



### **Review Article**

# Will the pill help defeat the coronavirus?

## Igor Klepikov\*

MD, Professor, Renton, Washington, USA

The onset of the pandemic has caused widespread concern about the rapid spread of the infection and serious concern about the lack of specific treatment for it. Calls and demands for strict compliance with sanitary and anti-epidemic measures, a sharp reduction in direct contacts and movements of people with the introduction of quarantine measures in large regions and even countries have become a familiar modern reality. All these efforts do not yet allow us to see and feel their positive results, and the next wave of infection destroys hopes for the likelihood of achieving rapid and complete success in the fight against this evil. At the same time, a detailed analysis of the material accumulated during this period allows us to identify the most problematic links in the process of diagnostics and providing care to such patients and to note the reasons that require priority solutions.

Currently, the primary diagnosis of coronavirus infection is based on specific testing covering a heterogeneous population group. Among those examined, many do not have any signs of infection and remain asymptomatic carriers in the future. The proportion of this group in the total number of infected people varies greatly in different parts of the world and depends, in particular, on the breadth of testing. Such cases only require isolation and observation, and such patients do not need medical care.

Despite such a successful fate, patients in this group are of great interest for conducting analytical assessments. First of all, no one can indicate even the approximate number of such cases around us. Such statements require the results of almost total testing, which is difficult to imagine even theoretically. Second, such hidden carriers of an infectious agent are a source of infection spread, without attracting attention until a test is performed. Therefore, no one can foresee where, when, and during what contact they may become infected, but it becomes an obvious necessity to observe all precautions in this regard. Finally, the example of this group of observations clearly shows that the very fact of infection does not mean that the disease is imminent, and many of our environment perfectly tolerate such a "meeting".

The next group, which has its own criteria for combining,



consists of patients who not only have a positive test confirming infection, but also show signs of a mild form of the disease. In this case, we are talking about patients with a coronavirus infection, whose appearance of signs of the disease is not accompanied by a noticeable deterioration in their condition and does not require hospitalization. Such patients carry the infection and disease independently, without resorting to professional medical care.

Thus, if we sum up the number of cases in the two abovementioned groups, these cases will make up the vast majority of the entire infected population. This correlation can be seen both in world statistics and in the dynamics of these indicators in individual countries. These figures show very clearly that the vast majority of cases of infection during the current pandemic pass without any serious consequences and, most importantly, without special medical assistance from professional medicine. According to statistics, it turns out that for the majority of infected people, the coronavirus does not pose such a deadly threat, which forces to take the most stringent quarantine measures in different regions of the world. And such indicators are already available even before the start of universal vaccination of the population.

An analysis of the last group of people infected with coronavirus provides an answer to the question of why strict quarantine conditions are imposed in many countries and why the current situation has such a strong psychoemotional impact. Representatives of this group have a disease clinic with negative dynamics and deterioration of their condition, which requires their hospitalization to provide the necessary



care and monitoring. If there were no such observations, the spread of the coronavirus infecting the population would hardly have attracted such close attention.

The main cause of disease and death in a pandemic is viral inflammation of the lung tissue. The latter circumstance underlies the severe clinical manifestation and provides additional diagnostic data. In this regard, it should be emphasized that the appearance of clinical and laboratory, radiological and pathoanatomic signs of inflammation (!) characterizes a new stage of infection development [1-5]. It is the development of viral pneumonia, as a rule, that marks further negative dynamics and creates unpredictability of the forecast. Therefore, the very fact of hospitalization of such observations does not cause any doubts, as well as the possibility of conducting comprehensive professional monitoring in a hospital setting. The whole essence of the problem is due to the actual lack of specific treatment of such patients in modern hospitals.

At present, the specifics of the development of the pandemic have focused General attention on the pathogen as the main and only cause of all the observed disasters. At first glance, this approach seems logical in light of the danger and spread of infection. The natural solution to the problem with this understanding of its essence is to search for and use drugs to suppress the pathogen itself. Versatile approaches in this direction do not yield any tangible results [6-10]. In this situation, it is not only that such searches can take a long time when many patients need effective help right now, but that previous experience of dealing with the causative agent of acute pneumonia (AP) is not fully understood and not internalized. In this regard, it is very important to clarify the priorities of various aspects of the disease in its dynamics and how to provide emergency care at different stages of its development.

