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ETIOLOGY AND THERAPEUTIC MANAGEMENT OF LOWER RESPIRATORY TRACT INFECTIONS: A CURRENT REVIEW

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ABSTRACT

Lower respiratory tract infections remain a primary global cause of morbidity and mortality, particularly devastating for children under five and adults over seventy. This study focuses on analyzing the diverse etiology of these infections – including viral, bacterial, and atypical pathogens – to establish therapeutic algorithms that ensure effective treatment while curbing the critical issue of antimicrobial overuse. Based on an extensive review of current literature and epidemiological data, the research highlights community-acquired, hospital-acquired, and ventilator-associated pneumonia. Findings from 2023 indicate that general mortality rates have returned to pre-pandemic levels, though mortality remains highest when pneumonia precedes mechanical ventilation. While Streptococcus pneumoniae is the leading bacterial cause of death globally, Staphylococcus aureus and Pseudomonas aeruginosa dominate hospital settings. Among young children, Respiratory Syncytial Virus (RSV) is the primary pathogen. Management strategies identify amoxicillin as the first-line treatment for community-acquired cases, whereas hospital-acquired infections require empirical coverage for MRSA and Gram-negative bacteria. Prevention is bolstered by vaccinations and monoclonal antibodies like Nirsevimab for RSV. Ultimately, because lower respiratory tract infections etiology is highly dependent on age and comorbidities, rapid differential diagnosis is essential to combat antibiotic resistance. Effective prevention through immunization and patient education remains the most successful strategy for reducing hospitalizations related to severe respiratory infections.

KEYWORDS

Lower Respiratory Tract Infections, Pneumonia, Etiology, Antibiotic Therapy, Diagnostics, Streptococcus Pneumoniae

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Introduction

Lower respiratory tract infections remain one of the main medical problems and causes of death in the general population. This applies to both patients treated in outpatient settings and patients hospitalized in all hospital wards. Such infections are a significant problem, especially in risk groups where, if left untreated, they can pose a direct threat to life. Data on the epidemiology of lower respiratory tract infections have changed recently due to the COVID-19 pandemic.

In 2016, the incidence rate for lower respiratory tract infections was 45.5 per 1,000 people in the general population. The highest incidence concerned two specific groups: people over 70 years of age, where the incidence rate was 155.4 per 1,000 people, and children under 5 years of age, where the incidence rate was 107.7 per 1,000. The mortality rate was 32.2 per 100,000 people in the general population and 267.4 and 103.3 per 100,000 people respectively in the population of adults over 70 and children under 5 ("Estimates of the global, regional, and national morbidity, mortality, and aetiologies of lower respiratory infections in 195 countries, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016," 2018).

At the beginning of the pandemic, during the global application of restrictions on personal contact, the data changed. The incidence rate for lower respiratory tract infections for the general population in 2020 was 43.694 per 1,000 people, while in 2021 it was 43.542 cases per 1,000 people. This number is slightly lower compared to the data from 2016. The incidence rate for children under 5 years of age significantly decreased. In 2020, it was 59.408 per 1,000 people, while in 2021 it was 57.475 per 1,000 people. In the case of people over 70, the differences compared to pre-pandemic data are less significant. In 2020, the incidence rate in this group was 192.794 per 1,000 people, while in 2021 it was 188.977 per 1,000 people (Infections & Antimicrobial Resistance, 2024).

Mortality data show similar relationships. The mortality rate in the general population in 2020 and 2021 was 29.1 and 27.7 per 100,000 people, respectively. This means that mortality due to lower respiratory tract infections at that time fell by about 9.6% in 2020 and by about 14% in 2021 relative to 2016 data. Mortality in

high-risk groups also fell in 2020 and 2021: in children under 5, the mortality rate was 83.1 and 76.2 per 100,000 people respectively; in people over 70, it was 238.5 and 224.6 per 100,000 people respectively (Infections & Antimicrobial Resistance, 2024).

Statistics from 2023 show a partial return to pre-pandemic proportions. The incidence rate in the general population was 30.017 per 1,000 people, which means that the return to the pre-pandemic state does not apply to the incidence, which is lower than in 2016 as well as in 2020 and 2021. In the population of children up to 5 years of age, the incidence rate was 77.004 per 1,000 people. This is higher than the data from 2020 and 2021, but lower than the 2016 data. In the group over 70 years of age, the incidence rate was 124.839 per 1,000 people. This is lower compared to 2016 data and significantly lower compared to 2020 and 2021 data (Infections & Antimicrobial Resistance, 2025).

