Acta Scientific MEDICAL SCIENCES (ISSN: 2582-0931)

Volume 9 Issue 11 November 2025

Review Article

Mythology of Diagnostics of Sepsis and Septic Shock in Acute Pneumonia

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Received: May 26, 2025

Published: October 30, 2025

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Abstract

The successful appearance in medical practice of antibiotics, which are exclusively etiotropic agents, has concentrated professional attention on the etiological direction of treatment of non-specific inflammations with the loss of attention to their pathogenesis. The narrow antimicrobial action of antibiotics, which does not affect such a basis of inflammatory processes as the mechanisms of their development, strangely enough, has not been subjected to a logical revision of therapeutic principles, having turned over the years into the dominant worldview. The so-called microbial concept of inflammatory diseases of non-specific etiology, despite the gradual accumulation of facts contradicting it, has formed a deeply rooted conviction in the exceptional role and indispensability of antibiotics in the treatment of such pathology. Misconceptions in the interpretation of the nature of inflammatory processes are especially clearly noticeable in the analysis of examination and treatment materials for patients with acute pneumonia. One of the illustrative examples of the existing deformation of professional views on the nature of this disease is the distorted diagnosis of sepsis and septic shock in acute pneumonia, which entails an inadequate approach to providing medical care.

Keywords: Acute Inflammation; Nonspecific Etiology; Antibiotics; Pathogenesis; Sepsis; Septic Shock; Acute Pneumonia; Pulmonary Blood Flow Characteristics; Regulation of Blood Circulation

Introduction

In recent years, sepsis (S) has become one of the most serious problems in global health, and its negative statistics are of great concern to specialists who are intensively searching for an effective solution to this problem. Just a decade ago, the total number of S diagnoses worldwide per year was estimated at 30 million cases, of which 6 million were fatal [1]. Currently, according to the World Health Organization (WHO), the number of patients with S has increased to 49 million per year, and the number of deaths - to 11 million [2]. In the United States, the total number of S cases has remained stable in recent years, amounting to 1.7 million cases per year, but the number of deaths over the past 6 years has increased from 270 thousand [3] to 350 thousand [4]. The average length of hospital stay for patients with S remains twice as long as for any other fatal outcome [5,6]. The hospital mortality rate, which reached 20% a few years ago [5,6], has risen to 40% in recent years in Europe and North America, i.e., in the most advanced health care systems [7]. At the same time, in the USA, S is the leading diagnosis of hospital mortality [8].

Discussion

The source of S can be inflammatory processes of various localization and clinical manifestations, which is the reason for significant heterogeneity of this complication [9,10]. However,

in recent years, the diagnosis of S, including septic shock (SS), is carried out according to generally accepted uniform criteria [11], regardless of the underlying cause and its functional characteristics. Such a combination of various sources of S and SS creates a precedent for using one diagnostic assessment scale for situations that are incomparable in terms of development mechanisms. In this regard, to make it clear what we are talking about, it should be noted that all primary foci of S and SS are divided into two fundamentally different groups. The first group consists of the overwhelming majority of inflammatory processes localized within the systemic circulation. The second group is actually represented by only one nosology - acute nonspecific inflammation of the lung tissue or acute pneumonia (AP). This division into two groups must be foreseen in advance, since, despite the continuity of blood circulation in the two circulatory circles, their indicators demonstrate complete opposites, but such vital proportions are automatically maintained by autonomous regulatory mechanisms.

Despite such significant numerical differences in the representation of these two groups of inflammatory diseases, AP has always been the leader among the causes of S and SS, creating conditions for the occurrence of almost half of these conditions [12-14], and recently, according to combined statistics, has been the source of such complications in more than 60% of cases [15]. Currently, there is a desire for the earliest possible diagnosis of the initial manifestations of S using biomarkers for timely triage of patients and prediction of further development of events up to fatal outcomes [16-20]. This direction in research has recently become dominant, creating an aura of novelty around this area, but at the same time, the basic principles of treatment, which for many years did not bring the expected results, remain untouched. In this regard, it is still worth noting that the final results of treatment in each specific case depend not on the place of treatment and the potential capabilities of the hospital departments, but on the specifics of the efforts made, right?

In particular, over the past two decades, such an indisputable fact as the growth of viral forms of AP and, accordingly, associated variants of S has emerged, the validity of which is based solely on analogies with bacterial variants of S and which have no other convincing arguments in favor of the septic nature of the observed symptom complex. This important detail of the interpretation of S should be remembered in further analysis of modern circumstances in this area. In addition, it should be added that viral forms of inflammation are most likely to cause damage to the lung tissue, in contrast to inflammatory processes in other organs and structures of the body, which can lead to the development of S. However, in real practice, the principles of treating S continue to demonstrate unwavering stability, representing a single scheme for all observations of this complication. The primary basis of medical care for patients with S remains antibacterial therapy with parallel infusion therapy and various symptomatic and auxiliary means [21-24].

