ECRONICON OPEN ACCESS

EC PULMONOLOGY AND RESPIRATORY MEDICINE

Review Article

A Chronicle of the Solution to the Problem of Acute Pneumonia and the Reasons that Slow this Process Down

Igor Klepikov*

MD, Professor, Retired, Renton, WA, USA

***Corresponding Author:** Igor Klepikov, MD, Professor, Retired, Renton, WA, USA.

Received: September 29, 2025; **Published:** November 17, 2025

Abstract

In recent years, severe forms of acute pneumonia (AP) have emerged as a distinct group of diseases due to low treatment efficacy, frequent complications, and high mortality. However, amid the apparent rise in viral pneumonias, which, according to some data, already outnumber bacterial pneumonias, attempts to address this problem continue to stubbornly rely on the leading and decisive role of antibiotics. This article, drawing on the author's unique experience and accumulated material on this topic, critically analyzes existing misconceptions about the nature of AP and proposes ways to overcome the main obstacles to solving this problem.

Keywords: *Acute Pneumonia; Antibiotics; Side Effects; Etiology; Pathogenesis; Disease Concept*

Abbreviations

AP: Acute Pneumonia; COVID-19: Coronavirus Disease 2019; ICU: Intensive Care Units; MERS: Middle East Respiratory Syndrome; MRSA: Methylene-Resistant *Staphylococcus aureus*; SARS: Severe Acute Respiratory Syndrome; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2; WHO: World Health Organization

Introduction

Advances in clinical microbiology and pharmacology at the beginning of the last century led to the so-called microbial theory of acute pneumonia (AP), according to which the main role in the development of this disease was assigned to its etiology [1]. The advent of antibiotics with their amazing first results in such a previously prepared environment served as the reason for the rapid and unconditional recognition of this antimicrobial therapy as the main method of treating inflammatory processes, including AP. In the first decades, the use of antibiotics and the expected effects of this therapy significantly exceeded their potential capabilities, and the tactics of treating AP for a long time were based on the principle of "antibiotics alone". No one paid serious attention to the fact that these drugs have an exclusively antibacterial effect and are not able to directly affect the mechanisms of inflammation, and that in practical medicine, patients with various diseases began to receive one drug as the main treatment.

Soon after the start of clinical use of antibiotics, side effects began to be observed, which were initially predicted on the basis of the reactions of microflora to the action of these drugs during their initial study and the inevitability of which was warned by the authors of this therapy even before its widespread use [2,3]. The first consequences of the use of antibiotics in the form of a decrease in their

effectiveness and a change in the etiological landscape of AP manifested themselves quite quickly and over time became increasingly significant and large-scale. However, the initial awareness of clinicians about the side effects of antibiotic therapy and long-term observation of this phenomenon in practice did not at all mean the development and application of a system of measures to reduce the severity of such consequences.

Practical medicine showed a keen interest only in restoring the primary activity of antibiotics and persistently tried to solve this problem for many years, but without the expected success. The utopian nature of achieving this goal from a biological point of view has become an obvious fact over the years. The causative agents of AP, which formed a stable basis for the etiology of the disease in the pre-antibiotic era [4-8], became increasingly rare representatives of the microflora, giving way to other agents. However, at present, in the conditions of critical growth of viral forms of the disease, antimicrobial drugs continue to be considered the main means of treating inflammatory processes. Such widespread confidence in the exclusive role of antibiotics is declarative in nature, since it is not based on the results of a comprehensive analysis of the global consequences that have occurred as a result of the long-term use of these drugs, and the inevitable prospects for their development. Let us try to understand the origins of the vicious circle in solving this urgent problem and find a way out of these misconceptions.

The experience of radically reconsidering the essence of the problem and its success

For the author of these lines, visual acquaintance with the problem under discussion began more than 50 years ago and since then this topic has been a constant object of observation. I spent the first half of my working life in the Soviet Union, where, as a student, I became interested in the topic of pulmonary surgery, which determined my subsequent choice of surgical specialty. However, real practice turned out to be completely different from student ideas. At that time, a significant proportion of hospitalizations in many surgical departments were patients with purulent-destructive complications of acute pneumonia (AP), so instead of the expected surgical practice, daily intense work on the timely diagnosis of dangerous complications and their immediate elimination by methods of so-called minor surgery prevailed.

