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## Review Article

# The main reasons why emergency care for acute pneumonia does not help much

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## Abstract

Despite the successful solution of many issues and impressive achievements in various fields, modern medicine is far from successful in providing effective care to patients with acute nonspecific inflammation of the lung tissue. This pathology, known since ancient times as acute pneumonia, has gradually become an important global problem in recent decades. Modern ideas about the nature of the disease and the basic principles of its treatment were formed under the didactic influence of antibiotics and are of a narrowly targeted etiotropic nature. First aid and emergency care methods for this category of patients do not provide the immediate expected effect, and arguments in favor of their use ignore the pathogenetic mechanisms of the disease, which leads to side effects. A radical revision of professional views on this problem, taking into account the unique pathogenesis of inflammatory processes in the pulmonary circulation, is an inevitable step in solving this problem.

## Introduction

One of the axioms of medical practice is the provision of timely medical care to patients. The fulfillment of this task is especially important in acute diseases when a sudden pathological process is characterized by a rapid deterioration in the condition of patients and not only the time of first aid but also its nature determines the further course of events and the final result. Practitioners and many of their patients know from their own experience how important this rule is. Therefore, the set of measures that are provided for acute diseases as first aid measures should contain actions that can slow down the dynamics of an impending catastrophe and bring noticeable relief to most patients with a certain nosology. Another old rule of medicine can serve as a control for assessing the adequacy of emergency care, which tells us that if therapy does not bring positive results, then it does not correspond to the nature of the disease.

These principles of attitude to emergency medical care and its consequences are the result of centuries of practice, which

have turned into natural unwritten laws that habitually and naturally determine our requirements for initial therapeutic measures. Unfortunately, today, in the 21<sup>st</sup> century, we can still observe situations where for many years unsuccessful attempts by modern medicine to solve certain problems can continue, ignoring the obvious discrepancy between the efforts made and the results obtained. A striking example of such inconsistencies is the problem of acute nonspecific inflammation in the lungs (ANSIL). The main nosology of such diseases is Acute Pneumonia (AP), which in recent years has appeared under various terms reflecting the currently dominant ideas about the essence of ANSIL.

### Imperfections of modern principles of providing first and emergency aid for AP

For at least eight decades, antibiotics have been the main treatment for AP, as well as many other inflammatory processes. At the same time, representatives of official medicine have been well aware since the appearance of these drugs that their effect is only to neutralize certain types of pathogenic



microorganisms but does not directly affect the mechanisms of the advanced inflammatory process that arose with their participation. Long before the discovery of antibiotics, it was reliably known that the clinic of each disease depends on the localization of the focus of inflammation and dysfunction of a particular affected organ. However, these long-proven features of inflammatory processes were not an obstacle for a long period of treatment of patients with AP on the principle of «antibiotics alone». In other words, the use of antimicrobial therapy as an etiotropic treatment method has completely replaced any types of pathogenetic care that were empirically tested even before Galen described the classic fifth sign of inflammation, «loss of function,» about two millennia ago.

In recent years, with the constant growth of viral forms of pneumonia, no one has attempted a radical revision of the concept of this disease. This creates a very real impression that representatives of modern medicine cannot imagine the development and features of AP without the main role of the pathogen, and the treatment of such patients without antibiotics. Doubts about such statements were finally dispelled during the SARS-CoV-2 pandemic. Patients with COVID-19 pneumonia, when bacterial coinfection was detected within ten percent, received antibiotic treatment in 70% - 80% of cases or more [1-5]. At the peak of the pandemic, instead of a logically consistent search for optimal solutions, the persistent continuation of efforts to develop bacterial methods for rapid diagnosis of AP is striking [6,7], and the search for the most optimal choice of antibiotics [8,9].

The latest data are a vivid example of the profound negative didactic effect of antibiotics on the professional worldview on the problem under discussion. For many years, both theoretical and practical approaches to the treatment of patients with AP have been reduced to a narrow etiotropic solution to the problem. The latter fact, including the period of use of therapy based on the principle of “antibiotics alone”, means that this type of drug treatment was the main type of medical care, while simultaneously performing the function of first aid. A logical question that any specialist in this problem should think about concerns the speed and mechanism of action of such emergency care in the context of an acute and rapidly progressing inflammatory process. Repeated attempts to achieve a striking effect from the earliest possible administration of antibiotics were unsuccessful, but the principle of achieving the expected result using this technique reflected the desire to use such therapy as an emergency, from which it was expected to obtain a very real effect.

As is known, antibiotics can only suppress the bacterial pathogen as one of the factors supporting the mechanisms of the inflammatory process. However, over a long period of use of antibiotics in medical circles, there was an opinion that a rational choice of antibiotics should lead to a significant improvement in the condition of patients and normalization of functional changes in the respiratory and cardiovascular systems. For example, the extended forum of two leading US societies on the problem of thoracic and infectious diseases, recognizing the lack of influence of bacteriological diagnosis on

treatment results, makes recommendations on the prescription of antibiotics to patients with community-acquired pneumonia for a period of at least 5 days. Experts consider the criterion for the duration of this therapy, which forms the basis of treatment, to be the clinical stabilization of the patient's condition and the normalization of pulmonary ventilation, gas exchange, cardiac activity, and blood circulation [10].

