
# MANIFESTATION OF VIRAL AND INFECTION COMPLICATIONS

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**Abstract.** A variety of respiratory viruses infect every person many times throughout life and are a risk factor for the development of bacterial complications. The most dangerous among the causative agents of acute respiratory viral diseases is the influenza A virus, which can cause catastrophic pandemics, the high mortality rate of which is largely due to secondary bacterial pneumonia. Numerous studies in recent years have shown that, regardless of the type of respiratory virus, the main mechanism for provoking bacterial infections is an unbalanced response of the innate antiviral immune system - an excessive interferon response and uncontrolled inflammation.

**Keywords:** virus, infection, secondary bacterial infection, influenza, secondary pneumonia, interferon.

## INTRODUCTION

*According to the World Health Organization (WHO), 3.9 million people die from acute respiratory viral infections (ARVI) per year [1]. These infections affect all age groups, but especially affect the health of children, as well as the elderly and those with chronic diseases. The danger of ARVI is determined by their ability to provoke both viral pneumonia and secondary bacterial complications, such as pneumonia, otitis media, meningitis, as well as chronic pulmonary diseases.*

## MATERIALS AND METHODS

*Thus, it is respiratory viruses that are involved in approximately 50% of cases of community-acquired pneumonia (CAP) in children and provoke more than 90% of cases of bronchiolitis in infants and 85-95% of cases of exacerbation of asthma in children. In adults, outside the pandemic influenza period, ARVI determines 30–50% of cases of CAP, 80% of exacerbations of asthma and 20–60% of exacerbations of chronic obstructive pulmonary disease (COPD). In general, ARVI is one of the five leading causes of death worldwide, and in many developing countries it is the leading cause of death in children under 5 years of age.*

## RESULTS AND DISCUSSION

Even in the early 21st century, with the availability of anti-influenza drugs and broad-spectrum antibiotics, people with seasonal influenza are still likely to develop virus-induced acute respiratory distress syndrome (ARDS) within the first week of infection or secondary bacterial pneumonia by 6– 7 days after the onset of the viral disease. According to WHO, influenza causes up to 650,000 deaths worldwide each year. In the United States, with a population of about 300 million people, according to the Centers for Disease Control and Prevention (CDC, Atlanta, USA), mortality from influenza ranges from 16,000 to 56,000 cases annually.

*Flu in the absence of antibiotics, antiviral drugs and vaccines*

The pandemic caused by the influenza A(H1N1) virus at the end of the First World War (1918) and called the "Spanish flu" was the largest ever recorded: 50% of the world's population was infected and about 50 died. million people [4]. The main group of people affected by this pandemic were people aged 20–40 years old who were drafted into the army. It should be noted that at the time of the Spanish Flu, at the beginning of the 20th century, the etiological agent of the disease was not yet known: the influenza virus was discovered only in 1933. Microbiologists of that time tried to associate the Spanish flu with various bacterial agents and, in particular, with Haemophilus influenzae (H. influenzae) [5].

*Pandemic influenza in the era of antibiotics in the absence of vaccination and antiviral drugs*

In 1957, the Asian flu pandemic affected 40–50% of people worldwide. The cause was the influenza A (H2N2) virus strain. Global mortality estimates range between 1.5 and 4 million [3], with the US death toll estimated at 69,800. When analyzing postmortem samples, bacterial infection was detected in 80% of severe cases and deaths. It should be noted that in developed countries by this time antibiotics such as penicillin and streptomycin were already used. However, during this pandemic, the United States and many other countries have seen an increase in hospitalizations associated with pneumonia, predominantly caused by S. pneumoniae, H. influenzae, and S. aureus. Similar data are presented in reports from the Netherlands, where out of 148 deaths analyzed, presumably caused by Asian influenza, 75% were associated with bacterial pneumonia, caused in 59% of cases by S. aureus and in 15% by S. pneumoniae. It is possible that the presented data from the bacteriological examination could be greatly distorted, since many patients were already taking antibiotics.