Soon the volume of work of the department with this contingent of patients increased even more noticeably due to a non-standard administrative decree. The reason for this decision was the large number of patients with severe AP in the region with the rapid development of purulent-destructive complications and high mortality. The current situation led to the instruction to immediately refer such patients with an aggressive onset of the disease to the surgical department immediately after the initial diagnosis. Such considerations were dictated by the fact that only here it was possible to provide full-fledged intensive therapy. Over a long period, up to 15-20 or more patients with severe AP with various stages of the inflammatory process were in the surgical department at the same time.

Thus, under the influence of a number of conditions and circumstances, a unique clinical situation arose, when the most severe cases of AP with varying degrees of lung tissue damage were collected under simultaneous observation and dynamic control with equivalent approaches to treatment tactics and criteria for assessing the results obtained. This opportunity for synchronous comparative study and critical analysis made it possible to see the shortcomings of the so-called microbial concept of disease [1] and to question the legitimacy and logic of choosing antibiotics as the main method of treating this category of patients. The questions that arose and the paradoxes identified required not only reasoned explanations, but also objective evidence, and most importantly, a search for ways to achieve encouraging results.

At that time, one of the reasons for such a severe course of AP was considered to be *Staphylococcus*, which, according to some statistics, was recognized as the causative agent of complicated forms of the disease in almost 100% of cases. In the literature, there were no substantiated explanations for such an unexpected change in the etiology of the disease with the abrupt disappearance of pneumococcus, which had previously been its main causative agent. At the same time, the results of bacteriological studies from foci of purulent

complications were distinguished by significant variability, and *Staphylococcus* was not absolutely dominant. It was also known about the unfavorable environmental situation in the air basin of our large industrial center of Western Siberia, and only a limited circle of specialists had access to such important results of air sample studies within the city. It is also noteworthy that among those who fell ill, city residents significantly predominated, for whom the severity of the dynamics of AP differed significantly compared to residents of nearby villages and districts.

Not only the above-listed prerequisites, but above all the lack of the expected effect from the therapy, against the background and in spite of which the condition of many patients continued to deteriorate, served as an incentive to search for a solution to the problem. As a result, a huge clinical and experimental work was initiated, the results of which demonstrated the possibility of targeted pathogenetic treatment of AP with a confident prospect of rapid elimination of inflammation and prevention of complications. The obtained materials formed the basis of the doctoral dissertation of the author-surgeon, and the significance of its results served as the basis for its fundamental defense in the specialty of "pulmonology" [9]. Such paradoxes, when a surgeon solves exclusively therapeutic problems, receives an academic degree in a non-surgical specialty, while continuing to work as an operating surgeon, were probably possible only in the specific conditions of the Soviet Union.

Despite the successful defense of the presented dissertation materials, specialists in the therapeutic profile were skeptical about the achieved results and showed no signs of their practical implementation. Antimicrobial treatment principles continued to dominate in the therapy of AP, which was explained not only by the strength of established habits. The vast majority of specialists did not encounter a situation similar to the one described above and did not feel the need to change treatment standards. At that time, bacterial forms of AP had a total predominance, and antibiotics remained a justified etiotropic agent, maintaining in most cases the imitation of an effective "anti-inflammatory drug". At the same time, severe cases of the disease in other regions, in contrast to our conditions, were relatively rare, but the preservation of previous approaches to treatment suited many clinicians.

The proposed concept of views on the nature of AP and approaches to its treatment was initially presented and published only in Russian, which limited access to this information within the Soviet Union. At the same time, political and social reforms began in the country, which were chaotic in nature and violated the usual foundations and traditions of life of the population. Science, in the context of the emerging reassessment of norms and lifestyle, was rapidly losing its value and relevance, which served as one of the reasons for emigration.