As follows from the materials in the given example, antibiotics are considered not only as antimicrobial therapy but also as a means of normalizing functional disorders. At the same time, the clarity of recommendations for the use of some antimicrobial drugs raises natural doubts against the backdrop of a clear recognition of such an important fact as the inability to accurately determine the etiology of AP, as well as the increasing role of viruses among the causative agents of the disease. How, under such unclear etiological conditions, one can expect the desired result from the “blind” prescription of antibiotics remains a mystery. At the same time, recommendations for the empirical selection of individual drugs taking into account the real situation in this section of the problem do not go beyond the declaration of assumptions. For example, today it can be stated that the differential diagnosis of not only bacterial pneumonia depending on the pathogen remains an unsolved problem, but also the separation of bacterial and viral forms of inflammation does not achieve its goals [11,12], including studies at the genetic level [13,14]. It should be added that, despite the increasing change of leaders among the pathogens of AP and the expansion of their list, the clinical picture of this nosology remains relatively constant.

In this last connection, it is puzzling that, despite numerous inconsistencies between theoretical premises and specific results, persistent attempts to divide pneumonia by etiology continue. Recent efforts, from my point of view, are due to the dominance of the established stereotype of “antibiotic versus microbe” and the desire to maintain the same therapeutic principles. The wide dissemination of such a worldview on this problem leaves without due attention such important circumstances as the stereotyping of the AP clinic, regardless of etiology, and its difference from inflammatory processes in other localizations. Meanwhile, all of the above circumstances are due to such a classic sign of inflammation as dysfunction of the affected organ, which is currently, unfortunately, considered in a sharply reduced partial version.

The assessment of the effective action of antibiotics, based on the restoration of functional disorders, was unexpectedly and without any justification transferred to patients with COVID-19 pneumonia, in whom these drugs lose the meaning of their purpose. The authors of the study focused on the duration of hypoxemia and the need for respiratory support as a criterion for the effect of antibiotics in such patients [15,16]. It would be useful for supporters of this point of view to analyze the statistics of patients of this profile in recent years. In this case, we are talking about a complete discrepancy between this statement and the results of treatment of patients with COVID-19 pneumonia during the pandemic. Patients with acute coronavirus inflammation of the lung tissue were deprived of

basic etiotropic treatment in accordance with modern standards. However, as statistics show, this undoubted fact did not affect the final results of this group of patients, whose indicators turned out to be comparable to those of bacterial forms of the disease receiving etiotropic treatment [17]. This didactic lesson of the pandemic should be firmly learned in further solving the whole problem, as it allows us to understand how the hypnotic effect of antibiotics has distorted professional ideas in this field of medicine. Therefore, we should not support self-deception and attribute actions to antibiotics that they do not possess.

In recent years, many forums of specialists on the problem of AP have begun to adopt recommendations on the duration of a course of antibiotics, depending on the presence of aggravating circumstances, ranging from 5 to 7-8 days [10,18,19]. Reducing the duration of antibiotic use in patients with AP is consistent with clinical studies that show that the duration of antimicrobial treatment does not affect the results [20,21]. At the same time, many experts completely allow a reduction in the initial dose if clinical stability is observed in the first 48 hours - 72 hours after the start of treatment [10]. However, the main feature of this approach to treatment is not what dosage of the antibiotic and the duration of its administration is used in such situations. It is enough to recall once again about patients with viral pneumonia without coinfection, who, as a rule, are deprived of etiotropic care, and the use of antiviral drugs can give a positive result in the first 48 hours after infection [10], that is until the virus has penetrated inside the cell. When starting etiotropic therapy as the main method of treatment, medical personnel have high hopes for the success of this particular therapy. This means that patients will be monitored over the coming days until their condition stabilizes. And is this the first and emergency care?

However, the development of the AP does not always allow us to continue a purely observational position. In the case of aggressive development of the disease, the body does not have time to adapt its systems to new conditions and a situation arises that requires additional help. Such a scenario of the continuation of the disease is still considered in professional circles as a result of the action of virulent microflora, despite such refuting facts as the difference in clinical manifestations of AP in conditions of identical etiology and, conversely, an indistinguishable picture of the disease in the presence of different pathogens. In such cases, the fight against the infectious factor of the disease continues without taking into account the uniqueness of the pathogenesis of pulmonary processes. With the development of AP, diagnosis, and treatment of the disease do not take into account such a feature of the lung tissue as the inextricable connection and inverse proportion between the pulmonary and systemic circulation. Primary damage to the pulmonary vessels, unlike other localizations of inflammation, disrupts blood flow in the pulmonary circulation, which affects the overall blood circulation in the body.

