Letter to the Editor

Was there really sepsis?

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This article not only refers to a long-standing and very stable problem, but is also based on the analysis of the most significant studies from different parts of the modern world. Therefore, the results discussed and the conclusions obtained can be considered as a universally dominant position. In this regard, it is important to note that the research materials analyzed in this article mainly relate to the last decade. This fact indicates that the most advanced views and approaches to the diagnosis and treatment of this group of patients have been critically evaluated. Such selection of the analyzed sources allows to expect cardinal conclusions, exact and reliable recommendations for the near future. However, the essence of the presented materials leaves no other possibility, and the conclusion again focuses the attention of readers on the importance and inviolability of the priority of antibacterial therapy. All other aspects of the problem remain unclear and non-specific. The conclusion of this article is not much different from similar thoughts presented in the foreseeable past, and is, in my opinion, the result of a General misconception and overestimation of the role of antibiotics among other means and directions of medical care.

The discovery of antibiotics and the initial triumph of their use for many years directed the solution to the problem of acute pneumonia (AP) only on the narrow path of suppressing its pathogens. The gradual distortion of views on the nature of the disease has led to the oblivion of its biological basis as an inflammatory process and the modern interpretation of the leading cause as infectious. AP regardless of the introduction of new terms (community-acquired, health-related, hospital-acquired, ventilator-related, etc.) remains a classic example of acute inflammation of non-specific etiology.

AP, despite the shift of interpretations of its essence towards infection, is not a contagious disease and remains a classic inflammatory process of nonspecific etiology, where the microbial factor may be one of the trigger causes, but not its main source. In the presence of appropriate conditions, many microorganisms present in the body as a concomitant microflora can take part in the inflammatory process. At the same time, the true participant of this process in the vast majority of patients remains unknown, and discussions about the etiology of the disease, as a rule, are based on indirect studies, which can not be considered an objective argument and do not have a significant impact on the final results (1,2).

In connection with the above remark, attention is drawn to the fact that in this article the verification of sepsis pathogens, as its diagnostic confirmation and the most important characteristic, has not received the usual reflection in our time, both in the cited results and in the Discussion section. This is an additional confirmation of the declarative nature of many modern provisions of the doctrine of AP. In addition, the stagnation of the infectious trend in addressing AP causes many researchers and clinicians to look for other criteria to explain the observed phenomena. Thus, among the diagnostic biomarkers that have been used in recent years, attention is drawn to the

* The author conducted research on the topic under discussion in the USSR at the State Institute for advanced training of doctors (Novokuznetsk). To date, the USSR and the mentioned Institute no longer exist. However, research and clinical trials of new approaches to the treatment of children with acute pneumonia and the results of this work can provide answers to a number of questions facing us today, which allows us to consider the research of thirty years ago relevant and worthy of mention.

attempt to return to the category of mandatory research and rehabilitation of some long-known tests, such as C-reactive protein (CRP). The blood test for CRP has a fairly long history and is not any diagnostic novelty, but the increased attention to this biomarker in AP is, in my opinion, a positive shift towards assessing the inflammatory response as such, and not just the bacterial factor. To understand how important the evaluation of the inflammatory response in AP is, it is necessary to recall the fundamental foundations of this pathological transformation and weigh their role in this disease.

(I) Inflammatory transformation of tissues occurs due to the vascular reaction in the lesion, which is accompanied by a change in the permeability of vascular membranes and strictly sequential change of stages.

(II) The rate of development of inflammatory transformation is determined by the ability of the body to respond to the emerging focus of irritation and is an individual characteristic that can have both a lightning nature and a relatively smooth development (the so-called immune response reaction).

(III) In the most aggressive cases, the inflammatory process can proceed at lightning speed by the type of Artus reaction. In such situations, it is possible to develop necrosis of inflamed tissues within a short time, and the body has great difficulty adapting to sudden functional disorders.

(IV) Like any other inflammation, AP is accompanied by five classic signs, which after their description by Celsus and Galen for several centuries are a mandatory characteristic of such diseases (heat, pain, redness, swelling, and loss of function).

(V) Of the five above-mentioned signs, the most practical importance is the loss of function, which, depending on the localization of inflammation, determines the clinical features and severity of the disease.

To the main characteristics of acute nonspecific inflammation listed above, the following cardinal and indisputable facts should be added. Of all the currently known list of acute nonspecific inflammatory processes, AP is the only one that develops in the vessels of the small, not the large circle of blood circulation. One of the important functions of the lungs is their integral regulatory role in the circulatory system of the body. Through the vessels of the pulmonary circulation passes all the blood circulating in the body and for the normal synchronous operation of the two halves of the heart, the blood pressure of the large circle should be several times higher than this indicator in the pulmonary vessels. Acute inflammation in the lung tissue affects the receptors of blood flow regulation in the small circle of blood circulation, including mechanisms of unloading of pulmonary vessels with a tendency to reduce systemic blood pressure (3,4).

It should also be noted that antibiotics, which continue to be considered as a panacea, have only antimicrobial action and are not able to directly affect the mechanisms of the inflammatory process.

To sum up the above reminders, many common areas of patient care receive a completely different explanation, allowing us to understand the lack of effectiveness of modern treatment of AP. For example, mandatory forced intravenous infusions in severe patients with AP give the opposite effect in contrast to other inflammatory processes, and the observed negative dynamics of the disease does not correlate with the virulence of the microflora (5). Under new conditions, the body tries to resist unexpected therapeutic aggression and therefore hypotension and the need for vasopressors logically follow from modern ideas about the pathogenesis of the disease.