The set of basic treatment methods presented today demonstrates, first of all, an uncritical commitment to and undying faith in the success of antibiotics. In this regard, it is not only their widespread use in viral pneumonia that is surprising [25-28]. Even more striking are the methods for assessing their effectiveness, which in previous years, despite repeated studies, did not give convincing results. For example, attempts continue to prove the greater effectiveness of antibiotics with their earlier hourly use, which, according to the authors, who found 7 similar studies in the literature over the past 5 years, reduces the risk of fatal outcomes [29]. On the other hand, the assessment of the effectiveness of such therapy at all stages of patient treatment after its initiation is up to 72 hours [20], which in the context of a rapidly progressing inflammatory process is an unforgivable waste of time, because antibiotics have only an etiotropic effect, without affecting the mechanisms of inflammation and the correction of emerging functional disorders, right?

Of even greater concern is the stereotypical approach to infusion therapy, which continues to be widely practiced regardless of the source of the suspected S [11,23,24]. R. Gauer., *et al*. [21] consider infusion therapy to be a priority in the early treatment of S. At the same time, the appearance of signs of negative dynamics in the patient's condition serves as a reason for bolus infusions, and hypotension refractory to such therapy is an indication for the use of vasopressors [21,22]. Q. Guo., *et al*. [30], studying the development of S during the treatment of patients with AP using the qSOFA diagnostic scale, compared their results with a similar work by other authors, which was carried out almost 20 years ago [31]. To their inexplicable surprise, the results were identical with the frequency of S development in almost half (48%) of all observations. Agree that such results cannot serve as an indicator

of the success of medicine in solving the problem under discussion and should not leave specialists in this field in a serene state. In this case, it is time to recall the above-mentioned fundamental division of all inflammatory processes into two groups.

Our body is a complex biological organism capable of autonomously and imperceptibly adapting the work of its organs and systems to constantly changing conditions and unexpected loads. This occurs due to the presence of many protective and adaptive mechanisms that are not subject to our will, are autonomous in nature and automatically respond to the appearance of various irritants. These provisions are fully relevant to the present discussion, but modern medicine studies the parameters of such responses mainly at the cellular and molecular level and considers them as prognostic tests and objects for subsequent correction. For example, with S, activation of pro- and anti-inflammatory reactions, immunological indicators, shifts in the cardiovascular, hormonal, coagulation and other systems of the body are noted and studied [32-35]. In recent years, research in these areas has significantly deepened, but the focus on the transformation of microstructures does not provide practical breakthroughs, and the assessment of the patient's condition continues to rely on integral functional indicators, and not on molecular shifts.

In order to avoid further self-deception in our ideas about the nature and mechanisms of development of AP, it is necessary to recall and include in the process of revising the concept of the disease a number of classical canons of medical science, which are currently not given sufficient attention. Such worldviews have long had indisputable scientific evidence, have been tested by many years of practice and constitute the gold fund of fundamental principles of medical and biological science. Such rules and patterns will influence the features of the development of the disease we are studying, regardless of our desires and preferences. In this context, given the limitations of the presentation, it is necessary only to briefly mention the most significant factors that are most directly related to the problem discussed here.

First of all, we are talking about the features of the inflammatory process, such as the vascular reaction with which this phenomenon begins, which is accompanied by a sharp blood filling of the affected area and an extreme increase in the permeability of the vascular wall. All these mechanisms have an individual rate of development and are accompanied by significant morphological transformation of tissues with an inevitable change in its functional capabilities. In connection with the morphofunctional changes in inflamed tissues, medicine has been using 5 classic signs of inflammation for almost two thousand years, primarily for diagnostic purposes. Among these signs, the greatest clinical significance is the loss of function, which depends on the localization of the lesion and determines the specificity of the disease picture, maintaining it regardless of the etiology. It is necessary to take into account the rate of increase in changes and the body's ability to compensatory and adaptive reactions. In the most aggressive cases of the process, the autonomous nature of such reactions can go beyond the permissible useful limits, turning into an additional problem.

In addition, as is known, AP is the only nosology among acute inflammatory processes that occurs in the pulmonary circulation. At the same time, the classical work of the circulatory system is such that the arterial pressure in the pulmonary vessels is approximately 6-8 times lower than in the systemic circulation [36]. This difference is due to the functional purpose of two different types of vessels, but the disruption of pulmonary blood flow and the shift in this proportion require, first of all, the restoration of equality of volumes between the cardiac output of the two ventricles. This condition is vitally important, since it ensures the synchronous work of the two halves of the heart. In the case of the slightest shifts in this balance, mechanisms capable of maintaining this parity are automatically activated, but if they do not provide full adaptation, then external assistance is required, since an increase in pressure in the pulmonary artery above 25 mm Hg leads to pulmonary edema [37]. If there were no such protection, many lung diseases, especially acute inflammations, would threaten our body with inevitable fatal consequences.