Means of suppressing inflammatory pathogens have a strictly selective effect. A lot of experience in this area has been accumulated during the period of use of antibiotics. The use of these drugs at the time of development of inflammatory changes in the lung tissue led to the elimination of the pathogen as one of the causes of the disease, leaving the resolution of the already completed inflammatory transformation of tissues to the body itself. Using the principle of "only antibiotics" as the main method of treating AP for decades allows us to evaluate the effectiveness of such efforts.

The greatest effect of such point therapy was observed in the initial period of its use. As the resistance of microflora increased, new types of drugs and the introduction of additional means of assistance were required. In recent years, the success rate of such treatment has continued to fall, and the most vulnerable group of patients with AP has been concentrated in emergency departments during treatment, with a mortality rate of up to 50% [11-15]. Instead of analyzing the unique features of AP development in contrast

to other localizations of inflammation of the same etiology, all observed treatment failures were explained by the special virulence of pathogens. At the same time, special attention was not paid to such facts as, for example, the treatment of fundamentally different diseases with one antibiotic or the appearance of so-called sterile purulent pleurisy.

The sudden invasion of coronavirus broke the usual stereotype of treatment, although in this case the characteristic of surprise is very relative, since coronavirus epidemics have already been observed in the recent past, but have not led to a change in views on the essence of the problem [16]. Since the beginning of the pandemic, there has been only one significant change: medicine has lost moral hope for antibiotics. If earlier, when prescribing antibacterial therapy, every doctor, regardless of further results, considered such treatment a duty performed at the level of scientific justification, now this therapeutic and moral trump card has devalued. However, it should be noted that from 70% to 89.5% of patients with coronavirus continue to receive antibiotics, despite the lack of sense in their use and the presence of bacterial co-infection only in isolated cases [17-20], and in the UK cases of COVID-19 pneumonia are included in the care program together with patients with community-acquired pneumonia [1].

Otherwise, the current situation roughly repeats the dynamics of the distribution of patients with AP in terms of aggressiveness and severity of the course, which was observed before the outbreak of the pandemic. To make sure of this, it is enough to take another look at today's COVID-19 statistics, which we discussed above. Of course, there are quite significant differences between these groups of patients. Previously, patients with AP received a treatment package that was considered reasonable, and the disease itself was not contagious and had a wide range of pathogens.

At the moment, when analyzing patients with COVID-19 pneumonia, all specialists emphasize the lack of special treatment, the pathogen has the ability to spread quickly, but the infection itself remains monoetiological. Despite such a significant difference, especially in terms of treatment, the final results do not differ significantly from the previous ones. Overall mortality among hospitalized patients reaches 20% [21[, and the mortality of coronavirus patients concentrated in emergency departments is comparable to this indicator in bacterial forms, rising to the same 30% - 50% [22-24].

Today, a patient with coronavirus pneumonia during hospitalization can only count on oxygen insufflation with subsequent transfer to artificial ventilation. These procedures cannot change the dynamics of the disease, as they are supportive, not therapeutic. At the same time, the mortality rate among patients who were on assisted ventilation even increases [24]. However, comparing the results of treatment of patients with AP in the pre-pandemic period and at the present time, two undoubted circumstances draw attention to themselves.



First, the infinite variety of options for the course of coronavirus infection, from asymptomatic cases to critical conditions, convincingly demonstrates how nature, in the absence of medical intervention, sorts its patients by severity. A similar division of patients according to the severity of the disease was observed earlier, when patients received modern treatment for bacterial forms of AP. This raises the question of the second factor: how effective was this treatment and did it affect the results?

This statement of the question is not purely rhetorical and does not follow only from the comparison of statistical data. First, for many years, antibacterial therapy was extended and continued in patients with AP as long as x-ray signs of inflammation persisted. In other words, signs of inflammatory transformation, rather than the presence of a specific pathogen, served as a guideline for the duration of antibiotic use, but recently there has been a growing interest in the use of antibiotics in short courses, which does not worsen the final results [25-28].

