The Didactics of Acute Lung Inflammation

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This book is dedicated to my beloved daughters Yulia and Elena, who are always a source of inspiration in my work.

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ABBREVIATIONS

AP-acute pneumonia;

ARDS - Acute respiratory distress syndrome;

BSC - body surface cooling;

CAP-community-acquired pneumonia;

COVID-19 – coronavirus disease;

CPT – cupping therapy;

CRPG – comparative reopulmonography;

CVSB- cervical vagosympathetic blockade;

EP - Empyema of the pleura;

GBC - general body cooling;

HR - heart rate;

ICU- intensive care unit;

K v/p - coefficient of ventilation-perfusion ratio;

LG - lung gangrene

MBF - minute pulsatory blood flow;

MERS - Middle East respiratory syndrome;

MRSA - methicillin-resistant Staphylococcus aureus;

MTS – microtracheostomy;

MV - minute volume of ventilation;

PE - pulmonary embolism;

PM – Pneumomediastinum;

PP – Pneumopericardium;

RPG – reopulmonography;

RR – respiratory rate;

RV - respiratory volume;

SA - systolic wave amplitude;

SARS - severe acute respiratory syndrome;

VATS - video-assisted thoracic surgery

FROM THE AUTHOR

The successes and achievements of modern medicine surprisingly bypass the actual and widespread problem of acute inflammatory processes of lung tissue. In this section of medicine, the situation has not only not changed for many years, but, according to statistics, it tends to gradually and steadily worsen. This is all the more strange because acute pneumonia is considered one of the oldest nosological forms, which has been observed and studied throughout the entire historical period.

In medicine, there is a wise and business tradition to bring all controversial and unresolved problems to public discussion, as well as to present the results of their own research to a wide audience. The information below is a combination of these circumstances. Unlike the vast majority of works published on this topic and devoted to its currently relevant features and details, in this case we are talking about the principles of solving the problem, which depend on the existing concept of the disease. It is the strategy of solving the problem that determines the direction of scientific research and the success of applying the results obtained. Mistakes and misconceptions that arise in the process of forming general ideas about the subject of attention are the main obstacle to achieving the goal.

Attention is drawn to the origins of those didactic distortions that formed the problem of acute inflammation of the lung tissue in its current form. No matter how unexpected and stunning it may sound, but the main reason for the current state of this problem is connected with one of the greatest discoveries of medicine of the last century, which are antibiotics. The phenomenal success of this antimicrobial therapy has narrowed the idea of the essence of the disease to the leading role of its causative agent. Today, this

interpretation of the causes of pneumonia, despite significant changes in its etiology, remains an anchor that does not allow to move this problem from its place, and antibiotics, having lost their broad significance and initial effectiveness, continue to figure in the image of the main hope.

The modern ideology of acute inflammation of the lung tissue has been formed for many years under the influence of the priority of antibiotics. At present, firmly internalized stereotypes continue to serve as the basis for finding solutions in new situations and are not questioned, despite the presence of inconsistencies and refuting facts.

This feature of the problem under discussion goes beyond the scope of clinical medicine and is already an object of study in other disciplines. Such misconceptions, which gradually cover the consciousness and perception of an increasing part of society, despite the contradiction with existing facts and circumstances, are defined in modern psychology and sociology as a *“destructive meme”*. The ability of such defective material to further spread is designated by the term *"information cascade"*. These are just the factors that can serve as a vivid example of the psychological consequences of the use of antibiotics. However, the purpose of this work relates exclusively to the affected clinical topic, especially since the author is not a professional psychologist.

The information presented below includes, first of all, fundamental, well-known materials of medical science, which underlie professional ideas about inflammation and dysfunction of the affected organ, but which are not given sufficient attention in the modern concept of the disease. These materials were supplemented with the results of special studies and clinical trials.

Taking into account the imperative of the generally accepted concept of the disease in modern healthcare systems, as well as the fact that the duties of doctors and the limits of medical actions in any region of the world are determined by local laws and

regulations, this manuscript is offered as an informational message. Such material for reflection is necessary today and will be useful to every specialist related to the section of acute inflammatory processes of the respiratory system. The proposed information summarizes the facts and objective evidence of existing inconsistencies and contradictions in understanding the nature of acute pneumonia, which during the SARS-CoV-2 pandemic turned into a diagnosis that frightens patients and causes pessimism among medical personnel.