One of the most important mechanisms of emergency adaptation of pulmonary blood flow with an increase in blood pressure in the pulmonary circulation is the reflex from the baroreceptors of the pulmonary vessels, discovered almost a century ago by H. Schwiegk [38]. At present, this mechanism is designated as the unloading reflex, and its action as a result of stimulation of the baroreceptors helps to reduce systemic arterial pressure, deposit part of the circulating blood and reduce venous return. The action of this mechanism attracts attention, first of all, in such sudden

pathologies as, for example, pulmonary embolism, but remains aside in the interpretation of the mechanisms of AP and S.

The mechanism of action of the unloading reflex in AP begins as a result of the vascular reaction and subsequent blood flow disturbance in the inflammation zone, but reaches peak manifestations of clinical symptoms in patients with aggressive development of the process. In such situations, the rapid development of the process does not leave the body enough time for gradual adaptation of the blood flow. The compensatory mechanism goes beyond its positive limits as a result of generalized reflex spasm of the pulmonary vessels. The sudden relative excess of venous return requires further protection of the pulmonary circulation, which leads to a decrease in systemic pressure. Such a picture of blood circulation in such patients is currently considered a sign of S or SS. However, in reality, in patients with AP, due to the peculiarity of the pathogenesis of the disease, we can talk about a peculiar form of the so-called pulmonogenic shock without any evidence of its septic nature. A similar mechanism of circulatory disturbance in AP was confirmed and described more than 30 years ago [39]. At present, the results of the work done in the light of the current events of the last decades have been published in English [40].

In this context of discussion, it is necessary to present only objective arguments in favor of the reflex, rather than septic, origin of those signs that are today considered as manifestations of S and SS. In the Soviet Union, where the above-mentioned work was carried out [39,40], for the differential diagnosis of acute appendicitis and abdominal syndrome of AP, it was recommended to perform a cervical vagosympathetic block (CVSB) with novocaine. The result of this procedure could be assessed within a few minutes by the appearance of Horner's syndrome on the side of the block. For an objective assessment of the results, comparative records of rheopulmonograms (CRPG) before and immediately after the block were used (Figure 1 and 2).

The results of the CRPG, obtained literally at intervals of several minutes in a group of such patients after the CVSB, could only indicate a reflex, but not a septic nature of the corrected disorders. The initial predominance of ventilation over blood flow and the shift in the coefficient of their ratio immediately after

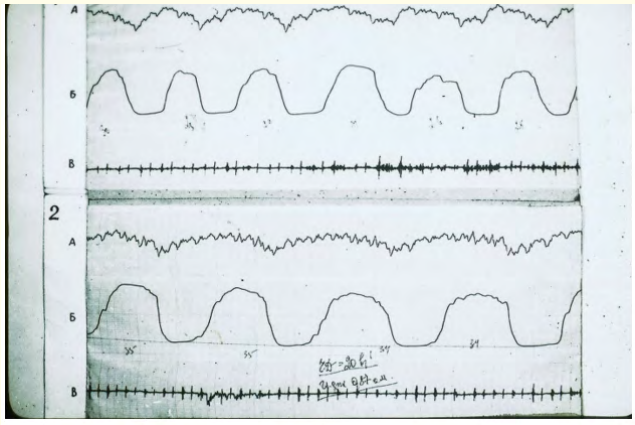

Figure 1: Rheogram of ventilation of the patient 8 years old, AP 7-10 segments of the right lung.

1-The original reopulmonography (RPG).

2-RPG after vagosympathetic blockade

A-differential RPGs

Б-Main RPG

B-phonocardiogram

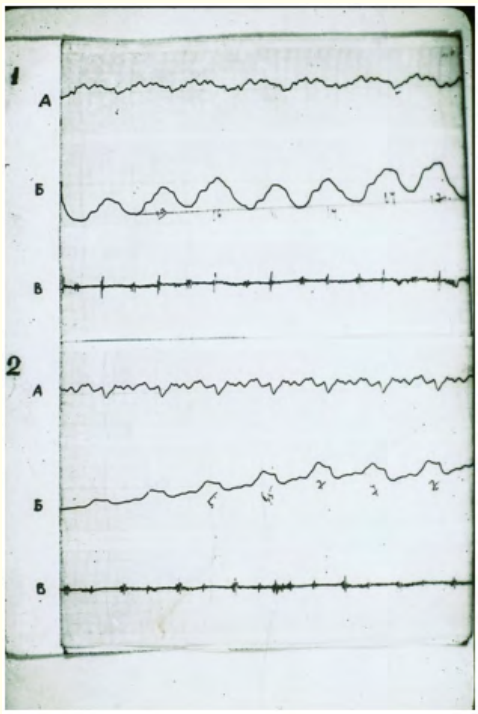

Figure 2: Rheogram of pulsatory blood flow of the same patient. The designations are the same.

