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Clinical Research in Pulmonology

Opinion

The Era of Viral Pneumonia

Igor Klepikov*

Department of Pediatric Surgeon, Tel Aviv University, USA

***Corresponding author**

Igor Klepikov, Department of Pediatric Surgeon, Tel Aviv University, Renton, Washington, USA, Email: igor.klepikov@yahoo.com

Submitted: 19 April 2022

Accepted: 25 May 2022

Published: 28 May 2022

ISSN: 2333-6625

OPINION

Pneumonia (AP) has been known to medicine throughout its foreseeable history as a severe inflammatory disease that does not pose a danger to others in contact with the patient. The origin and development of microbiology allowed us to establish that the etiological factors of AP are certain types of bacteria, which, however, can occur with different frequency among the symbiotic microflora of healthy people. This information confirmed the ancient postulate that people do not get infected with pneumonia, but get sick.

Among the bacteria involved in acute inflammation of the lung tissue, *Streptococcus pneumoniae*, isolated back in the 19th century, prevailed for a long time, and its special role in this disease was reflected in its name [1]. However, despite the obvious predominance of *Pneumococcus* among the pathogens of AP, it did not have an absolute monopoly in the etiology of the disease, since in the development of pneumonia could manifest other bacteria. Such etiological features have long allowed AP to be interpreted as acute nonspecific inflammation in the lungs, where the term "nonspecific" emphasized the possible diversity of pathogens.

With the advent of the possibility of microbiological characteristics of AP, the most aggressive and severe forms of the disease with bacterial etiology of the process were noted. The viral etiology of AP was also included in the list of causes of its development, but it was a fairly rare form of the disease, and viral infections were mainly considered as circumstances provoking the development of bacterial inflammation. Relatively rare forms of the disease are fungal and parasitic variants of inflammation, which usually do not differ in severity and severity of manifestations inherent in bacterial processes.

The noted features of bacterial forms of AP, which were established by the middle of the last century, became an ideal testing ground for the implementation of the effect of antibiotics that appeared in the medical arsenal of medicines of that time. Unfortunately, the first impressive successes of antibacterial therapy have been misinterpreted in the long run. This applies both to the targeted activity of these drugs and to the inevitable consequences of their use.

Antibiotics are able to affect only certain types of bacteria, without directly affecting the mechanisms of the resulting inflammatory process. In bacterial forms of inflammation, suppression of the pathogen helps the body to cope with the pathological cascade of the disease on its own. The faster the effect of the use of antibiotics is realized, the sooner it will be possible to observe positive changes in the condition of patients. This was the result that prevailed in the early years of antibiotic use among patients with AP.

However, such effectiveness of antibacterial therapy could not continue indefinitely. The widespread use of antibiotics disrupted the usual balance that existed between the body and its accompanying microflora. At the same time, bacteria, as representatives of wildlife, showed their adaptive functions in response to the aggression that arose. Today, the consequences of prolonged use of antibacterial agents in a wide medical practice are no longer a secret to anyone. The emergence of a whole galaxy of antibiotic-resistant strains, the periodic change of drugs and the steady decline in their effectiveness have been a real trend in this field of medicine for many years.

Despite the obvious and well-known circumstances, many sides of the problem under discussion, which were formed as a result of prolonged use of antibiotics and excessive preference for their place in the treatment of AP, remain aloof from discussions and new perceptions. The main role in preserving the usual stereotypes is played by the system of views on the nature of AP, which arose and developed under the influence of the meme about the exceptional importance of antibiotics in the treatment of this disease. The deepening of these traditions against the background of the observed phenomena turned into *a destructive meme* with its further spread through *the information cascade* [2,3].

One of these phenomena, which has been observed for several decades, is the periodic change of leaders among the pathogens of AP. In this regard, it is necessary to return once again to the history of the disease and recall that in the pre-antibiotic era, pneumococcus remained a constant favorite of this list until the sixties of the last century. It was during this period, that is, about 15-20 years after the start of clinical use of antibiotics, for the first time in a long period of microbiological diagnosis of AP, staphylococcus replaced pneumococcus. At the same time, according to numerous publications of that time, the frequency of detection of *staphylococcus* among the pathogens of AP was approaching 100%.