After emigration, the author continued to work as an operating surgeon, but no longer had professional access to patients with AP. However, the results of the enormous work on the discussed topic, which was an unpaid burden and was carried out on personal initiative and enthusiasm, could not be simply discarded. Personal interest in this topic, on the contrary, continued to grow, and clinical information was constantly replenished thanks to informal communication and discussions with doctors of neighboring departments where such patients were treated, as well as constant monitoring of literary thematic publications. This form of control over the dynamics of those transformations that have occurred and continue to occur in this section of medicine in recent years, significantly strengthened the belief in the correctness and validity of the conclusions and prospects proposed by the author. At the same time, new materials and facts that have appeared in recent years allow us to strengthen the argumentation of those delusions in which modern medicine has found itself in the issue of solving the problem of AP.

Underestimated factors in solving the AP problem

The facts and objective materials noted below are, in my opinion, such obvious phenomena that it is very difficult to explain the reason for their "invisibility" over many years. Meanwhile, the position of professional views that has determined and continues to determine the strategy for solving the problem under discussion, testifies to the amazingly powerful mental impact of such attitudes as

the dominance of the pathogen in the nature of AP and the unrivaled role of antibiotics in the treatment process. After receiving the first results of antimicrobial therapy, a distorted, one-sided concept of the disease was born, which turned into a long-standing and unshakable dogma. The literally hypnotic effect of such an ideology not only distorts the analysis of failures and the assessment of their causes, but also leaves "overboard" the classical principles of medical science. If half a century ago, substantiation and proof of already established misconceptions in understanding the nature of AP and the principles of its treatment presented quite serious difficulties, then by now the ongoing transformation of the main characteristics of the problem and the accumulation of new convincing facts in all subsequent years significantly facilitate the recognition of false ideas and beliefs.

Firstly, biased and distorted views on the problem of AP began to form already in the initial period of the antibiotic era, when excessive hopes for the use of this therapy arose. Drugs that have only a specific antimicrobial effect and do not directly affect the mechanisms of inflammation, that is, the basis and essence of such diseases, soon began to be considered as the main method of assistance in AP, often being the only method of treating such patients.

Secondly, the rapid decrease in the effectiveness of antibiotics was a consequence of their biological action, consisting in antagonism to inflammatory pathogens and the adaptive response of the latter. As a result, the microflora as an association of biological objects responded to the intervention with natural adaptation. On the one hand, antibiotic resistance of the microflora began to form and strengthen, and on the other, bacterial interchangeability appeared, when the most sensitive and susceptible strains began to be replaced by others, which was accompanied by a transformation of the etiology of the disease. The assessment of the above-mentioned consequences of antibiotic therapy and the use of corrective measures were due to the influence of the still unabated delight and amazement from its first results, which contributed to a distortion of the interpretation of the problem.

Thirdly, comprehensive efforts aimed primarily at restoring and maintaining the primary effect of antibiotics began. Already in the first three decades, the overwhelming majority of existing classes of antibiotics were developed and released into clinical practice [10]. Microbiological diagnostic methods were developed and improved, but the results of the study were of interest only from the standpoint of an earlier start of antimicrobial therapy, while prevention and reduction of side effects did not receive due attention. Such attempts to revive the initial activity of etiotropic therapy, mainly antibiotics, turned into one of the main trends in solving the problem of AP and continue to this day.

Fourth, during the long period of antibiotic use, programs to prevent and reduce the side effects of this therapy were virtually nonexistent. Moreover, the principles of antibiotic use and the emphasis on their improvement are astounding, effectively reflecting pharmaceutical companies' race to keep up with dynamic changes in disease etiology. Meanwhile, the side effects of this therapy have been accelerating and multiplying for many decades, without being recognized as a growing, irreversible catastrophe and without being subject to countermeasures.

This attitude toward the adverse effects of antibiotic use seems absurd and paradoxical, given the publication of preclinical data on the rapid development of a protective response in bacteria when exposed to these antimicrobials [2,3]. In his Nobel lecture, in the early years of antibiotic clinical use, A. Fleming, the discoverer of penicillin, warned of the serious burden of the development of resistant microflora with their overuse [11]. Just a couple of decades later, the first resistant strain-methylene-resistant *Staphylococcus aureus* (MRSA)-was officially registered [12]. However, the discovery of this pathogen, its identification in patients, and the subsequent emergence of other similar species continued to be important primarily for the selection of therapeutic agents, leaving the problem of preventing and mitigating such transformations unaddressed.