Contrary to the classical mechanisms of pathogenesis, modern medicine, focusing on the presumed cause of the severity of the disease, uses general therapeutic methods of

treatment, which may be contraindicated in patients with AP. The main problem that builds a further chain of pathogenetic mechanisms and prevents the normal functioning of this vital system is the overload of the vessels of the small circulatory circle as a result of their reflex spasm [22-24]. The use of such a widely demanded technique as infusion therapy in patients with AP in these conditions is based on assumptions that have no reasoned evidence, and therefore, instead of the expected benefit, this procedure, on the contrary, has a stimulating effect on the pathological process [22]. Performing the function of additional care, intravenous infusions, especially in the early stages of the disease, turn into a kind of negative first aid option and are one of the main causes of deterioration of patients' condition during inpatient treatment. This feature of infusion therapy in patients with AP has been proven not only by comparing clinical data but also by experimental studies [22].

In this context, there is no need to return to the description of the features of the pathogenesis of AP and objective evidence of the effectiveness of pathogenetic care, since by now these materials have been repeatedly described by the author and published in the public domain. At the same time, it is necessary to pay attention to the fact that modern medicine still ignores the use of techniques that contribute to the rapid relief of the condition of patients with AP. Etiotropic drugs, which are presented as emergency care for this category of patients, do not correspond to their prescribed role. With this type of help, even in the case of a favorable impression of therapy with a narrow etiotropic orientation, the suppression of the mechanisms of the inflammatory process and the elimination of its consequences completely falls on the patient's body.

Adherence to the previous strategy, in which the main role is assigned to the causative agent of AP, and persistent concentration of efforts in attempts to achieve success with the help of etiotropic drugs do not bring the planned results, which, contrary to expectations, continue to decrease [9,20,21]. The number of patients with AP requiring hospitalization in Intensive Care Units (ICU) in recent years has been characterized by gradual and stable growth [25], an increase in the number of complicated forms of the disease, and the mortality rate [26,27]. Authors of publications usually try to present positive rather than negative materials about their professional activities, however, the results of treatment of AP, especially with a rapid onset of the disease, are characterized by negative statistics. For example, up to 58% of patients treated with this disease in the ICU are referred there immediately after diagnosis due to a more threatening onset of the process [28]. Up to 25% of those who receive treatment in general departments are eventually referred there due to deterioration, often in the first 2 days [28,29]. The latest data are an additional characteristic of the above-mentioned modern AP therapy, which does not allow us to talk about its adequacy.

Attention should be paid to the situations in the condition of patients, which determine the need for their referral to ICU. The most important factors for placing patients in ICU are the vital provision of artificial ventilation and vasopressor support,





as well as the need for Extracorporeal Membrane Oxygenation (ECMO) and dialysis [25,29-33]. Unfortunately, the development of these situations indicates missed opportunities in the initial period of the disease, when the inflammatory process has not yet reached the stage of deep disorders and it would be possible to slow down the course of the disease and prevent its progression using emergency pathogenetic methods. The fact that treatment during the development of complications has a lower chance of success is evidenced by data on the mortality of patients with AP after their intubation and artificial ventilation or after ECMO, which is 2-3 times higher than this figure in patients who did not need such treatment [33-35].

It remains to express regret once again that the modern proposals of specialists in this field of medicine to get out of the long-standing situation, which was clearly manifested in providing care to patients with COVID-19 pneumonia during the pandemic, do not leave any hope for a speedy solution to the deepening problem. What positive results can be expected by adhering to the tactics of providing oxygen to patients with AP and constant monitoring to select the appropriate time if there is a need for their intubation [36]? Or, for example, what drastic changes in the results of treatment of this contingent of patients can be expected from the fulfillment of suddenly appeared calls for an increase in the production of artificial lung ventilation devices [37-41]?

The decisive role of the AP causative agent continues to dominate the professional perception of this disease, and the hypnotic influence of this deeply internalized stamp continues to manifest itself in all initiatives and proposals to solve the affected problem. For example, the classification of pneumonia according to the place and conditions of their occurrence (community-acquired, nosocomial, and others) was conceived in order to divide the disease depending on the pathogen and improve the results of etiotropic therapy. No one has given reasoned conclusions about why this innovation was not successful, but unsuccessful attempts to find differences in the etiology of these forms of the disease continue to this day [26].

The reasons for the fiasco of many years of attempts to learn how to determine inflammation of lung tissue by microbiological criteria remain an unrealized desire. Despite the absence of any noticeable and stable achievements in the field of early diagnosis of AP pathogens and the revival of the initial effectiveness of antibiotics, research in this direction is actively continuing to the present time. Moreover, the continuation of traditions in this section of medicine, which every year receives more and more facts refuting them, continues with the same intensity. Evidence of blind adherence to the usual trend is the isolation in recent years of another type of pneumonia acquired in the intensive care unit [42,43]. Once again, attempts to identify pathogens of a new form do not bring concrete results, and conclusions end with assumptions that "have yet to be clarified" [27].