The widespread invasion of staphylococcus turned out to be a temporary and not very long-lasting phenomenon, and the pathogen itself imperceptibly and gradually ceased to dominate

among the leading causes of AP. One of the constant reminders of the "staphylococcal catastrophe", which was accompanied by the widespread and targeted use of etiotropic drugs, was the appearance of MRSA, the first antibiotic-resistant strain [4]. Starting from the specified time period, the etiology of AP no longer had the same relative constancy and continued to be accompanied by systematic changes in the ratios between various bacterial pathogens.

A review of statistical data on the etiology of AP shows that in recent decades there has not been such a clear and permanent leader among microbial pathogens of the disease, the role of which was performed by *pneumococcus* in the pre-antibiotic era. *Streptococcus pneumoniae*, which tends to damage lung tissue, after the "staphylococcal catastrophe" gradually returned to the list of leading bacterial factors of AP, but the frequency of its detection in this disease has significantly decreased.

So, if before the start of clinical use of antibiotics, *pneumococcus* was the causative agent of AP in 90-95% of cases [5-7], in recent years its participation in this disease has been confirmed only in 33-50% of positive bacteriological studies in this category of patients [8]. But if we take into account the fact that in half or more cases of AP it is not possible to identify the causative agent, then the role of pneumococcus in the etiology of the disease is established only in 10.9% of outpatient patients, in 17.7% of hospitalized and in 22.5% of these patients in intensive care units [9].

This small review of materials on bacterial pathogens of AP over the past few decades has been undertaken in order to show in general terms how the list of leading bacterial factors of the disease has changed over the period of widespread use of antibiotics. Changes in the etiology of AP began to be observed only after the introduction of antibacterial therapy into medical practice, which should be considered as a logical consequence of this type of treatment. Details and variants of such dynamics among bacterial pathogens of AP can, if necessary, be traced and clarified by analyzing the relevant data, but this message has a different purpose.

For at least the past two decades, many experts in the analysis of acute inflammatory lung diseases have expressed extreme concern about the constant and significant increase in cases of AP viral etiology. This alarm was based on statistical data, according to which 200 million cases of viral pneumonia were registered annually in the world, which at the time of analysis accounted for almost half of all cases of AP [10-12]. If we return to the statistics of bacterial forms of AP just mentioned, in which half of the observations fail to isolate the pathogen [9], it is quite acceptable to assume that such cases were due to viral etiology, but timely virological diagnosis was not carried out.

To this information about the growing involvement of viruses in the etiology of AP, it is necessary to add such well-known facts as annual epidemics of influenza and other viral infections, which have become a "tradition", requiring widespread vaccination of the population and increasing the burden on health systems. In terms of the style and breadth of the spread of the flu epidemic, they began to resemble pandemics more and more, capturing countries and continents with their expansion.

The SARS-CoV-2 pandemic, which began against this background, was not much different from traditional flu epidemics. Its presentation as an unexpected catastrophe may still look understandable to the media, which take such a viral invasion as a given and replicate the incoming information. However, when the same trend is observed in the medical literature, it inevitably raises doubts about the professional validity of such an assessment of the surprise factor.

Along with the general tendency to increase the role of viruses in the etiology of inflammatory processes of the lungs, the main cause of the pandemic - coronavirus - was already well known to modern medicine. This acquaintance took place not only as a result of laboratory studies of the pathogen, which began in the last century. Over the past couple of decades, at least two major coronavirus epidemics have been observed - SARS and MERS [13]. These infectious outbreaks with severe lung damage and high mortality brought some clinical experience and even reflected in the terminology of the pandemic, emphasizing the consistent connection of these phenomena.

However, as reality shows, no radical conclusions and reliable ways to help this category of patients during this long period of constant growth of viral pneumonia have been proposed. The destructive meme about the infectious nature of AP and the dominant role of the pathogen in the development and features of the course of the disease, which arose and strengthened over a long period of preference for antibiotics, continues to dominate the search for solutions to the deepening problem. The main efforts today are still focused on determining the means and methods of neutralizing the pathogen.