Today, emergency care for patients with severe pneumonia is based on analogies with other inflammatory diseases, including terminology and causes of common complications. Monitoring of the condition of patients and evaluation of the effectiveness of treatment in patients with acute pulmonary pathology is carried out according to the same standards as in other variants of inflammatory processes. A common way to determine the effect of the tested therapy is to compare the dynamics of various cellular and molecular constants in the body, which do not allow us to assess the impact of a particular technique on the dynamics of the process and do not always reflect its clinical effectiveness.

Emergency care methods, which are currently widespread in patients with acute pneumonia, are palliative and supportive treatment. Modern treatment of such patients, especially with aggressive development of the disease, does not guarantee a favorable outcome, and often the negative dynamics of the process is observed against the background of intensive treatment and despite it. One of the main axioms of medicine, reflecting its purpose throughout history, says: if treatment does not bring relief to the patient and even more so does not prevent the further development of the disease, then such assistance does not correspond to the nature of the process, does it? This is one of the main issues underlying the following text.

In the current situation, the proposed information should serve as a reason to change the principles of monitoring patients with acute pneumonia. In particular, it is necessary to shift the priorities of control towards the dynamics of the main process and especially blood flow in the small circle of blood circulation, and not on the periphery, as it is customary to assess now, fixing attention on the consequences of the process instead of its main mechanisms. Such monitoring will first of all help to understand the reasons why the results of modern treatment of this category of patients do not have the desired effectiveness.

The general consequences of prolonged use of antibiotics are a topic of separate discussion, but the impact of this type of therapy on the problem of acute inflammation of the lung tissue, including its terminology, turned out to be more noticeable and tangible than in other diseases. Various variants of the designation of one process, such as community-acquired pneumonia, hospital pneumonia, COVID-19 pneumonia and others, are the product of the microbiological theory of the disease that dominates today and reflect mainly the supposed etiological characteristics, and not the scientific essence of the problem. Therefore, the following materials are purposefully devoted to one nosological form of the disease, which has been known to medicine throughout its centuries-old history as *"acute pneumonia"* (AP).

The term "AP" is used in the text as a single reflection of this nosological form, which continues to be divided into various variants in accordance with the assumed etiology. Modern classifications are declarative in nature and do not bring real practical benefits, pursuing only the choice of etiotropic therapy and concentrating all attention on one of the fragments of the whole problem. The absence of accurate and reliable differences in AP depending on the etiology of the process indicates the general basis of the disease, regardless of the pathogen. Various terms in the text are used only to denote information that is discussed in a particular fragment, and repeated descriptions of some materials allow us to

show in more detail their significance in the overall process and their relationship with other factors.

The work, the results of which formed the basis of the information presented below, was started more than 40 years ago, so its results may cause distrust and doubts about their significance and reliability for modern conditions. At that time, the author found himself in a situation where the local geography of aggressive forms of AP and the concentration of such patients in one department was an unusual and unique phenomenon. Over the past decades, there have been changes in the development of this disease, which have led to the spread of similar situations around the world.

The role of viruses in the development of AP has increased significantly. The inability to clearly separate the bacterial and viral forms of the disease led during the SARS-CoV-2 pandemic to the need for widespread use of antibiotics and concentration of patients with AP in specialized departments. The phenomenon of combining severe patients in one workspace made it possible to more clearly see the insufficient effectiveness of medical care, but the general principles of solving this problem and the desire to find a way out of the current situation remained the same as forty years ago.

The purpose of the information presented below is to draw the attention of a wide range of specialists to distortions of the essence of the AP problem, which contradict the basic medical and biological laws and real facts. Among the various factors of the development and course of the disease, a clear preference is given to the pathogen, and the probability of success is inextricably linked with the hopes for etiotropic therapy. The persistent desire to succeed with the help of learned patterns and schemes that have developed over the period of antibiotic use, in fact, leave unclaimed the unique features of the pathogenesis of the disease.

Over the past decades, one can observe a periodic change of the leading pathogens of AP, the appearance of which adds a new

terminology to the classification of the disease, reflecting its etiology, but does not change the foundations of this nosology. So, recently the term "COVID-19 pneumonia" has become widespread, which does not have clear differential diagnostic differences from bacterial forms of the disease (with the exception of microbiological tests). The mechanisms of the pathological process that distinguished AP from other localizations of inflammation have been the main characteristic of this disease throughout its history and will influence the features of its course regardless of our perception. The preservation of the current concept of AP only complicates the situation and makes it difficult to find a rational solution to this problem.