Today, more than ever before, it is becoming increasingly clear that the era of antibiotic use is not just ending, but also marks the appearance of numerous and persistent side effects. Not all the consequences of using these biologically

active drugs are realized in the professional environment and are taken into account. Only a decrease in the effectiveness of these drugs as a result of the development of resistance of microorganisms causes concern among specialists as a result of the loss of familiar remedies. However, such an obvious fact as the change of the most frequent pathogens of AP under the action of antimicrobial therapy with a radical change in the etiology of the disease and the displacement of antibiotics from the arsenal of popular drugs is a more serious consequence of the use of these drugs than the resistance of microflora. Wildlife, in response to interference in its life processes and established relationships, starting from the early stages of antibiotic use, demonstrates to us the results of its protection. Initially, resistant forms of bacteria appeared, which reduced the effectiveness of antibiotics. The persistent continuation of this therapy has led to a change in the pathogens of nonspecific forms of inflammation, where the most striking example is AP. The latter phenomenon has become particularly noticeable in recent years, which has led to a decrease in the indications for the prescription of antimicrobial drugs, but their use has not decreased.

However, an even more serious and difficult-to-correct consequence of long-term antibacterial therapy is its profound and sustained didactic effect on the professional worldview. Attempts to solve the problem of AP are the most obvious example of the mental effects of antibiotics. The loss of antimicrobial drugs of their previous purpose and effectiveness required the widespread use of additional treatment methods, but their effect in the context of the uniqueness of the pathogenesis of AP showed the depth and persistence of prevailing misconceptions. Generations of doctors have long been brought up in a spirit of reverence for the superiority and indispensability of antibiotics. Disregarding the classical materials of medical science, as well as inattention to facts that refute the logic of the efforts undertaken, eventually formed a narrowly focused point of view. The published proposals and discussion materials on solving the problem under discussion give the impression that some specialists do not see any prospects for further assistance to patients with AP without the use of antibiotics. Calls for the creation of a strategic system for the rational use of antibiotics are at least 75 years - 80 years late, and their meaning once again shows that the authors of such proposals, including WHO experts, do not see any other solutions to the problem other than further improvement of antimicrobials [44-47]. That is, we are talking about the revival of the cause that gave rise to this problem.

The above-mentioned inconsistencies between facts and scientific materials, on the one hand, as well as between the existing strategy and tactics for solving the problem of AP, on the other, led to the fact that this category of patients found themselves without proper pathogenetic care, including primary and urgent measures. Waiting for the results of first aid, which continues to be provided with etiotropic drugs, stretches for at least 2 - 3 days, and in most cases, it is 5 - 7 days. In conditions of acute rapidly progressive inflammation, these days in the initial period of the disease literally determine the further fate of patients. With the help of timely



pathogenetic treatment in the first 5 - 7 days, it is possible to achieve complete elimination of the focus of inflammation in the lung tissue, and such results may not be the exception, but the rule [22]. However, the generally accepted standard of expectation of an antimicrobial effect has been considered the main goal for many years and remains the first frontier, the achievement of which is considered a success of treatment. In connection with the latter, it is necessary to mention the phenomenon of the so-called "sterile" empyema of the pleura and other purulent complications observed for many years, which have not been given a reasonable explanation. In such cases, antibiotics ideally achieve their goal, but they do not save from the progression of the disease and severe complications, do they? Think about why this is happening.

## Conclusion

Incorrect interpretations of the essence of the AP problem are not only related to the leading role of antibiotics. The need for additional assistance, which is growing every year, is not perceived as a treatment that can aggravate the development of the main process. Therefore, continuing the fight against the pathogen and not delving into the nuances of the pathogenesis of AP, modern medicine does not notice the adverse side effects of general therapeutic techniques. A large number and increase in adverse outcomes are usually explained by an aging population and an increase in the number of elderly patients, but no one has provided a reasoned explanation of why young people without concomitant diseases literally "burn out" from AP. In order to understand why such transformations occur and stop blaming pathogenic microorganisms for all the troubles, which, despite their differences, continue to reproduce the same type of clinics, it is necessary first of all to conduct a radical revision of their own views on the problem under discussion. Then, in particular, the need for pathogenetically sound first aid will become a logically necessary action.