Secondly, the reduction in the duration of treatment with antibiotics was not dictated by their narrow antimicrobial effect and the lack of direct influence on the inflammatory process. Published materials indicate that these recommendations are due to an increase in the number of pulmonary inflammations of viral etiology, the lack of a clear understanding of the pathogenesis of AP, and the desire to maintain the usual method of treatment in the absence of others.

Third, at the time of development of inflammatory transformation in the lung tissue, these changes disrupt the function of the affected organ and come out on top among the causes that require emergency correction. Antibacterial therapy at this stage of the disease is of secondary importance and auxiliary in nature, which is especially noticeable in the aggressive development of the inflammatory process. The latter position was proved and confirmed by clinical materials much earlier, when the therapeutic priority of antibiotics did not cause the doubts that are observed now [29].

Assessing today the main cause of the severity of the condition of patients with coronavirus infection, it should be borne in mind that the basis of the pathological process is an inflammatory transformation of the lung tissue with a typical violation of organ function. Functional disorders and pathogenesis of the disease in this situation do not differ fundamentally from other forms of AP, since, regardless of the etiology of inflammation, the same organ structures are affected. At the same time, coronavirus inflammation is characterized by a greater tendency to damage the vessels of the small circle, which can cause more severe circulatory disorders and vascular complications [3,5].

At the moment, no one knows and no one can accurately predict the probability of the disease and the severity of its development in the event of infection with coronavirus. According to statistics, the number of cases is significantly lower than the number of infected. The most dangerous variant of coronavirus infection is observed in the older age group, but this does not guarantee that a young and strong body will be able to avoid the critical development of the process. In order to have such foresight, it is necessary to know all possible options for primary immunological testing, which determine the further reaction of the body to external aggression, including viral. Today, medicine does not have such scientific foresight, and the lack of effective means of assistance in case of illness has a strong psychoemotional impact on medical personnel working on the front line [30-33].

The preference for antibiotics in the treatment of AP in recent years has become particularly convincing to demonstrate the shortcomings of such narrow efforts to suppress pathogens and neglect the role of the inflammatory process. The experience and lessons of long-term use of antibiotics are still poorly understood, as current discussions and practical efforts to find solutions to the problem of coronavirus infection continue the previous traditions of fighting the pathogen, leaving aside the fact of the development of pulmonary inflammation and all related disorders.

In this regard, the whole situation presented today clearly draws our attention to the fact that it is necessary to distinguish the mechanism of development of pulmonary inflammation from other forms of damage that occur in the area of the large circle of blood circulation. Nature, without our help, regulates the individual dynamics of the disease and distributes infected patients according to options for overcoming it, giving many of them the opportunity to successfully resist. The main task of medicine today is to understand the direction of natural compensatory and adaptive mechanisms in the case of AP development and find ways to support them, avoiding any counteractions. Such assistance to the body in critical situations, as previous experience shows, is literally (!) more important and effective than oxygen insufflation [29].

Long-term use of antibiotics for AP has many facts and arguments that refute the false idea that the treatment of this disease is consistent with a single drug. The use of antibacterial therapy has already reached a level where it is safe to say that the negative effects of these drugs are beginning to exceed its previous successes. Unfortunately, the lessons of this gigantic experiment on human intervention in natural proportions and balance of the biological world remains poorly understood, and the current debate and practical efforts to find solutions to the problem coronavirus infection continue old traditions for the elimination of the pathogen, leaving aside the Central fact-the development of lung inflammation and its impact on the functioning of the organism.

Today, medicine is trying to find antiviral agents, but at the same time it assesses the condition of the most severe group of patients not by the virulence of the pathogen, but by the degree



of inflammatory damage to the lung tissue, isn't it? When such patients are diagnosed with cardiovascular disorders, which are usually secondary to the main focus, their correction begins, without taking into account the fact that these indicators have a feedback relationship with the pulmonary blood flow. The lack of a clear understanding between cause and effect cannot provide a reasonable pathogenetic therapy for AP, so if intensive treatment is necessary, the shortcomings of the disease concept are reflected in its results.