INTRODUCTION

WHY IS SUCH A BOOK NEEDED?

Among the nosologies known to modern medicine, acute pneumonia (AP) is one of the most ancient. Throughout its long history, AP has been considered a formidable disease with a severe course and high mortality. The unprecedented successes of the last few decades in many areas of medicine, the achievement of a fantastic level of modern diagnostics and pharmacology, impressive progress in the technical support of all stages of medical care create today, especially among residents of developed countries, an aura of reliability of health systems and a sense of confidence in the effective elimination of most existing threats to our health. This belief is not only fully justified, but also has read confirmation by the results of prevention and treatment of various pathologies.

But, it is only necessary to switch attention to the topic of AP, and you can see a situation that today does not correspond to positive assessments in any way. For many recent years, the results of AP treatment reflect a decrease in the effectiveness of medical care with a gradual increase in the number of complications and an increase in mortality rates. A more detailed analysis of the state of this problem shows that various attempts that have been made in recent decades to change this negative trend have failed to slow down this course. The current situation in this section of medicine creates a very real impression that the long history of acquaintance with this disease has not helped much in its study, and the rise of medical science and its successes bypass the affected topic.

Currently, AP remains one of the leading problems of medicine in all regions of the world, including developed countries with the most advanced healthcare systems and the latest achievements of medical science. The effectiveness of modern AP treatment is most accurately characterized by mortality rates that reflect situations lost by medicine. Thus, according to the World Health Organization, in 2016, 3 million people worldwide died from lower respiratory tract infections, the main place among which is occupied by AP (1). Among other diseases included in the infectious group, AP ranks first in the number of deaths, which account for 5% for outpatient patients, 12% for hospitalized patients and reach 30% for those who are placed in intensive care units (2).

It should be noted that for many decades, antibiotics were considered the main treatment for AP, but their effectiveness gradually decreased. In this regard, many efforts have been made in recent years to identify the microbe responsible for the disease, in order to start targeted treatment as early as possible. For this purpose, acute inflammatory processes in the lungs began to be divided into separate subgroups in accordance with the conditions in which the disease develops, which implies the probability of different etiologies of AP. Therefore, one of the most "mild" types of AP is the so-called community-acquired pneumonia (CAP), the mortality rates from which have just been presented above. Other variants of AP provided for by this classification, such as, for example, hospital-acquired or ventilator-associated pneumonia, occur, as can be seen from the names, in more difficult conditions and have an even higher mortality rate.

The fact that acute inflammation of the lung tissue remains in the group of the main causes of death for an infinitely long time is the basis for a deep and comprehensive analysis in order to clarify the factors of such stability. For example, in the United States of America, AP is constantly among the ten most deadly nosologies (3), and in Europe it is the fifth most important cause of death (4). These indicators demonstrate the situation in the most prosperous

regions of the planet. If we make such calculations on the scale of the world community, then, as the WHO materials show, acute lower respiratory tract infections occupy the fourth place among the causes of death of people (5).

The above statistics relate only to bacterial forms of AP, which, according to popular beliefs and general confidence, at this stage is provided with the highest possible level of medical care. At the same time, no one focuses on such a rather strange circumstance as the treatment of completely incomparable (except etiology) inflammatory diseases with one antibiotic. These drugs are considered as the main therapeutic agent for a wide range of processes, including AP, although they are used empirically, that is, mainly taking into account existing assumptions about the etiology of a particular case, experience, capabilities and preferences of the attending physician (6-10).

In addition to the peculiarities of the choice of antibiotics for patients with AP, it should be recalled that for many years the steady growth of viral lung infections has caused concern among specialists, and the number of cases of viral pneumonia reported annually has reached 200 million (11-13). This figure, which at the time of its publication accounted for almost half of all AP observations in the world, is twice (!) the annual number of people infected (!) during the current SARS-CoV-2 pandemic. At the same time, medicine is already familiar with the coronavirus and its consequences, which have caused at least two major epidemics - SARS and MERS (14). However, the observed trend of shifts in the etiology of AP did not entail a radical analysis, a change in the strategy of the disease and the resulting principles of treatment.