The mortality rate in the general population was 31.0 per 100,000 people, which means that mortality after the COVID-19 pandemic increased, approaching the 2016 level. In the population of people over 70, the mortality rate was 231.6 per 100,000 people. This value remains at a level like that during the COVID-19 pandemic, still lower compared to 2016 data. In the population of children under 5, the mortality rate was 94.8 per 100,000 people. Similar to the incidence data, mortality in this age group was higher than in 2020 and 2021, but lower than in 2016 (Infections & Antimicrobial Resistance, 2025).

The aim of the work will be to analyze the etiology in the case of the most common disease entities covered by the common term of lower respiratory tract infections, considering possible causative pathogens and possible effective methods of treatment and prevention of certain infections in special risk groups.

Materials and methods

The study was conducted based on a comprehensive review of the medical literature available in the PubMed database. The search focused on publications regarding the etiology, epidemiology, and treatment of lower respiratory tract infections. The analysis included clinical practice guidelines, systematic reviews, and epidemiological reports from the Global Burden of Disease studies. Particular attention was paid to the most recent data from 2016–2023 to account for the impact of the COVID-19 pandemic on infection trends.

Results

Clinical classification of lower respiratory tract infections:

The incidence and mortality data presented in the introduction concern lower respiratory tract infections understood as clinically diagnosed pneumonia or bronchitis. Pneumonia is the most common infection among patients treated in the hospital (Magill et al., 2014). For this reason, mainly this diagnosis will be discussed in the context of etiology and treatment.

A distinction can be made between hospital-acquired pneumonia and pneumonia diagnosed in an outpatient setting. Patients in such a situation may have the option of outpatient treatment, but in case of complications or failure of outpatient treatment, it should take place in the hospital. Among pneumonias treated in hospital, a clinically important distinction concerns the method of patient ventilation. Mechanical ventilation is a very important factor affecting the occurrence and severity of pneumonia. Among patients with pneumonia, one can distinguish a group of patients not requiring mechanical ventilation, those requiring mechanical ventilation in whom it was introduced after the diagnosis of pneumonia, and groups of patients with pneumonia where the infection was related to previously applied mechanical ventilation. In patients with pneumonia not related to mechanical ventilation, mortality was 11.70%. In patients with a diagnosis of hospital-acquired pneumonia related to mechanical ventilation, mortality was 21.25%. The highest mortality concerns the group of mechanically ventilated patients in whom pneumonia occurred before the start of mechanical ventilation and is 29.16% (Zilberberg et al., 2022).

Etiology of lower respiratory tract infections:

Among the pathogens causing lower respiratory tract infections, *Streptococcus pneumoniae* is the most common etiological factor; infection with this bacterium caused the most deaths among patients with lower respiratory tract infections. Other bacteria causing the most infections and deaths are, in order of occurrence, *Staphylococcus aureus* and *Klebsiella pneumoniae*. Among viruses, the influenza virus caused the most infections and the highest mortality (Infections & Antimicrobial Resistance, 2025).

In the case of patients under 5 years of age, the pathogens and clinical problems regarding lower respiratory tract infections are different than in older children and adults. RSV virus deserves special attention here, being the most common cause of lower respiratory tract infections in children up to 60 months of age. In

this age group, RSV infection was the cause of 2.0% of deaths, while in the age group 28 days - 6 months, the percentage was even higher and amounted to 3.6% (Li et al., 2022).

In patients with a diagnosis of hospital-acquired pneumonia, the most common pathogen isolated in patients, regardless of the method of ventilation, was *S. aureus*. Identification of a methicillin-resistant *S. aureus* strain was most common in non-mechanically ventilated patients. Methicillin-sensitive *S. aureus* strains were most often found in patients with a diagnosis of ventilator-associated pneumonia. The most common Gram-negative bacterium found in patients diagnosed with hospital-acquired pneumonia was *Pseudomonas aeruginosa* (Zilberberg et al., 2022).

Community-acquired pneumonia:

Lower respiratory tract infections are a group of diagnoses including, among others, pneumonia. Community-acquired pneumonia is the most common disease entity in the group of lower respiratory tract infections. It represents a significant global public health challenge, being a leading infectious cause of morbidity and mortality. It is estimated that the global incidence of community-acquired pneumonia in 2021 was 43.50 cases per 1,000 people, which translated to approximately 2.2 million deaths annually (Reyes et al., 2025).