The formation of a clinical worldview about the nature of AP with the priority value of its pathogen occurred over several generations. Therefore, despite the obvious misconceptions, the reform of views on this issue is unlikely to happen too quickly. Even if there is irrefutable evidence, it takes time to change the angle of view and perception of the phenomenon being studied. However, given the complex current situation and the likelihood of unforeseen surprises, we can offer for reflection the following information, which does not require any obligations, but is offered for the readers 'assessment and at the discretion of each in case of critical circumstances.

The formation of a clinical worldview about the nature of AP with the priority of its pathogen occurred over several medical generations. Therefore, despite the obvious, from my point of view, misconceptions, the reform of views on this issue is unlikely to happen too quickly. Even in the presence of irrefutable evidence, it takes time to change the angle of view and perception of the phenomenon being studied. However, given the complex current situation and the likelihood of unforeseen events, the following information should be offered for reflection, which does not require any obligations, but is offered for evaluation and at the discretion of everyone in case of critical circumstances.

In this case, we mean a situation in which not only an infection occurred, but also a clinic of pulmonary inflammation develops with an increase in signs of respiratory failure. If this situation progresses and its development catastrophically reduces the chances of a favorable outcome, then the further course of events has two most likely continuations: either rely on chance and wait for a possible transfer to auxiliary ventilation with an unknown outcome, or try to help your own body interrupt the cascade of pathological mechanisms of the disease.

The latter decision can only be made consciously by the patient himself, especially since in this case we are not talking about any specific means of assistance. In order to have a figurative idea of the nature of such an impact, it is enough to imagine yourself suddenly falling into an ice hole. This version of the extreme procedure is necessary for the body in the initial stage of pneumonia in order to avoid further escalation of the process. The essence of this procedure is to immerse the entire body and limbs in a bath with cold (preferably ice) water for a few minutes (up to 8-10, but no more). A guide to

the end of the procedure can serve as a persistent paling of the skin, the appearance of a feeling of chills and a decrease in shortness of breath. After that, you should dry your skin well, put on warm underwear and warm up well, adding a warm drink.

Elderly people and those who suffer from other diseases, it is better not to carry out this procedure alone, and people with problems of the cardiovascular system, especially of an ischemic nature, should avoid sudden immersion in cold water.

It should be noted that this procedure, despite its excellent effectiveness, cannot be considered as a legitimate recommendation for the conditions of official medicine. Any innovation in healthcare systems requires special permission. However, it is quite acceptable to present this material as ordinary information, as a "last chance" for complex and critical situations, especially when official medicine cannot perform its duties effectively enough.

The hope for the future development of drugs for coronavirus should not create a wait-and-see attitude when choosing care for the seriously ill, because even if such effective drugs appear and are used, they will not be able to have an absolute impact in aggressive and super-aggressive forms of the disease. there is an urgent need to bring the system of views on the nature of AP in line with the features of the inflammatory process in the lungs as a consistent biological phenomenon [34,35], which will require a revision of therapeutic approaches and will significantly improve the results.

### Conclusion

Clinical and radiological features of ap, as a separate nosological form, are determined by the development of the inflammatory process in the lungs and its unique pathogenesis. The etiology of AP performs the same role as the first stage of a rocket in cosmonautics, being one of the starting factors of the cascade of inflammatory changes in the parenchyma of the organ, but not having a fundamental impact on the further clinic of the disease. The change of AP pathogens observed in recent decades and the increase in the number of viral lesions have not made drastic changes in the clinical picture of this nosology, which remains dependent on its own localization, which determines the specifics of functional disorders. The necessary attention to the mechanisms of AP development will help to start using pathogenetic treatment methods that can radically improve the results and reduce the causes of social tension in society.

## References

 Lipman M, Chambers RC, Singer M, Brown JS. SARS-CoV-2 pandemic: clinical picture of COVID-19 and implications for research. Thorax 2020; 75: 614-616.