## References

- Huttner BD, Catho G, Pano-Pardo JR, Pulcini C, Schouten J. COVID-19: don't neglect antimicrobial stewardship principles! *Clin Microbiol Infect.* 2020 Jul; 26(7):808-810. doi: 10.1016/j.cmi.2020.04.024. Epub 2020 Apr 30. PMID: 32360446; PMCID: PMC7190532.
- Beović B, Doušak M, Ferreira-Coimbra J, Nadrah K, Rubulotta F, Belliato M, Berger-Estilita J, Ayoade F, Rello J, Erdem H. Antibiotic use in patients with COVID-19: a 'snapshot' Infectious Diseases International Research Initiative (ID-IRI) survey. *J Antimicrob Chemother.* 2020 Nov 1; 75(11):3386-3390. doi: 10.1093/jac/dkaa326. PMID: 32766706; PMCID: PMC7454563.
- Rawson TM, Moore LSP, Zhu N. Bacterial and fungal co-infection in individuals with coronavirus: A rapid review to support COVID-19 antimicrobial prescribing [published online ahead of print, 2020 May 2]. *Clin Infect Dis.* 2020; 530. doi:10.1093/cid/ciaa530
- Lipman M, Chambers RC, Singer M, Brown JS. SARS-CoV-2 pandemic: clinical picture of COVID-19 and implications for research. *Thorax.* 2020 Aug; 75(8):614-616. doi: 10.1136/thoraxjnl-2020-215024. Epub 2020 May 27. PMID: 32461230.
- Puzniak L, Finelli L, Yu KC, Bauer KA, Moise P, De Anda C, Vankeepuram L, Sepassi A, Gupta V. A multicenter analysis of the clinical microbiology and antimicrobial usage in hospitalized patients in the US with or without COVID-19. *BMC Infect Dis.* 2021 Feb 27; 21(1):227. doi: 10.1186/s12879-021-05877-3. PMID: 33639862; PMCID: PMC7910773.

- Kyriazopoulou E, Karageorgos A, Liaskou-Antoniou L, Koufargyris P, Safarika A, Damoraki G, Lekakis V, Saridakis M, Adamis G, Giamarellos-Bourboulis EJ. BioFire® FilmArray® Pneumonia Panel for Severe Lower Respiratory Tract Infections: Subgroup Analysis of a Randomized Clinical Trial. *Infect Dis Ther.* 2021 Sep; 10(3):1437-1449. doi: 10.1007/s40121-021-00459-x. Epub 2021 Jun 13. PMID: 34120316; PMCID: PMC8197784.
- Enne VI, Aydin A, Baldan R, Owen DR, Richardson H, Ricciardi F, Russell C, Nomamiukor-Ikeji BO, Swart AM, High J, Colles A, Barber J, Gant V, Livermore DM, O'Grady J; INHALE WP1 Study Group. Multicentre evaluation of two multiplex PCR platforms for the rapid microbiological investigation of nosocomial pneumonia in UK ICUs: the INHALE WP1 study. *Thorax.* 2022 Dec; 77(12):1220-1228. doi: 10.1136/thoraxjnl-2021-216990. Epub 2022 Jan 13. PMID: 35027473.
- Montes-Andujar L, Tinoco E, Baez-Pravia O, Martin-Saborido C, Blanco-Schweizer P, Segura C, Prol Silva E, Reyes V, Rodriguez Cobo A, Zurdo C, Angel V, Varona O, Valero J, Suarez Del Villar R, Ortiz G, Villanueva J, Menéndez J, Blanco J, Torres A, Cardinal-Fernández PA. Empiric antibiotics for community-acquired pneumonia in adult patients: a systematic review and a network meta-analysis. *Thorax.* 2021 Oct; 76(10):1020-1031. doi: 10.1136/thoraxjnl-2019-214054. Epub 2021 Mar 15. PMID: 33723019.
- Cillóniz C, Torres A, Niederman MS. Management of pneumonia in critically ill patients. *BMJ.* 2021 Dec 6; 375:e065871. doi: 10.1136/bmj-2021-065871. PMID: 34872910.
- Metlay JP, Waterer GW, Long AC, Anzueto A, Brozek J, Crothers K, Cooley LA, Dean NC, Fine MJ, Flanders SA, Griffin MR, Metersky ML, Musher DM, Restrepo MI, Whitney CG. 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. *Am J Respir Crit Care Med.* 2019 Oct 1; 200(7):e45-e67. doi: 10.1164/rccm.201908-1581ST. PMID: 31573350; PMCID: PMC6812437.
- Heneghan C, Plueddemann A, Mahtani KR. Differentiating viral from bacterial pneumonia. April 8, 2020. The Centre for Evidence-Based Medicine. Evidence Service to support the COVID-19 response. University of Oxford. 2020. <https://www.cebm.net/covid-19/differentiating-viral-from-bacterial-pneumonia>.
- Lhomme C, Garot D, Grammatico-Guillon L, Jourdainnaud C, Asfar P, Faisy C, Muller G, Barker KA, Mercier E, Robert S, Lanotte P, Goudeau A, Blasco H, Guillon A. Predicting the microbial cause of community-acquired pneumonia: can physicians or a data-driven method differentiate viral from bacterial pneumonia at patient presentation? *BMC Pulm Med.* 2020 Mar 6; 20(1):62. doi: 10.1186/s12890-020-1089-y. PMID: 32143620; PMCID: PMC7060632.
- Kamat IS, Ramachandran V, Eswaran H, Guffey D, Musher DM. Procalcitonin to Distinguish Viral from Bacterial Pneumonia: A Systematic Review and Meta-analysis. *Clin Infect Dis.* 2020 Jan 16; 70(3):538-542. doi: 10.1093/cid/ciz545. PMID: 31241140.
- Suarez NM, Bunsow E, Falsey AR, Walsh EE, Mejias A, Ramilo O. Superiority of transcriptional profiling over procalcitonin for distinguishing bacterial from viral lower respiratory tract infections in hospitalized adults. *J Infect Dis.* 2015 Jul 15; 212(2):213-22. doi: 10.1093/infdis/jiv047. Epub 2015 Jan 29. Erratum in: *J Infect Dis.* 2015 Dec 15; 212(12):2023. PMID: 25637350; PMCID: PMC4565998.
- Tsalik EL, Henao R, Nichols M, Burke T, Ko ER, McClain MT, Hudson LL, Mazur A, Freeman DH, Veldman T, Langley RJ, Quackenbush EB, Glickman SW, Cairns CB, Jaehne AK, Rivers EP, Otero RM, Zaas AK, Kingsmore SF, Lucas J, Fowler VG Jr, Carin L, Ginsburg GS, Woods CW. Host gene expression classifiers diagnose acute respiratory illness etiology. *Sci Transl Med.* 2016 Jan 20; 8(322):322ra11. doi: 10.1126/scitranslmed.aad6873. PMID: 26791949; PMCID: PMC4905578.
- O'Kelly B, Cronin C, Connellan D, Griffin S, Connolly SP, McGrath J, Cotter AG, McGinty T, Muldoon EG, Sheehan G, Cullen W, Doran P, McHugh T, Vidal L, Avramovic G, Lambert JS. Antibiotic prescribing patterns in patients hospitalized with COVID-19: lessons from the first wave. *JAC Antimicrob Resist.* 2021 Jun 30; 3(2):dlab085. doi: 10.1093/jacamr/dlab085. PMID: 34223144; PMCID: PMC8242139.