In subsequent years, the tactic of primarily monitoring resistant bacterial strains with an emphasis on finding effective methods to suppress them has led to the emergence of new resistant species, which in recent years have already constituted a fairly impressive

group of microorganisms [13]. Thus, throughout the entire period of antibiotic use, not only was the inevitable development of resistant strains known, but their emergence and spread in medical practice was also observed. In this regard, another paradox was the relatively unexpected declaration by the World Health Organization (WHO) of resistant microflora as a global catastrophe [14]. Additional information provided below will help explain why such a document appeared only in recent years.

Fifth, the clinical use of antibiotics has marked a constant change in the etiology of AP. If in the pre-antibiotic era for several decades, regardless of the regions of study, among the causative agents of the disease in 95% or more cases was *Streptococcus pneumoniae* [4-8], then after the introduction of antimicrobial therapy into widespread practice, the proportion of this pathogen has significantly decreased and no longer approached the initial indicators [15]. The enthusiasm of researchers and practitioners regarding the constant search for the most effective antibiotics gradually turned into the main goal that everyone was striving for in the process of treating patients with AP. At the same time, the fact remained unaccounted for that if in the initial period of the antibiotic era, the interchangeability of bacteria was observed, then by the beginning of the current century about half of all cases of AP in the world were the result of viral aggression [16-18]. This turn of events is quite natural and is a consequence of the long-term suppression of the bacterial segment of the microflora, which began to be replaced by viruses.

Despite significant changes in the etiology of AP, the principles of treatment of this disease have not undergone the necessary and significant revision. The published recommendations on this problem still focus on the most probable bacterial pathogens and the list of antibiotics proposed as the optimal choice. At the same time, taking into account the bacterial-antimicrobial parallels, specialists are increasingly confident in recommending an empirical choice of antibiotics, thereby emphasizing the futility of a long "chase" for early diagnosis of AP pathogens, but do not provide a critical assessment of these failures [19,20].

A significant illustrative moment in the problem under discussion was the beginning of the SARS-CoV-2 pandemic. Modern medicine, which did not change its principles of treating AP during the period of growth of viral forms of inflammation, turned out to be unprepared for a situation when the flow of such patients increased relatively suddenly and sharply. Calls for further widespread use of antibiotics did not affect the results, once again confirming the senselessness of their use in viral inflammations [21-23]. Continuing to consider and analyze the situation from the standpoint of the so-called "etiotropic concept" of AP and trying to find an explanation for the failures of medical care, "conspiracy theories" arose with a suspicion of deliberate spread of coronavirus. However, a thorough study of materials on this topic with the involvement of diverse experts, including intelligence agencies, did not reveal any evidence [24].

Before examining these suspicions, it's important to remember that human coronaviruses only came to the attention of physicians in the 1960s [25]. However, by the turn of this century, new variants of the virus, emerging without laboratory intervention, triggered two major epidemics (SARS and MERS), which began similarly to pandemics. Because the main foci of these epidemics remained localized and did not affect the vast majority of healthcare systems worldwide, data analysis of the origins of these events and the outcomes of medical care was more of a statement than a critical and analytical approach with far-reaching conclusions. But the most important thing in this story is that two severe outbreaks of coronavirus infection with high mortality rates, amid a general rise in viral pneumonia, did not force specialists to look at this problem from a different perspective or lead to any changes in patient management strategies, right?

It is also important to remember that medicine's acquaintance with coronavirus was not limited to the above-mentioned epidemics. In the periods between them and on the eve of the pandemic, coronavirus remained among the causative agents of acute pneumonia, reaching, according to some statistics, 5% in the etiology of the disease [26,27]. In addition, the materials of the pandemic itself showed that most of the population suffered from the infection in mild and moderate forms, coping with this condition on their own, without specific medical care, and in 20-40% of cases, coronavirus infection did not have signs of the disease and was detected only by tests. Hospitalization was required for only about 15% of infected people, of which 5% were placed in intensive care units (ICU) [28-31]. It was

the latter group of patients with coronavirus pneumonia that became one of the reasons for the growing alarming situation in society, which was explained by the unforeseen occurrence of critical situations. When it became obvious that the usual treatment stereotypes were not helping, and no new ideas for treating coronavirus pneumonia were found, a WHO document appeared, which focused on resistant microflora as one of the important reasons for treatment failure [14].