Despite the growing trend of viral etiology of AP, the focus continued to be on the bacterial factor, which remained the main goal of therapeutic efforts, and antibiotics continued to be considered the "cornerstone" of therapy for these patients (6,15). The appearance in such an atmosphere of a large number of

patients with COVID-19 pneumonia, against the causative agent of which the main "anti-pneumonic" remedy turned out to be incapacitated, turned out to be unexpected for most specialists. The new conditions violated the previous treatment stereotypes, which were actually focused on the antimicrobial approach, and clearly demonstrated the lack of comprehensive treatment for this localization of inflammation.

The feeling of a sudden loss of rational treatment of AP today is the reason for the intensive search for new means of etiotropic effects, which continues to focus steadily on the leading role of the etiology of the disease and is carried out in a "combat situation". At the same time, as A. H. Attaway and co-authors rightly point out (16), modern respiratory care revolves around auxiliary measures.

Despite the dramatic transformation that occurred both with the etiology of the inflammatory process in the lungs and with its treatment, there were no significant changes in the statistical results during the SARS-CoV-2 pandemic. 80% of patients infected with coronavirus tolerate this contact on an outpatient basis and without special medical care. At the same time, at least a quarter of them learn about this event only through diagnostic tests, since they have no signs of the disease (17-20). It is easy to see that this is the same 80% as in the outpatient group among patients with CAP (2). The only difference is that during a pandemic, the total figure takes into account the number of infected people, while the CAP statistics show only cases of the disease.

The statistical proportions have hardly changed among hospitalized patients, who during the pandemic make up the same 20% of the total contingent of coronavirus infected as hospitalizations among patients with CAP. However, it is the results of inpatient treatment that are of greater interest for reflection, since it is possible to compare a group of patients with CAP who receive optimal treatment in accordance with modern standards, and patients with COVID-19 pneumonia, whose medical care is supportive and

symptomatic. No matter how surprising the result of such a comparison may seem, the fact is obvious - there is no significant difference in the main statistical indicators. For example, the percentage of patients who need to be transferred to intensive care units and the mortality rate reaching 30-50% in both groups (21-29) require an in-depth analysis of the current situation.

Despite maintaining the stability of the main statistical indicators, the emergence of the SARS-CoV-2 pandemic has significantly worsened the psychological situation. If earlier the CAP refers to infectious diseases, but did not require strict epidemiological measures, now the rapid and easy spread of the coronavirus has forced them to comply. To the contagiousness of this infection was added the uncertainty of a favorable outcome in the case of the disease. Although we are talking only about the spread of the pathogen, and not about the transmission of inflammation of the lung tissue, but the usual hope for antibiotics has lost its relevance. Finally, the epidemiological situation forced to change the rules for hospitalization of patients with COVID-19 pneumonia. Now, severe respiratory patients began to concentrate in specialized departments for this pathology.

The organization of specialized departments to combat coronavirus was not just a heavy, but an extremely heavy burden for the medical staff working in them. If earlier such patients were distributed to different departments, which significantly reduced the atmosphere of tension, now there are clusters of the most severe clinical situations when each patient requires extreme attention and super-maximum efforts. The aggressive dynamics of the disease and the rapid change of situations in each patient require immediate solutions and timely correction, but, most importantly, the percentage of observations in which the efforts expended were unsuccessful turned out to be too high. A reflection of such organizational movements turned out to be a whole series of articles devoted to mental shocks and depressive moods among employees of such specialized units (30-36).

The author of these lines found himself in a similar situation at the dawn of his career. At that time, the world was gripped by the so-called "staphylococcal catastrophe". A large number of patients with severe forms of AP appeared, which more often affected children, were characterized by rapid development and high mortality, and pathogenic strains of staphylococcus were considered the cause of this. The provision of medical care to this contingent of patients in a large Siberian city, where the author began working, was put in critical conditions. Most of the small city hospitals where such patients were admitted were not ready to provide intensive care, which newcomers often needed. In this regard, the city health department decided to hospitalize all patients with aggressive onset of AP in the surgical department of a multidisciplinary hospital, which worked in close contact with the intensive care unit.

The only difference between the circumstances in which the author found himself and the current concentration of patients with COVID-19 pneumonia was the absence of an epidemic situation. Otherwise, the intense atmosphere of work was ensured by the presence of 10-15, and sometimes more than 20 severe patients with AP at the same time in the department.