The versatile efforts that are being made to suppress viruses and achieve tangible results in seriously ill patients remain fruitless. Virus neutralization is demonstrated in laboratory studies when the tested drug is in direct contact with the object [14-16]. However, in the real conditions of a living organism, the laboratory effect of such attempts is not achieved, which has its own logical reasons and explanations, which are not always given importance.

First of all, it is well known that clinical signs of viral pneumonia appear during the period of the disease when the pathogen is already inside the cell. In such a situation, drugs that can affect the virus in the laboratory are not always able to follow the pathogen into the cell, and when they have this ability, they can aggravate the toxic effect on cellular structures [14].

In addition, suppressing the pathogen at a time when the patient needs urgent care due to an increasing cascade of severe functional disorders is a belated measure. At this stage of the disease, the pathogen does not determine the intensity and severity of clinical manifestations, which was noted when attempting differential diagnosis of AP on an etiological basis. For example, long-term attempts to separate bacterial forms of the disease by the nature of the pathogen ultimately had no effect on clinical symptoms and further treatment results [17,18].

During the SARS-CoV-2 pandemic, previous ideas that the causative agent of pneumonia is of leading importance for clinical manifestations remained the cause of differential diagnosis between bacterial and viral forms of lesions. Such a diagnosis is

still considered necessary for the selection of etiotropic agents that preserve the image of the main treatment. Again, the results showed that the features of the development and course of AP do not depend on its etiology, and it is impossible to draw clear boundaries between bacterial and viral inflammation of the lung tissue [19-21].

Thus, the hypertrophied belief in the leading role of the pathogen, developed under the didactic influence of antibacterial therapy, continues to determine the search for a solution to the problem in new conditions, when the frequency of viral processes has increased significantly, but the need for antibacterial agents has significantly decreased. In this situation, according to the logic of the observed trends in the etiology of AP, a radical revision of the prevailing views on the doctrine of the disease is required. However, contrary to logical regularity, many experts are trying to find a solution through old stereotypes when the treatment of COVID-19 pneumonia continues with the widespread use of antibiotics [22-26].

A long period of antibiotic use could not but affect the accompanying microflora of the body. The specific effect of this therapy affected only representatives of the bacterial sector, initially causing a change in the proportions between them. The subsequent expansion of the spectrum of action of antibiotics and the constant release of more advanced drugs enhanced and maintained the antimicrobial effect, freeing up the field of activity for other representatives of the microbiome.

Suppression of the bacterial segment of the microbiome cannot ensure the sterility of the body tissues, since other microbiological agents fill the vacated space. For example, it is well known that prolonged courses of antibiotics can lead to the activation of a fungal infection, which is often a consequence of such treatment. Moreover, inflammation of fungal etiology usually does not have the aggressiveness that is inherent in bacterial processes. At the same time, as the events of recent years show, the widespread use of antibacterial therapy has become the main cause of constant shifts in the etiology of nonspecific inflammatory processes of the lungs and, ultimately, contributed to the growth of viral forms of the disease.

What has been happening with the etiology of AP for many recent years is one of the consequences of long-term and widespread use of antibiotics. This statement can currently be presented only as a postulate, since it does not yet have sufficient arguments for its absolute confirmation and at the same time cannot be rejected due to the presence of compelling signs. Nevertheless, this postulate should be used as an important guideline for further research on the problem of AP and assessment of the origin of the disease.

The growth of viral forms of AP can be traced in the features of the current SARS-CoV-2 pandemic. The lack of convincing and long-term vaccination results, as well as multiple changes of pathogen strains in a relatively short period of time, more resemble an outbreak of growing viral expansion than an infectious catastrophe scenario. However, approaches to finding effective help for viral pneumonia remain tied to the lost positions of antibiotics, and ideas about the essence of the disease are based on the concept that arose under the didactic influence of this therapy. Without the elimination of existing misconceptions, further progress in the treatment of this category of patients remains unattainable.

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Cite this article

Klepikov I (2022) The Era of Viral Pneumonia. Clin Res Pulmonol 8(1): 1050.