Signs of the development of resistant microflora have been observed throughout the antibiotic era, and in recent decades such bacterial transformation has already been considered an important task in solving the whole problem, but a notable feature of the mentioned WHO document was its "timely" appearance. When specialized departments created in many hospitals during the pandemic were overcrowded with patients with coronavirus pneumonia, and their treatment was narrowed to symptomatic and palliative measures, an authoritative organization suddenly (after so many years of observation!) declares resistant bacteria as the cause of ineffective treatment, focusing the attention of the reading public on this information and trying to maintain the "honor of the uniform". However, the appearance of such a WHO document during the pandemic was a forced and logical result of transformations that remained out of sight and practically not subject to discussion.

Sixthly, such a factor, the role and significance of which remained insufficiently appreciated in the observed "unexpected" events of recent decades, was the steady change in the etiology of AP. In this case, we are talking not only and not so much about the loss of this disease of initially stable microbiological causes of inflammation under the influence of antibiotics, but about a gradual dynamic shift of microflora towards viruses. It is worth noting the already mentioned signs of such shifts: an increase in the frequency of viral epidemics that have become an annual "tradition", the emergence of new pathogens, such as coronavirus, up to the development of a pandemic, the predominance of viral forms of inflammation over bacterial ones among positive diagnostic results for the etiology of AP [32-34]. If such a transformation received the necessary critical assessment, then one of the cardinal conclusions for taking the necessary measures would be the statement of a sharp decrease in the number of patients with AP, for whom the prescription of antibiotics, especially as the main and primary treatment, is an unfounded approach. The situation in which the long-term use of antibiotics led to their gradual displacement from traditional treatment reached its peak during the pandemic, but was misunderstood [35].

Seventh, the interpretation of the reasons for the decrease in the effectiveness of AP treatment based on the microbial theory of disease has led to declarative statements about the negative role of resistant microflora. Such demonization of resistant bacterial strains is usually not accompanied by statistical evidence. Only a few publications report that antibiotic-resistant microorganisms are the causative agents of AP in only 0,7-1.4% of cases [36,37]. At the same time, clinicians do not discuss or provide explanations for such long-known facts that among certain segments of the population and in a number of professions, the carriage of resistant strains among healthy individuals can reach 6-10 percent or more [38-40]. Despite such a long and asymptomatic symbiosis, there are still recommendations regarding the use of sanitizing courses of antimicrobial therapy in such cases [41].

Despite the ominous characteristics of resistant strains, no one has presented evidence that such microorganisms, having acquired their own protection from external aggression, themselves become more aggressive. In this regard, a pressing issue, logically arising from the outdated concept of the disease, is the difficulty of using etiotropic agents as leading methods of treatment. This is why both WHO experts [14] and other specialists [42-44] see a way out of the current situation in the development and release of new, more active drugs. The paradox lies in the strengthening of biologically active antimicrobial therapy, the results of long-term use of which are discussed in this case. And again, no one expresses concern about the consequences that such a leap in antimicrobial pharmacology may lead to.

Finally, the established unshakable idea of the nature of AP has determined the principles of providing additional and auxiliary care, among which counterproductive methods are used. Considering the pathogen as the main cause of AP, you will not be able to find in

expert opinions an explanation for such an obvious fact as the preservation of the clinical foundations and signs of the disease regardless of the etiology options. At the same time, acute inflammations of different localizations, but with the participation of one pathogen, give completely incomparable diseases, don't they? For example, AP, meningitis and otitis media caused by one of the pneumococcal strains have completely different clinical symptoms, right?

Focusing efforts on diagnosing the pathogen and suppressing it emphasizes the focus on the hegemony of the disease etiology, but ignores its pathogenesis, the unique mechanisms of which determine the clinical features and development of signs that underlie the observation of patients and are the goal of correction with the help of auxiliary measures. However, such an etiological approach to assessing the severity of patients' condition does not attach due importance to the difference in the pathogenesis of various diseases. It is necessary to pay attention to the fact that among all inflammatory processes, AP is the only nosology that occurs in the pulmonary circulation. Such localization of inflammation with its vascular reaction and classical stages of development has far-reaching consequences, which, oddly enough, remain unaccounted for many years.