It should be noted that the very change in organizational measures to provide medical care to patients with AP did not significantly affect the results of treatment. The most severe category of these patients had the opportunity to be in the best observation conditions for that time and received optimal treatment in accordance with international standards. However, the dynamics of inflammatory processes was characterized by aggressive development, rapid addition of pleural complications and high mortality, which exceeded 10%. Such results forced us to look for ways to improve the effectiveness of therapeutic measures, and the first doubts about the adequacy of the therapy arose at the moment of realizing that staphylococcus is not the main cause of such a severe and complicated course of AP.

While all the information on this problem presented staphylococcus as the main cause of the crisis, and the professional literature was overflowing with reports about the exceptional virulence of this pathogen and options for its suppression, the real facts contradicted the validity of such a concept. Bacteriological studies of purulent contents from the inflammatory zone already at the early stages of the disease revealed other types of pathogens, and often such material for research turned out to be sterile.

To the doubts that arose about the leading role of etiotropic treatment in AP, uncertainty was added in the correct choice of a number of treatment methods, which from general therapeutic practice were transferred to the exceptional conditions of localization of the focus of inflammation in the small circle of blood circulation. In the end, a lot of research work was started, which was based on a radical revision of the entire concept of AP. The result of this work and clinical approbation of pathogenetic principles of treatment was a unique success of therapy with the possibility of guaranteed prevention of complications of the disease.

The combination of a number of circumstances did not allow timely translation and presentation of the results achieved to a wide range of specialists at the international level. However, over the past period of time, inconsistencies between existing ideas about the nature of AP and real facts, which are especially inherent in the most acute forms of the disease, have not only not become a thing of the past, but, on the contrary, have become more pronounced. In this regard, the importance of the results of the work done earlier to solve the problem of AP in its current state has only increased.

It should be noted that in recent decades there has been a periodic change of the leading pathogens in the etiology of AP, which was reflected only in tactical nuances. The information base of scientific data on the topic under discussion has also expanded significantly in recent years, but the strategy for solving the problem has not changed. Today, the desire to find a universal drug that can help

with the development of AP, especially with its aggressive course, and bring, if not instantaneous, then a very rapid positive effect, continues to prevail. Such illusory hopes were formed and strengthened in the process of reducing the effectiveness of antibiotics, stimulating the search for equivalent replacements, and continue to determine the directions of ongoing research under the influence of the established AP concept.

Today, a broad but fruitless search for etiotropic antiviral drugs continues in the hope of repeating the success of the initial use of antibiotics and again achieving a revolutionary breakthrough in the treatment of AP (37). However, the absence of direct parallels when comparing antibacterial and antiviral methods of exposure remains beyond the scope of discussion. Currently, efforts are being made to find therapeutic options for blocking the penetration of viruses into the cell. That is, there are searches for ways to prevent the disease, and not medical care when it occurs.

When viral pneumonia has already been diagnosed, by this time the virus has not only "hidden" in the cells, but also contributed to the development of inflammatory changes in tissue structures. Those manifestations of the disease that we can see and evaluate in clinical conditions are the result of organ damage and disruption of its functions, but not a reflection of the characteristics of the pathogen. After all, bacterial forms of pneumonia have similar manifestations, and therefore, in most cases, it is extremely difficult or impossible to make a differential diagnosis between them according to etiological signs, isn't it? Therefore, drugs that can prevent the virus from entering the cells can, at best, prevent the further spread of the process, but cannot provide the necessary therapeutic effect of the disorders that have already occurred.

Dreams of creating a universal etiotropic treatment for pneumonia largely determine today's plans and directions in solving the problem of AP. No, no one claims the need to develop a so-called "pneumonia pill", which a priori cannot exist in nature, but the main

efforts of research and clinical trials are aimed at finding remedies against the pathogens of AP. Stereotypes of ideas that have arisen as a result of prolonged use of antibiotics continue to dominate the interpretation of changes occurring in the etiology of AP.

The exclusively antimicrobial effect of antibiotics was initially used as an additional agent in the treatment of AP, which corresponded to its main pharmacological characteristic. However, in the future, contrary to logic and professional ideas, this type of therapy began to be interpreted as the only and main method of treating acute nonspecific inflammation (!), and the initial treatment of patients with AP was for a long time designated by the term "antibiotics alone".