*Influenza pandemic in the presence of influenza vaccines, antiviral drugs and antibiotics*

In 2009, an influenza outbreak caused by the A(H1N1)pdm09 strain spread to 41 countries within 4 weeks. The variants of seasonal influenza vaccines released during the 2009 season did not match the antigenic properties of the newly emerged pandemic strain in the H1 component. The epidemic is believed to have killed 284,000 people worldwide. In the United States, during the 2009 influenza pandemic, secondary bacterial infections, mainly S. pneumoniae and S. pyogenes, were also common causes of death. American researchers found that 77 deaths between May and August 2009 were associated with bacterial infections in almost 30% of cases, 46% of which were caused by S. pneumoniae, 9% by S. aureus and 1% – H. influenzae. Palacios et al. examined nasopharyngeal swab samples from almost 200 patients with pandemic influenza: H. influenzae was found in 52%, S. pneumoniae in 31% and S. aureus in 18% of samples. The severity of the disease most often correlated with the isolation of S. pneumoniae.

*Respiratory viral infections of non-influenza etiology as triggers of secondary bacterial pneumonia*

The current state of diagnostics makes it possible to analyze bacterial complications in various respiratory infections of non-influenza etiology. Table 1 summarizes the results of numerous studies that have linked respiratory viral infections with certain bacterial pathogens associated with complications such as pneumonia, otitis media, sinusitis and meningitis. Despite the lack of pandemic potential, other representatives of respiratory viruses turned out to be no less dangerous triggers of secondary bacterial complications than influenza viruses. For example, a member of the Paramyxoviridae family, human

metapneumovirus (hMPV) is not inferior to the influenza virus in the severity of complications. Complications include both viral pneumonia with the development of ARDS and secondary bacterial pneumonia [3].

Table 1. Respiratory viruses and associated bacterial secondary infections

| **Virus** | **Associated secondary infection** |
|---|---|
| Influenza virus | S. pneumoniae, S. aureus, Staphylococcus pyogenes, |
| RSV | H. influenzae, Moraxella catarrhalis, |
| Adenovirus | Neisseria meningitidis |
| Human rhinovirus | S. pneumoniae |
| Parainfluenza virus | S. pneumoniae, H. influenzae, |
| hMPV | Moraxella catarrhalis |

Studies conducted in different regions of the world, although there are common conclusions about the relationship between viral and bacterial infections, may differ in conclusions about the role of various pathogens in the development of CAP, since climatic conditions and genetic characteristics of the population can significantly influence the prevalence of one or another viral and bacterial pathogen.

The US study included 1024 patients with CAP and 759 patients without significant symptoms [4]. It turned out that influenza viruses, RSV, hMPV, and also, to a lesser extent, parainfluenza viruses and coronaviruses were significantly more common in the group of patients with pneumonia, regardless of the age of the patients. At the same time, rhinoviruses were a common cause of PFS in adults, but were practically not found in pneumonia in children, while adenoviruses were associated with CAP only in children under 2 years of age.

*Pathogenesis of secondary bacterial infections in ARVI*

The human body hosts a variety of bacterial species, collectively referred to as microbiota [5]. Normally, these bacteria are considered so-called commensal strains, living in a mutually beneficial symbiosis with the host and providing a variety of useful functions, for example, protecting the body through competition with pathogenic strains. Typically, small numbers of pathogenic bacteria, including S. pneumoniae, S. aureus, H. influenzae, S. pyogenes, Moraxella catarrhalis and MRSA, are present in the microbiota of the human upper respiratory tract without serious consequences for the body [2]. Violation of the microbiota composition towards an increase in pathogenic flora can occur during viral respiratory infections due to the suppression of antibacterial defense factors. In this regard, secondary bacterial infections of the respiratory tract most often do not require infection of the body with pathogenic bacteria from the outside, but are the result of colonization provoked by a virus.

**CONCLUSION**

Advances in medicine in recent decades associated with the discovery of antibiotics and the development of vaccines against viruses and bacteria have significantly reduced the likelihood of a recurrence of the catastrophic Spanish flu pandemic of 1918, when bacterial superinfections turned out to be the main cause of mortality [2]. However, influenza viruses

and other respiratory viruses remain one of the main causes of bacterial complications and a common etiological cause of CAP. An alarming aspect is the increasing resistance of bacterial pathogens to modern antibiotics due to their widespread use. Unfortunately, the relative success in the development of influenza vaccines and anti-influenza drugs practically does not apply to other respiratory viruses, which, as shown above, are also infectious agents that provoke secondary bacterial complications. Despite progress in the development of pneumococcal and other antibacterial vaccines and multiple efforts to develop vaccines against respiratory viruses, it is difficult to imagine that an effective combination vaccination system against the major viral and bacterial respiratory pathogens will be developed in the foreseeable future. The likelihood of creating specific antiviral drugs against different groups of respiratory viruses that significantly affect the viral load, especially when used late, is also low.

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