17. Klepikov I. As Evidenced by the Statistics of the Pandemic. *J Neo Res Pedia Care*. 2020; 3(3): 180032.
18. Kalil AC, Metersky ML, Klompas M, Muscedere J, Sweeney DA, Palmer LB, Napolitano LM, O'Grady NP, Bartlett JG, Carratalà J, El Solh AA, Ewig S, Fey PD, File TM Jr, Restrepo MI, Roberts JA, Waterer GW, Cruse P, Knight SL, Brozek JL. Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. *Clin Infect Dis*. 2016 Sep 1; 63(5):e61-e111. doi: 10.1093/cid/ciw353. Epub 2016 Jul 14. Erratum in: *Clin Infect Dis*. 2017 May 1; 64(9):1298. Erratum in: *Clin Infect Dis*. 2017 Oct 15; 65(8):1435. Erratum in: *Clin Infect Dis*. 2017 Nov 29; 65(12):2161. PMID: 27418577; PMCID: PMC4981759.
19. Torres A, Niederman MS, Chastre J, Ewig S, Fernandez-Vandellos P, Hanberger H, Kollef M, Li Bassi G, Luna CM, Martin-Loeches I, Paiva JA, Read RC, Rigau D, Timsit JF, Welte T, Wunderink R. International ERS/ESICM/ESCMID/ALAT guidelines for the management of hospital-acquired pneumonia and ventilator-associated pneumonia: Guidelines for the management of hospital-acquired pneumonia (HAP)/ventilator-associated pneumonia (VAP) of the European Respiratory Society (ERS), European Society of Intensive Care Medicine (ESICM), European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and Asociación Latinoamericana del Tórax (ALAT). *Eur Respir J*. 2017 Sep 10; 50(3):1700582. doi: 10.1183/13993003.00582-2017. PMID: 28890434.
20. Tansarli GS, Mylonakis E. Systematic Review and Meta-analysis of the Efficacy of Short-Course Antibiotic Treatments for Community-Acquired Pneumonia in Adults. *Antimicrob Agents Chemother*. 2018 Aug 27; 62(9):e00635-18. doi: 10.1128/AAC.00635-18. PMID: 29987137; PMCID: PMC6125522.
21. Lan SH, Lai CC, Chang SP, Lu LC, Hung SH, Lin WT. Five-day antibiotic treatment for community-acquired bacterial pneumonia: A systematic review and meta-analysis of randomized controlled trials. *J Glob Antimicrob Resist*. 2020 Dec; 23:94-99. doi: 10.1016/j.jgar.2020.08.005. Epub 2020 Aug 28. PMID: 32866643.
22. Klepikov I. *The Didactics of Acute Lung Inflammation*. Cambridge Scholars Publishing. 2022; 320: ISBN: 1-5275-8810-6, ISBN13: 978-1-5275-8810-3
23. Thillai M, Patvardhan C, Swietlik EM, McLellan T, De Backer J, Lanclus M, De Backer W, Ruggiero A. Functional respiratory imaging identifies redistribution of pulmonary blood flow in patients with COVID-19. *Thorax*. 2021 Feb; 76(2):182-184. doi: 10.1136/thoraxjnl-2020-215395. Epub 2020 Aug 28. PMID: 32859733.
24. Dierckx W, De Backer W, Lins M, De Meyer Y, Ides K, Vandevenne J, De Backer J, Franck E, Lavon BR, Lanclus M, Thillai M. CT-derived measurements of pulmonary blood volume in small vessels and the need for supplemental oxygen in COVID-19 patients. *J Appl Physiol* (1985). 2022 Dec 1; 133(6):1295-1299. doi: 10.1152/jappphysiol.00458.2022. Epub 2022 Oct 21. PMID: 36269576; PMCID: PMC9722246.
25. Laporte L, Hermetet C, Jouan Y, Gaborit C, Rouve E, Shea KM, Si-Tahar M, Dequin PF, Grammatico-Guillon L, Guillon A. Ten-year trends in intensive care admissions for respiratory infections in the elderly. *Ann Intensive Care*. 2018 Aug 15;8(1):84. doi: 10.1186/s13613-018-0430-6. PMID: 30112650; PMCID: PMC6093821.
26. Wise KR, Kempker JA, Neamu RF, Kobaidze K. Increased Long-Term Mortality in Patients Admitted to the Intensive Care Unit with Health-Care Associated Pneumonia. *medRxiv*. 2021;12.23.21267010; doi: <https://doi.org/10.1101/2021.12.23.21267010>
27. Lakbar I, Medam S, Ronflé R, Cassir N, Delamarre L, Hammad E, Lopez A, Lepape A, Machut A, Boucekine M, Zieleskiewicz L, Baumstarck K, Savey A, Leone M; REA RAISIN Study Group. Association between mortality and highly antimicrobial-resistant bacteria in intensive care unit-acquired pneumonia. *Sci Rep*. 2021 Aug 13; 11(1):16497. doi: 10.1038/s41598-021-95852-4. PMID: 34389761; PMCID: PMC8363636.