The periodic change of the main pathogens of AP observed in recent decades has clearly shown that the type of pathogen does not determine the severity of the course and features of the development of the disease. For example, clinical manifestations of bacterial forms of AP did not allow to determine the type of pathogen in each specific case for a targeted choice of antibiotics. Antimicrobial action as the basis for the treatment of this group of patients posed the task of accurately diagnosing the etiology of the process, which researchers had unsuccessfully tried to solve for many years, although the answer lay on the surface: the stability of the disease clinic, regardless of the etiology, was due to a constant violation of lung function as a result of the development of the inflammatory process.

Microbiological factors in the development of AP can influence certain nuances of inflammatory tissue transformation and some clinical and laboratory shades of the process, but even with the help of special diagnostic methods, it is not always possible to identify and determine those features that depend on the etiology of the disease, which is nonspecific in nature. At the same time, the focus of inflammation by its occurrence inevitably affects the function of the affected organ, determining, depending on the localization, all

the further originality of the clinic. That's why inflammation in the lung cannot be confused with inflammation of another localization, for example, with osteomyelitis, sore throat or hepatitis, right?

A detailed acquaintance with the modern strategy for solving the problem of AP allows us to note that it is focused on the etiology of the disease, but does not attach due importance to a number of important axioms of medical science. Having recently received a large influx of patients with COVID-19 pneumonia and having lost the possibility of using specific treatment methods in this group of patients, medicine finally drew attention to the need to revise strategic directions for solving the problem. During the SARS-CoV-2 pandemic, publications with proposals for revising general approaches to helping with inflammatory lung processes became more frequent.

When the solution of the problem by existing methods does not bring the expected results, the analysis and revision of the current strategy is absolutely the right and logical step from which to begin the search for new developments. However, the materials proposed today concerning changes in strategic solutions to the AP problem actually contain only individual tactical techniques, while maintaining the suppression of the pathogen of the process as the main goal (38-44). Thus, in addition to the indicated desire to change the basis of strategic approaches to solving this problem, no real changes in the strategy have yet been proposed.

The strategy for solving the AP problem depends entirely on our conceptual ideas about the nature of the disease. The introduction of any new proposals to the list of therapeutic measures, the interpretation of their expected effect and even the explanation of the results of their testing will be determined by our understanding of the essence of the development of the process. At the same time, the process that has arisen will develop according to its biological laws, regardless of how we imagine and understand it, right? Such a course of events in the absence of additional external influences

remains a natural variant of the development of the disease, which has its own individual characteristics.

However, when there is a need to provide medical care to patients with AP, professional recommendations are inevitably determined by prevailing ideas about the nature of the disease and, consequently, the existing concept. In this case, the treatment is an intervention in the natural course of the process, and its results will depend on the nature and direction of therapeutic actions. As experience and facts show, therapeutic measures can have a certain impact on the dynamics of the disease, and such an impact can be both positive and negative.

Thus, a detailed study of the causes that currently do not allow finding an effective solution to the problem of acute inflammation of the lung tissue shows that the main obstacle is the nature of the mental perception of the nature of the disease at the professional level. Justification of the existing misconceptions in this section of medicine, facts and objective evidence of such a conclusion are presented in the proposed publication. Such information is necessary today for a wide range of specialists related to this category of patients, and therefore the publication of the proposed materials should play the role of an explanatory manual, which is extremely necessary for understanding the current situation.

CHAPTER 1

A BRIEF HISTORY OF TREATMENT OF ACUTE PNEUMONIA

1.1. Pre-antibiotic period

AP has been familiar to medicine since the time of Hippocrates for more than two and a half millennia (45). However, despite such a long history and wide progress of medical science, the problem of effective treatment of these patients not only remains unresolved, but, contrary to logic and expectations, its relevance and acuteness in recent decades continue to grow worldwide.

Historical experience in any discipline is invaluable for its future, as studying the results of previous practice allows you to use and develop previous successes and achievements at a new level, but at the same time avoid the mistakes of the past. Looking from these positions at the current state of the AP problem, it seems that this disease, which has one of the longest histories in medicine, does not have worthy results of centuries of experience.

Today we can say with confidence that the history of AP treatment is divided into two fundamentally different periods. Initially, for many centuries, medicine scrupulously accumulated experience and information about methods of treating this disease. This lengthy process was purely empirical. The constructiveness of such searches was very difficult, unproductive and often tragic. The lack of basic medical knowledge and scientific ideas about the laws of the biological world, dubious plans and the lack of technical support for ongoing tests and research were difficult obstacles. Nevertheless, over a long period of time, certain medical traditions and a set of