the procedure were practically leveled due to a decrease in the frequency and some increase in the depth of respiratory excursions with a parallel decrease in the number of heart contractions and a decrease in the amplitude of the systolic wave (see figures). Interestingly, a similar effect was recorded after cupping therapy. The assumption that these procedures eliminate reflex generalized spasm of the pulmonary vessels was confirmed by the results of recently published studies. A number of specialists drew attention to the discrepancy between the volume of lung tissue damage and the level of hypoxemia in patients with COVID-19 pneumonia. Analysis of computed tomography data of the lungs in such patients showed a widespread decrease in blood volume in small (less than 2 mm in diameter) vessels of the pulmonary circulation [41,42]. The authors noted that the more pronounced the vascular spasm and changes on tomograms, the more pronounced the respiratory disorders.

In connection with the latter, it is necessary to note the features of modern diagnostics of S, which are based on a single assessment scale, regardless of the localization and pathophysiology of inflammatory processes. In particular, it is necessary to pay attention to the accelerated formula for diagnostics and sorting of patients qSOFA, in which the main role is played by such indicators as respiratory rate and systemic systolic blood pressure. If for the overwhelming majority of inflammatory processes the shift of these two indicators does not belong to the category of characteristic signs and can be regarded as a manifestation of the generalization of infection, then for patients with AP these clinical features, especially an increase in the frequency of respiratory excursions, are an integral manifestation of the disease already at the very beginning, contributing to the «accelerated diagnostics» of S. At the same time, AP is the only inflammatory process in which circulatory disorders begin with the vessels of the pulmonary circulation, but the assessment of shifts is carried out according to the indicators of systemic blood flow, actually determining not the degree of disorders, but the level of compensatory deviations.

Bacteriological examination of the blood of such patients is currently used to clarify antibacterial therapy, but no longer has the diagnostic value that was previously attributed to it. At the same time, in the recent past, some specialists drew attention to the reliably low, only a few percent, frequency of bacteremia in patients with AP who were diagnosed with S, compared with other localizations [43-45]. These data serve as additional, albeit weak, confirmation of the existing overdiagnosis of S in AP, but inattention to the features of the pathophysiology of this disease has no reasoned explanations, being the reason for the undisputed leadership of pulmonary processes among such complications. Unfortunately, such an approach to the interpretation of the pathogenesis of AP and the diagnosis of S and SS serves as an excuse for failures in providing medical care to such patients.

Current information on the treatment of S and SS indicates that the principles of treatment remain the same for all patients, regardless of the primary source of these complications. The two main lines of treatment are empirical antimicrobial therapy, which is used for all bacterial and fungal and many parasitic and viral infections causing S, and intravenous crystalloid infusion, the first-line therapy given as a bolus [22,30,46]. In addition, adjuvant and maintenance therapy are used. The results of such efforts remain variable, and the optimal volume of fluids to be administered to these patients remains unknown [46,48,49]. Moreover, all recent guidelines recommend the use of vasopressors in case of persistent hypotension after intravenous fluid administration.

First of all, the use of antibiotics cannot be considered as the first and emergency aid capable of bringing immediate results to seriously ill patients with AP, especially since the etiotropic nature of their action does not directly affect the pathogenetic mechanisms of the process that cause functional disorders. At the same time, infusion therapy in such patients will have an effect directly opposite to the expected one. The mysterious heterogeneity of the obtained results acquires a different interpretation if we take into account that AP is the source of C in a good half of the observations, and look at this group of patients, first of all, from the position of the pathophysiology of the disease. The fluid administered intravenously to such patients first reaches the vessels of the pulmonary circulation, not only preventing their unloading, but also stimulating the processes of edema and tissue infiltration in the inflammation focus. These phenomena have been proven and documented by us in experimental and clinical studies [39,40]. However, the details of this section are beyond the scope of the topic under discussion.

Conclusion

Thus, the diagnosis of sepsis and septic shock in patients with AP is currently based on a long-outdated concept of the disease

that does not correspond to the classical canons of medical science and accumulated facts. The cardinal changes in the etiology of the disease that occurred during the period of antibiotic use and the shift in emphasis towards pathogens that do not require this therapy have not led to the much-needed revision of views on this problem. The use of such general therapeutic methods in patients with AP as infusion therapy, the effect of which, especially in the initial period of the disease, contradicts its unique pathogenesis, can stimulate the development of the process. All this requires an urgent revision of the established views on solving the problem and a radical change in the principles of diagnosing S and SS, the number of which is currently clearly overestimated.

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.

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