28. Boëlle PY, Delory T, Maynadier X, Janssen C, Piarroux R, Pichenot M, Lemaire X, Baclet N, Weyrich P, Melliez H, Meybeck A, Lanoix JP, Robineau O. Trajectories of Hospitalization in COVID-19 Patients: An Observational Study in France. *J Clin Med*. 2020 Sep 29; 9(10):3148. doi: 10.3390/jcm9103148. PMID: 33003375; PMCID: PMC7600846.
29. Cavallazzi R, Furmanek S, Arnold FW, Beavin LA, Wunderink RG, Niederman MS, Ramirez JA. The Burden of Community-Acquired Pneumonia Requiring Admission to ICU in the United States. *Chest*. 2020 Sep; 158(3):1008-1016. doi: 10.1016/j.chest.2020.03.051. Epub 2020 Apr 13. PMID: 32298730; PMCID: PMC9458541.
30. Mandell LA, Wunderink RG, Anzueto A, Bartlett JG, Campbell GD, Dean NC, Dowell SF, File TM Jr, Musher DM, Niederman MS, Torres A, Whitney CG; Infectious Diseases Society of America; American Thoracic Society. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. *Clin Infect Dis*. 2007 Mar 1; 44 Suppl 2(Suppl 2):S27-72. doi: 10.1086/511159. PMID: 17278083; PMCID: PMC7107997.
31. Vidal A, Santos L. Comorbidities impact on the prognosis of severe acute community-acquired pneumonia. *Porto Biomed J*. 2017 Nov-Dec; 2(6):265-272. doi: 10.1016/j.pbj.2017.04.009. Epub 2017 May 26. PMID: 32289091; PMCID: PMC6806761.
32. Salluh JIF, Ramos F, Chiche JD. Delivering evidence-based critical care for mechanically ventilated patients with COVID-19. *Lancet Respir Med*. 2020 Aug; 8(8):756-758. doi: 10.1016/S2213-2600(20)30266-6. Epub 2020 Jun 16. PMID: 32559420; PMCID: PMC7837367.
33. Reddy R, Dovidio J, Baram M. Outcomes of extracorporeal membrane oxygenation in ARDS due to COVID-19: comparison of the first and the second wave. *Chest, Critical Care*, V. 160, Issue 4, Supplement, A 1065, October 01, 2021. DOI:<https://doi.org/10.1016/j.chest.2021.07.9851>
34. Karagiannidis C, Mostert C, Hentschker C, Voshaar T, Malzahn J, Schillinger G, Klauber J, Janssens U, Marx G, Weber-Carstens S, Kluge S, Pfeifer M, Grabenhenrich L, Welte T, Busse R. Case characteristics, resource use, and outcomes of 10 021 patients with COVID-19 admitted to 920 German hospitals: an observational study. *Lancet Respir Med*. 2020 Sep; 8(9):853-862. doi: 10.1016/S2213-2600(20)30316-7. Epub 2020 Jul 28. PMID: 32735842; PMCID: PMC7386882.
35. Gupta S, Wang W, Hayek SS. Association between early treatment with tocilizumab and mortality among critically ill patients with COVID-19. *JAMA Intern Med*. 2020;180(11):1436-1446. doi:10.1001/jamainternmed.2020.3596
36. Berlin DA, Gulick RM, Martinez FJ. Severe Covid-19. *N Engl J Med*. 2020 Dec 17; 383(25):2451-2460. doi: 10.1056/NEJMc2009575. Epub 2020 May 15. PMID: 32412710.
37. Ranney ML, Griffith V, Jha AK. Critical Supply Shortages - The Need for Ventilators and Personal Protective Equipment during the Covid-19 Pandemic. *N Engl J Med*. 2020 Apr 30; 382(18):e41. doi: 10.1056/NEJMp2006141. Epub 2020 Mar 25. PMID: 32212516.
38. Johns Hopkins Center for Health Security. Ventilator stockpiling and availability in the US. 2020. (<http://www.centerforhealthsecurity.org/resources/COVID-19/200214-VentilatorAvailability-factsheet.pdf>)
39. Truog RD, Mitchell C, Daley GQ. The Toughest Triage - Allocating Ventilators in a Pandemic. *N Engl J Med*. 2020 May 21; 382(21):1973-1975. doi: 10.1056/NEJMp2005689. Epub 2020 Mar 23. PMID: 32202721.
40. Gafford. The Vanderbilt Open-Source Ventilator: From Napkin Sketch to Ready to Save Lives in Three Weeks. in *IEEE Robotics & Automation Magazine*. 2021; 28:1; 101-114. doi: 10.1109/MRA.2020.3045668.
41. Rice TW, Janz DR. In Defense of Evidence-based Medicine for the Treatment of COVID-19 Acute Respiratory Distress Syndrome. *Ann Am Thorac Soc*. 2020 Jul; 17(7):787-789. doi: 10.1513/AnnalsATS.202004-3251P. PMID: 32320268; PMCID: PMC7328187.