PubMed: https://pubmed.ncbi.nlm.nih.gov/32461230/



- Stone JH, Frigault MJ, Serling-Boyd NJ, Fernandes AD, Harvey L, et al. Efficacy of Tocilizumab in Patients Hospitalized with Covid-19. N Engl J Med. 2020; 383: 2333-2344.
  - PubMed: https://pubmed.ncbi.nlm.nih.gov/33085857/
- Ackermann M, Verleden SE, Kuehnel M, et al. Pulmonary Vascular Endothelialitis, Thrombosis, and Angiogenesis in Covid-19. N Engl J Med. 2020; 383: 120-128.
  - PubMed: https://pubmed.ncbi.nlm.nih.gov/32437596/
- Martines RB, Ritter JM, Matkovic E, Gary J, BollwegBC, et al. COVID-19 Pathology Working Group (2020). Pathology and Pathogenesis of SARS-CoV-2 Associated with Fatal Coronavirus Disease, United States. Emerg Infect Dis. 2020; 26: 2005-2015. PubMed: https://pubmed.ncbi.nlm.nih.gov/32437316/
- Englisch CN, Tschernig T, Flockerzi F, Meier C, Bohle RM. Lesions in the lungs of fatal corona virus disease Covid-19. Annals of Anatomy -Anatomischer Anzeiger. 2020; 234: 151657.
   PubMed: https://pubmed.ncbi.nlm.nih.gov/33279630/
- Beigel JH, Tomashek KM, Dodd LE, et al. Remdesivir for the Treatment of Covid-19 — Final Report. N Engl J Med. 2020; 383:1813-1826. PubMed: https://pubmed.ncbi.nlm.nih.gov/32445440/
- Simonovich VA, Pratx LDP, Scibona P, Beruto MV, Vallone MG. A Randomized Trial of Convalescent Plasma in Covid-19 Severe Pneumonia. 2020; N Engl J Med. 384: 619-629.
   PubMed: https://pubmed.ncbi.nlm.nih.gov/33232588/
- Mitjà O, Corbacho-Monné M, Ubals M, et al. A Cluster-Randomized Trial of Hydroxychloroquine for Prevention of Covid-19. N Engl J Med. 2020; 384: 417-427.
  - PubMed: https://pubmed.ncbi.nlm.nih.gov/33289973/
- WHO. Solidarity Trial Consortium. Repurposed Antiviral Drugs for Covid-19 — Interim WHO Solidarity Trial Results. 2020.
- Huang E, Jordan SC. Tocilizumab for Covid-19 The Ongoing Search for Effective Therapies. December 10, 2020. N Engl J Med. 2020; 383:2387-2388.
  - PubMed: https://pubmed.ncbi.nlm.nih.gov/33296566/
- Liapikou A, Rosales-Mayor E, Torres A. The management of severe community acquired pneumonia in the ICU. Expert Rev Respir Med. 2014; 8: 293-303.
  - PubMed: https://pubmed.ncbi.nlm.nih.gov/24838089/
- Kim JW, Kim JJ, Yang HJ, et al. The Prognostic Factors of Pneumonia with Septic Shock in Patients Presenting to the Emergency Department. Korean J Crit Care Med. 2015; 30: 258-264.
- Jason P, Dean NC, Guo Q, Kuan WS, Lim HF, et al. Severe community-acquired pneumonia: timely management measures in the first 24 hours. Crit Care. 2016: 20: 237.
   PubMed: https://pubmed.ncbi.nlm.nih.gov/27567896/
- Vidal A, Santos L. Comorbidities impact on the prognosis of severe acute community-acquired pneumonia. Porto Biomed J. 2017; 2: 265-272.
   PubMed: https://pubmed.ncbi.nlm.nih.gov/32289091/
- Ceccato A, Torres A. Sepsis and community-acquired pneumonia. Ann Res Hosp. 2018; 2: 7.
- 16. https://en.wikipedia.org/wiki/Severe\_acute\_respiratory\_syndrome
- Rawson TM, Moore LSP, Zhu N, Ranganathan N, Skolimowska K, et al. Bacterial and fungal co-infection in individuals with coronavirus: A rapid review to support COVID-19 antimicrobial prescribing. Clin Infect Dis. 2020; 71: 2459-2468.
  - PubMed: https://pubmed.ncbi.nlm.nih.gov/32358954/
- Beović B, Doušak M, Ferreira-Coimbra J, Nadrah K, Rubulotta F, et al. Antibiotic use in patients with COVID-19: a 'snapshot' Infectious Diseases. International Research Initiative (ID-IRI) survey. J Antimicro

