand the scale and seriousness of the changes that have already occurred in the antibiotic era. However; the didactic consequences of antibiotic use remain an obstacle to such a critical analysis and optimal conclusions.

Another side effect of the widespread and prolonged use of antibiotics; not subject to substantive discussion and cited only as a reason for changes in etiotropic therapy; is the dynamic change in the pathogens that cause AP. This phenomenon has played and continues to play a significant role in the observed transformation of the initial conditions in this area of medicine and is the main reason for the current collapse of antibiotic therapy. As is well known; this side effect began to be observed soon after the onset of clinical use of antibiotics; which initially necessitated the intensive development and release of new; more advanced drugs. However; during the first three decades; the process of updating the drug potential slowed [29]; and then a period of intensified attempts at early diagnosis of the pathogen began. These latter efforts continue to this day [30-32]; but the futility of this long-term work is now recognized thanks to recommendations for the empirical selection of antibiotics [33,34].

The primary significance of this side effect of antibiotics lies not in the optimal choice of medications; but in the fact that prolonged suppression of bacterial pathogens has inevitably and naturally forced nature to develop its own defenses against this aggression. Thus; viral epidemics have begun to occur annually; becoming a sort of traditional phenomenon; requiring the resumption of vaccination due to the lack of effective treatments. Gradually; but quite steadily; the incidence of viral pneumonia has increased significantly in recent years. This circumstance represents a rather peculiar mechanism for the self-displacement of antibiotics from the list of in-demand etiotropic agents. The fact that antibiotics continue to be widely used for viral pneumonia is completely unfounded and does not confirm their effectiveness. Experience with the recent pandemic has shown that the indications for antibiotic prescriptions significantly exceeded the permissible limits [35-37]. Moreover; many patients with COVID-19 pneumonia were cured without the use of traditional etiotropic agents. Moreover; the mortality rate among those who received and did not receive antibiotics did not differ significantly [38-43].

The SARS-CoV-2 pandemic has clearly demonstrated that the human body's response to infection with the same pathogen is extremely diverse [44,46]. Add to this the lack of convincing criteria for differentiating pneumonia by etiology; even between bacterial and viral forms [6-8]; and the role of the pathogen; especially as a leading factor; becomes extremely problematic. At the same time; the clinical picture of the disease retains its key distinguishing characteristics; and a certain percentage of patients develop a severe course of the disease; regardless of the etiology; requiring additional treatment. This latter group of patients with acute pneumonia has been considered and analyzed separately in recent years; as disease progression in such cases is unpredictable and often leads to complications and critical situations [46-49].

Various attempts to improve the outcomes of emergency care for patients with severe AP also represent a return to an outdated understanding of the disease. All inflammatory processes; regardless of their location and pathogenesis; are separated and considered based on their characteristic complications; which are presented as identical and subject to equivalent treatment. For many years; the blatant misconception about the uniqueness of the pulmonary circulation; which is fundamentally different from the systemic circulation and has diametrically opposed parameters; the synchronous; vital regulation of which is carried out autonomously; was ignored. In this situation; a widely used general therapeutic method such as infusion therapy has a negative impact on the course of AP; especially in the early stages of the disease; stimulating the progression of inflammation [50].

If we attempt to answer the question of the source of modern misconceptions regarding the pathogenesis of AP; then in this situation; where all the key details of the functional parameters of blood circulation in the two halves of the cardiovascular system and their inextricable interconnection are known; then; in my opinion; there can be no other answer than the professional factor. This conclusion once again points to the strong influence of the so-called microbial concept of disease as a psychological dictate on the professional understanding of the nature of AP; despite contradictions with existing and long-established scientific data.

Didactic biases persist in professional understanding of the problem under discussion; which is reflected in current research. For example; there remains a deep belief in the positive value of classifying AP by site of origin; which; as was the case many years ago; presupposes a spectrum of expected pathogens and calculated antimicrobial therapy [51]. Similarly; a large group of experts from various countries and continents notes that severe AP is associated with high mortality worldwide; yet their proposed new recommendations are once again formulated based on old concepts and principles [52]. Logically; such recommendations have not led to significant improvements in outcomes; but the authors attribute this to other issues hindering the implementation of the proposed changes.

Thus; by not changing the strategy for combating AP and attempting to achieve established goals with minor tactical adjustments; medicine is effectively making no progress in this direction. However; given the ongoing changes in the etiology of the disease; which have already gone beyond the scope of current therapy; the situation is clearly worsening. However; the conclusions of most publications continue to predict the likelihood of successful treatment for this group of patients in the future if ongoing research continues. No specific timeframe for this eventuality is indicated; and the flow of such self-deception continues to grow. A review of publications on this topic from 20-30 years ago reveals numerous optimistic and encouraging conclusions in the articles; claiming that further research promises (!?) successful results. Analysis of such conclusions; reflecting assumptions stemming from a preconceived notion of AP; seems to be material for a larger

study of professional self-deception. However; this topic is already of interest to psychologists.

Conclusion

The final conclusions from the above analysis of factors hindering progress in addressing the problem of AP indicate the exceptionally strong didactic influence of antibiotics on the formation of professional worldviews. This side effect of this group of drugs significantly outweighs their biological consequences. This assessment is based on a strict requirement: to successfully solve any problem; it is first necessary to understand its causes and the underlying factors creating the complex situation. This requires the use and analysis of all relevant materials; rather than relying solely on traditionally selected sources. This approach will allow for a dynamic expansion of understanding of the essence of a specific problem; facilitating its solution.

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Conflict of Interest

No Conflict of interest.

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