Even such a method of assistance in AP, as oxygenotherapy, which is of the most specific nature and is used allegedly because of the violation of gas exchange in the area of inflammation, raises a reasonable question: "Why a small focus of acute inflammation in the lung causes more severe hypoxemia than atelectasis of the lobe or even the entire lung?"

It is possible to significantly expand the understanding of the pathogenesis of AP and radically change the results of treatment of these patients only by revising the doctrine of the disease. This first step in solving this problem is not only difficult because of the need to break the stereotypes that have developed over the years, but also absolutely necessary to achieve real, not declarative, success.

The first step in this direction was taken more than 30 years ago. Clinical testing of other approaches to the treatment of AP, arising from new ideas about the nature of the disease, confirmed the validity of the chosen course.

This work was performed and tested in clinical conditions in 1976–1985 in the clinic of pediatric surgery of the state Institute of advanced training (Novokuznetsk, USSR). Unfortunately, life circumstances did not allow the author to continue the research, to develop the results achieved and to present them at the international level in a timely manner. Over the past period, there have

been many significant events, in particular, instead of the collapsed Soviet Union, another country appeared on the map. The above-mentioned institution in which the author worked no longer exists, having radically changed its status. However, the solution of the AP problem remained true to the previous direction and only accumulated new questions and tasks. In this regard, research and clinical trials of pathogenetic approaches to the treatment of patients with AP and the results of this work can provide answers to a number of questions facing us today, which allows us to consider the research of thirty years ago relevant and worthy of mention.

The peculiarity of this material was that the most severe patients with initial forms of AP were concentrated in the surgical Department. Such hospitalization of non-surgical patients was explained by the rapid development of complications, high mortality and lack of conditions for intensive care and resuscitation in other hospitals. The administrative decision regarding the concentration of severe patients did not correct the situation and did not change the results of treatment. At that time, the aggressiveness of AP development was explained solely by the presence of Staphylococcus in the development of the disease, although some facts contradicted this opinion. That is why the search for a solution to the problem was started with a revision of views on the nature of AP.

The main and first step in the study was a radical revision of views on the nature and mechanisms of development of AP. The new doctrine was based on well-known scientific medical axioms and facts that already had the previous justification and confirmation.

In addition, the following studies were carried out: (I) experimental model AP (4 series of experiments, 44 animals) to obtain a model of pleural complications (certificate for invention No. 1631574, A1, November 1, 1990, USSR); (II) X-ray examination with contrast of 56 anatomical lung preparations with various forms of AP taken from deceased patients; (III) record of comparative rheopulmonography before and after treatment procedures (36 patients); (IV) analysis of monitoring and treatment of 994 children with AP and its various destructive and pleural complications (6).

The revised treatment guidelines were applied in 101 patients in the initial period of aggressive forms of AP. The analysis of the results showed that compared with the same group of patients who received the previous complex of care, the number of pleural and pulmonary complications significantly decreased (T=8,65; P<0,001), the length of hospital stay was reduced by three times, respectively, material and financial costs of treatment were significantly reduced, there were no deaths. The received results allow to speak about possibility of the guaranteed prevention of suppurative and destructive complications of the disease.

The revised treatment package was also used in 102 patients who already had pleural changes at the time of hospitalization, despite the initial period of the disease. In this group of patients, rapid recovery without fatal outcomes was also achieved, but the final results depended on the nature of the initial pleural reaction. The more intense and saturated the pleural effusion was at the time of hospitalization, the greater was the probability of the appearance of destructive cavities in the lung with the resolution of inflammatory infiltration.

The main results of research, clinical trials and the results obtained can be summarized as follows. AP is a classic inflammatory process of nonspecific etiology, where the microbial factor may be one of the trigger causes, but not its main source. In the presence of appropriate conditions, many microorganisms present in the body as a concomitant microflora can take part in the inflammatory process. At the same time, the true causative agent of the disease in the vast majority of patients remains unknown.

However, in patients with relatively slow development of the disease, treatment by the type of "antibiotics alone" manages to suppress the revolt of the microflora and allow the body to cope with the problem. Despite the significant decrease in the effectiveness of antibiotics compared to their first results, such observations support the illusion of the exclusive role of these drugs, as well as the impression of the infectious nature of AP. Therefore, when this type of treatment does not give the desired result or the disease initially begins aggressively and requires the use of additional methods of care, the situation begins to get out of the influence of the treating doctors.

Hemodynamic disorders, decreased blood oxygenation and other laboratory and metabolic shifts, which are considered in the analyzed article as signs of sepsis and septic shock, have, from my point of view, a different origin and are a reflection of the unique pathogenesis of AP. All these shifts are not the result of infection entering the bloodstream and generalizing. In addition, the review does not provide objective evidence of the septic nature of these phenomena. The absence of such important arguments in the diagnosis of sepsis allows us to consider the presented concepts as declarative and incorrect, which direct further research on the wrong path.

The use of specific methods of treatment of AP and the

possibility of real inhibition of the disease should be based on an understanding of the dynamics and mechanisms of the process. This requires a radical revision of views on the nature of AP with a modification of its doctrine, which is the first, but necessary and inevitable step in this direction (7-9).

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Footnote

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