- Chemotherapy. 75: 3386-3390. PubMed: https://pubmed.ncbi.nlm.nih.gov/32766706/
- Kim D, Quinn J, Pinsky B, Shah NH, Brown I.. Rates of co-infection between SARS-CoV-2 and other respiratory pathogens. JAMA. 2020;
  - PubMed: https://pubmed.ncbi.nlm.nih.gov/32293646/

323: 2085-2086.

- Ocampo-Torres M. Characterization of Mortality by Covid-19 in a Health System in Central Mexico. EC Pulmonology and Respiratory Medicine. 2020; 9: 20-22.
- Boëlle PY, Delory T, Maynadier X, Janssen C, Piarroux R, et al. Trajectories of Hospitalization in COVID-19 Patients: An Observational Study in France. J Clin Med. 2020; 9: 3148.
   PubMed: https://pubmed.ncbi.nlm.nih.gov/33003375/
- 22. Seligman R, Seligman BGS. Pandemic in the 21st Century. The Challenge of COVID-19". EC Pulmonology and Respiratory Medicine. 2020; 9: 30-31.
- Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, et al. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy region, Italy. JAMA. 2020; 323: 1574-1581.
  - PubMed: https://pubmed.ncbi.nlm.nih.gov/32250385/
- Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. JAMA. 2020; 323: 2052-2059.
  - PubMed: https://pubmed.ncbi.nlm.nih.gov/32320003/
- WHO classification and treatment of childhood pneumonia at health facilities. Geneva: World Health Organization, 2014. https://apps.who. int/iris/bitstream/handle/10665/137319/9789241507813\_eng.pdf
- Jehan F, Nisar I, Kerai S, Balouch B, Brown N, et al. Randomized Trial of Amoxicillin for Pneumonia in Pakistan. N Engl J Med. 2020; 383: 24-34.
   PubMed: https://pubmed.ncbi.nlm.nih.gov/32609980/
- Chang AB, Grimwood K. Antibiotics for Childhood Pneumonia Do We Really Know How Long to Treat? N Engl J Med. 2020; 383: 77-79.
   PubMed: https://pubmed.ncbi.nlm.nih.gov/32609987/
- Ginsburg AS, Mvalo T, Nkwopara E, McCollum ED, Phiri M, et al. Amoxicillin for 3 or 5 Days for Chest-Indrawing Pneumonia in Malawian Children. N Engl J Med. 2020; 383: 13-23.
   PubMed: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7233470/
- 29. Klepikov I. Acute pneumonia. New doctrine and first treatment results. LAP-Lambert Academic Publishing. 2020.
- Lai J, Ma S, Wang Y, Cai Z, Hu J, et al. Factors associated with mental health outcomes among health care workers exposed to coronavirus disease 2019. JAMA Netw Open. 2020; 3: e203976-e203976.
   PubMed: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7090843/
- Leiter RE. Reentry. N Engl J Med. 2020; 383: e141.
  PubMed: https://pubmed.ncbi.nlm.nih.gov/33053276/
- Rosenquist JN. The Stress of Bayesian Medicine Uncomfortable Uncertainty in the Face of Covid-19. N Engl J Med. 2020; 384: 7-9.
   PubMed: https://pubmed.ncbi.nlm.nih.gov/33027563/
- 33. Chen X. Avoiding Defensive Medicine among Pandemic. EC Emergency Medicine and Critical Care. 2020; 4: 49-53.
- 34. Inflammation. https://en.wikipedia.org/wiki/Inflammation
- Chandrasoma P, Taylor CR. Part A. "General Pathology", Section II.
  "The Host Response to Injury", Chapter 3. "The Acute Inflammatory Response", sub-section "Cardinal Clinical Signs". Concise Pathology (3rd ed.). McGraw-Hill. 2005.