The strangeness of the position in relation to the inevitable consequences of the localization of AP is that modern medicine knows the diametrically opposite difference in arterial pressure between the two circles of blood circulation, in which normal values in the pulmonary artery are approximately 8 times lower than in the systemic vessels [45,46]. Such dissonance is ensured by the parity in the work of the two halves of the heart and, being one of the most important vital equilibria, is autonomously maintained by the unloading reflex with the participation of baroreceptors of the pulmonary circulation [47,48]. In the event of a trigger in the pulmonary vessels and a sudden increase in arterial pressure in them, the adaptive reaction is a decrease in vascular tone in the periphery and unloading of the pulmonary circulation. The sudden development of such a mechanism leaves the body no chance for adaptation. The most typical example of such situations are unforeseen critical situations up to a fatal outcome in pulmonary embolism [49-52].

With the aggressive development of AP, the body's response is characterized by an identical mechanism, the clinical manifestations of which correspond to the picture of pulmonary shock [9,35]. However, the unified scheme for recognizing septic conditions, which has been generally accepted in recent decades, including in patients with AP [53], leads to an erroneous diagnosis of "sepsis." As a result, an absolute predominance of patients with AP is observed, which already exceeds half of the patients with sepsis. The most dramatic aspect of this situation is the standard therapy of all patients with sepsis and septic shock, regardless of the localization of inflammation. The insignificance of the latter factor is recently reflected in the lack of information about the underlying disease of these patients [54,55]. In the latter case, intravenous infusions, instead of unloading the pulmonary vessels, achieve the opposite effect in patients with AP. The negative effect of such therapy has been proven by objective arguments and comparative results [9,35].

Conclusion

The above materials from recent years demonstrate a scientific colorblindness in the approach to the problem of AP. The persistent search for a solution to an increasingly complex situation using the long-outdated microbial concept of disease defies logical explanation. The author's successful experience in this area of medicine several decades ago pointed to the need to rely on the classical foundations of biomedical science when searching for an optimal solution strategy. The narrow interpretation of the essence of the AP problem through the leading role of the "antibiotic versus microbe" tandem is a thing of the past, and the mental perception of this pathology has long required a decisive and fundamental rethink, as it remains the main obstacle to success.

Funding Support

This manuscript is a full initiative of the author and does not have any funding.

Conflict of Interest

The author states that he has no conflict of interest.

Bibliography

1. Podolsky SH. "The changing fate of pneumonia as a public health concern in 20th-century America and beyond". *American Journal of Public Health* 95.12 (2005): 2144-2154.

2. Abraham EP and Chain E. "An enzyme from bacteria able to destroy penicillin, 1940". *Reviews of Infectious Diseases* 10.4 (1988): 677-678.

3. Rammelkamp T. "Resistance of *Staphylococcus aureus* to the action of penicillin". *Experimental Biology and Medicine* 51.3 (1942): 386-389.

4. Avery OT., *et al*. "Acute lobar pneumonia: prevention and serum treatment". Monographs of the Rockefeller Institute for Medical Research. Rockefeller Institute for Medical Research, New York (1917).

5. Cole RI. "Acute pulmonary infections". De La Mar Lectures. Williams & Wilkins, Baltimore (1927-1928).

6. Sutliff WD and Finland M. "The significance of the newly classified types of pneumococci in disease: types IV to XX inclusive". *Journal of the American Medical Association* 101.17 (1933): 1289-1295.

7. Heffron R. "Pneumonia, with special reference to pneumococcus lobar pneumonia". Cambridge: Harvard University Press (1939).

8. Small JT. "A short history of the pneumococcus with special reference to lobar pneumonia". *Edinburgh Medical Journal* 55.3 (1948): 129-141.

9. Klepikov I. "Acute pneumonia and its purulent and destructive complications in children in the midst of a major industrial centre of Western Siberia". Dissertation for the degree of Doctor of Medical Science. Leningrad, USSR (1989).

10. Aminov RI. "A brief history of the antibiotic era: lessons learned and challenges for the future". *Frontiers in Microbiology* 1 (2010): 134.