42. Llitjos JF, Bredin S, Lascarrrou JB, Soumagne T, Cojocar M, Leclerc M, Lepetit A, Gouhier A, Charpentier J, Piton G, Faron M, Stoclin A, Pène F. Increased susceptibility to intensive care unit-acquired pneumonia in severe COVID-19 patients: a multicentre retrospective cohort study. *Ann Intensive Care*. 2021 Jan 29; 11(1):20. doi: 10.1186/s13613-021-00812-w. PMID: 33512602; PMCID: PMC7844782.
43. Johnstone J, Muscedere J, Dionne J, Duan E, Rochweg B, Centofanti J, Oczkowski S, Lauzier F, Marshall J, Heels-Ansdell D, Daneman N, Mehta S, Arabi Y, Zytaruk N, Dodek P, Adhikari NK, Karachi T, Charbonney E, Stelfox HT, Kristof AS, Ball I, Hand L, Fowler R, Zarychanski R, Arnaud CS, Takaoka A, Kutsogiannis J, Khwaja K, Sligl W, Loubani O, Tsang J, Lamarche D, Bowdish D, Surette M, Cook D; Prevention of Severe Pneumonia and Endotracheal Colonization Trial (PROSPECT) Investigators and the Canadian Critical Care Trials Group. Definitions, rates and associated mortality of ICU-acquired pneumonia: A multicenter cohort study. *J Crit Care*. 2023 Jun; 75:154284. doi: 10.1016/j.jcrc.2023.154284. Epub 2023 Mar 3. PMID: 36870801.
44. Hoffman SJ, Outtersson K, Røttingen JA, Cars O, Clift C, Rizvi Z, Rotberg F, Tomson G, Zorzet A. An international legal framework to address antimicrobial resistance. *Bull World Health Organ*. 2015 Feb 1; 93(2):66. doi: 10.2471/BLT.15.152710. PMID: 25883395; PMCID: PMC4339972.
45. Behdinan A, Hoffman SJ, Pearcey M. Some Global Policies for Antibiotic Resistance Depend on Legally Binding and Enforceable Commitments. *J Law Med Ethics*. 2015; 43 Suppl 3:68-73. doi: 10.1111/jlme.12277. PMID: 26243246.
46. WHO. Antimicrobial resistance. 17 November 2021.- <https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance>
47. Bankar NJ, Ugemuge S, Ambad RS, Hawale DV, Timilsina DR. Implementation of Antimicrobial Stewardship in the Healthcare Setting. *Cureus*. 2022 Jul 8; 14(7):e26664. doi: 10.7759/cureus.26664. PMID: 35949742; PMCID: PMC9357433.

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