11. Fleming A. "The Nobel Prize in Physiology or Medicine 1945 - Penicillin: Nobel Lecture". NobelPrize.org. (1945).

12. "MRSA History Timeline: The First Half-Century, 1959-2009". The University of Chicago Medical Center (2010).

13. WHO. "Global antimicrobial resistance and use surveillance system (GLASS) report: 2022" (2022).

14. WHO. "Antimicrobial resistance" (2021).

15. Gadsby NJ and Musher DM. "The microbial etiology of community-acquired pneumonia in adults: from classical bacteriology to host transcriptional signatures". *Clinical Microbiology Reviews* 35.4 (2022): e00015-22.

16. Shoar S and Musher DM. "Etiology of community-acquired pneumonia in adults: a systematic review". *Pneumonia* 12 (2020): 11.

17. Carlos P., *et al*. "CURB-65 and long-term mortality of community-acquired pneumonia: a retrospective study on hospitalized patients". *Cureus* 15.3 (2023): e36052.

18. Palomeque A., *et al*. "A review of the value of point-of-care testing for community-acquired pneumonia". *Expert Review of Molecular Diagnostics* 24.8 (2024): 729-742.

19. Metlay JP., *et al*. "Diagnosis and treatment of adults with community-acquired pneumonia. An official clinical practice guideline of the American thoracic society and infectious diseases society of America". *American Journal of Respiratory and Critical Care Medicine* 200.7 (2019): e45-e67.

20. Martin-Loeches I., *et al*. "ERS/ESICM/ESCMID/ALAT guidelines for the management of severe community-acquired pneumonia". *Intensive Care Medicine* 49.6 (2023): 615-632.

21. Huttner BD., *et al*. "COVID-19: don't neglect antimicrobial stewardship principles!". *Clinical Microbiology and Infection* 26.7 (2020): 808-810.

22. Beović B., *et al*. "Antibiotic use in patients with COVID-19: a 'snapshot' Infectious Diseases International Research Initiative (ID-IRI) survey". *Journal of Antimicrobial Chemotherapy* 75.11 (2020): 3386-3390.

23. Rawson TM., *et al*. "Bacterial and fungal coinfection in individuals with coronavirus: a rapid review to support covid-19 antimicrobial prescribing". *Clinical Infectious Diseases* 71.9 (2020): 2459-2468.

24. LO Gostin and GK Gronvall. "The origins of covid-19 - why it matters (and why it doesn't)". *New England Journal of Medicine* 388.25 (2023): 2305-2308.

25. Monto AS. "Coronaviruses". In Evans AS (ed.) Viral Infections of Humans: Epidemiology and Control. Springer US (1984): 151-165.

26. Visseaux B., *et al*. "Prevalence of respiratory viruses among adults, by season, age, respiratory tract region and type of medical unit in Paris, France, from 2011 to 2016". *PLoS One* 12.7 (2017): e0180888.

27. Shah MM., *et al*. "Seasonality of common human coronaviruses, United States, 2014-2021". *Emerging Infectious Diseases* 28.10 (2022): 1970-1976.

28. Oran DP and Topol EJ. "Prevalence of asymptomatic SARS-CoV-2 infection: a narrative review". *Annals of Internal Medicine* 173.5 (2020): 362-367.

29. Wu Z and McGoogan JM. "Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: Summary of a report of 72 314 cases from the Chinese center for disease control and prevention". *Journal of the American Medical Association* 323.13 (2020): 1239-1242.

30. Murad M and Martin JC. "Pathological inflammation in patients with COVID-19: a key role for monocytes and macrophages". *Nature Reviews Immunology* 20.6 (2020): 355-362.

31. Zhou B., *et al*. "COVID-19 pathogenesis, prognostic factors, and treatment strategy: Urgent recommendations". *Journal of Medical Virology* 93.5 (2021): 2694-2704.

32. Rabin EE., *et al*. "Clinical significance of culture-negative, PCR-positive bronchoalveolar lavage results in severe pneumonia". *ERJ Open Research* 9.6 (2023): 00343-2023.

33. Pickens CI., *et al*. "Microbiology of severe community-acquired pneumonia and the role of rapid molecular techniques". *Seminars in Respiratory and Critical Care Medicine* 45.2 (2024): 158-168.

34. Maricar Malinis., *et al*. "Community-acquired pneumonia: a US perspective on the guideline gap". *Journal of Antimicrobial Chemotherapy* 79.5 (2024): 959-961.

35. Klepikov. "Myths, legends and real facts about acute lung inflammation". Cambridge Scholars Publishing. Pages: 334. ISBN: 1-0364-0293-2 ISBN13: 978-1-0364-0293-8 (2024).

36. Sakamoto Y., *et al*. "In-hospital mortality associated with community-acquired pneumonia due to methicillin-resistant *Staphylococcus aureus*: a matched-pair cohort study". *BMC Pulmonary Medicine* 21.1 (2021): 345.

37. Ding H., *et al*. "Incidence of drug-resistant pathogens in community-acquired pneumonia at a safety net hospital". *Microbiology Spectrum* 12.8 (2024): e00792-24.

38. Albrich WC and Harbarth S. "Health-care workers: Source, vector, or victim of MRSA?" *Lancet Infectious Diseases* 8.5 (2008): 289-301.

39. Aubry-Damon H., *et al*. "Antimicrobial resistance in commensal flora of pig farmers". *Emerging Infectious Diseases* 10.5 (2004): 873-879.

40. Graveland H., *et al*. "Methicillin resistant *Staphylococcus aureus* ST398 in veal calf farming: Human MRSA carriage related with animal antimicrobial usage and farm hygiene". *PLoS ONE* 5.6 (2010): e10990.

41. C Liu and M Holubar. "Should a MRSA nasal swab guide empiric antibiotic treatment?" *NEJM Evidence* 1.12 (2022): EVIDccon2200124.

42. Serwecińska Liliana. "Antimicrobials and antibiotic-resistant bacteria: a risk to the environment and to public health". *Water* 12.12 (2020): 3313.

43. World Health Organization. "Antimicrobial resistance" (2023).

44. Madhavi Thara. "Antibiotic Stewardship". *Medicon Medical Sciences* 6.3 (2024): 01-02.

45. Colledge NR., *et al*. "Davidson's Principles and Practice of Medicine (21st edition)". Edinburgh: Churchill Livingstone/Elsevier. ISBN 978-0-7020-3084-0 (2010).

46. "Normal Hemodynamic Parameters - Adult". Edwards Lifesciences LLC (2010).

47. Schwiegk H. "Der Lungenentlastungsreflex". *Pflügers Archiv* 236 (1935): 206-219.

48. Olivia Vynn. "Cardiology secrets". Chapter 41. Adair Edition: 2, illustrated Published by Elsevier Health Sciences, 2001 ISBN 1-56053-420-6, 978-1-56053-420- (2001): 210.

49. M Stein and SE Levy. "Reflex and humoral responses to pulmonary embolism". *Progress in Cardiovascular Diseases* 17.3 (1974): 167-174.

50. Mohanty PK., *et al*. "Reflex effects of prolonged cardiopulmonary baroreceptor unloading in humans". *American Journal of Physiology* 254.2 (1988): R320-R324.

51. Fu Q., *et al*. "Evidence for unloading arterial baroreceptors during low levels of lower body negative pressure in humans". *American Journal of Physiology-Heart and Circulatory Physiology* 296.2 (2008): H480-H488.

52. Busch S., *et al*. "Evidence for a physiological role of pulmonary arterial baroreceptors in sympathetic neural activation in healthy humans". *Journal of Physiology* 598.5 (2020): 955-965.

53. Singer M., *et al*. "The third international consensus definitions for sepsis and septic shock (Sepsis-3)". *Journal of the American Medical Association* 315.8 (2016): 801-810.

54. Self WH., *et al*. "Liberal versus restrictive intravenous fluid therapy for early septic shock: rationale for a randomized trial". *Annals of Emergency Medicine* 72.4 (2018): 457-466.

55. Shapiro NI., *et al*. "Early restrictive or liberal fluid management for sepsis-induced hypotension". *New England Journal of Medicine* 388.6 (2023): 499-510.

Volume 14 Issue 12 December 2025