The profile of pathogens causing community-acquired pneumonia depends on the patient's age, comorbidities, and geographical region. Among the most common etiological factors for this disease entity are Gram-positive bacteria such as *S. pneumoniae* and *S. aureus*. Among the Gram-negative bacteria causing community-acquired pneumonia, the most common pathogen is *H. influenzae*, while among atypical bacteria, *Chlamydophila pneumoniae* and *Legionella pneumophilia* play an important role (Herold & Sailer, 2004).

Among viruses, the most important role is played by the influenza virus, responsible for the most infection cases and deaths, and the RSV virus, especially in children up to 5 years of age. Illnesses caused by rhinovirus are also frequently observed. Viral infections can also be complicated by bacterial superinfection, conditioning a more severe course of the disease (Jain et al., 2015).

Risk groups for community-acquired pneumonia are the elderly, children, and immunocompromised individuals, but also those with chronic diseases. Diseases that have a particularly strong impact on increasing the risk of illness are a history of pneumonia and chronic lung diseases - chronic obstructive pulmonary disease, asthma, as well as heart disease and diabetes. Lifestyle and socioeconomic status also have a significant impact on the risk of illness. Malnutrition, cigarette smoking, and alcohol abuse are significant modifiable risk factors. Air pollution, poor housing conditions, and low socioeconomic status are also of significant importance (Almirall et al., 2017; Bordon et al., 2020).

The diagnosis of community-acquired pneumonia is based on clinical symptoms and laboratory and imaging tests. Clinical symptoms often include cough, dyspnea, chest pain, fever, and tachypnea. Imaging tests useful in diagnosing community-acquired pneumonia are chest X-ray, lung ultrasound, and CT in case of doubt. Laboratory tests are primarily markers of inflammation - procalcitonin and CRP. They are particularly important in monitoring treatment (Aliberti et al., 2016).

Assessing the severity of community-acquired pneumonia can be important when choosing a treatment method. The decision on hospitalization can be made using the result in the CURB-65 or PSI scale. The CURB-65 scale is simpler and faster; an alternative to it is the PSI scale, which better predicts mortality within 30 days (Zaki et al., 2023). The SMART-COP scale can be useful for assessing the need for respiratory and circulatory support (Ehsanpoor et al., 2019).

Hospital-acquired pneumonia:

Hospital-acquired pneumonia is defined as an infection 48 hours after hospital admission. In intubated patients, mortality is much higher, while non-mechanically ventilated patients suffering from pneumonia are particularly patients with chronic illnesses. This primarily concerns patients with neoplastic diseases and chronic respiratory system diseases (Zilberberg et al., 2022). Ventilator-associated pneumonia is defined as an infection 48 hours after endotracheal intubation. It can also apply to patients who have already been extubated (Modi & Kovacs, 2020).

Diagnosing hospital-acquired pneumonia can be difficult due to the lack of specific rapid laboratory tests clearly indicating the diagnosis. Clinical symptoms such as fever, cough, or dyspnea are important for the diagnosis. Among laboratory test results, an elevated concentration of procalcitonin is of great importance. A significant increase in this parameter may suggest a typical bacterial etiology; lower concentrations may indicate infection with atypical bacteria or viruses. Determination of this parameter can also be useful for evaluating treatment

effectiveness. A diagnosis of hospital-acquired pneumonia can be made based on the presence of at least two symptoms among fever, productive cough, and leukocytosis (Kalil et al., 2016; Metlay et al., 2019).

A bacteriological examination in the form of a culture of material from the respiratory tract is also important. When an infection is suspected, even before microbiology test results are available, empirical treatment should take place based on knowledge of hospital bacterial flora and existing patterns of strain resistance to antibiotics. In the absence of such data, empirical treatment should include antibiotics effective against methicillin-resistant *S. aureus* and Gram-negative bacteria, including *P. aeruginosa* (Kalil et al., 2016).

Prevention of hospital-acquired pneumonia includes oral hygiene, use of proton pump inhibitors and antihistamines as needed, and early diagnosis and treatment of dysphagia. These actions allow for the prevention of nasopharyngeal colonization by pathogenic flora, thereby reducing the risk of infection because of the transfer of bacterial flora to the respiratory tract (Kaneoka et al., 2015).

Methods of treatment and prevention:

Treatment of community-acquired pneumonia in the initial phase of the disease is empirical. Amoxicillin or doxycycline is used for this purpose. In the case of a patient with chronic lung disease or asplenia, amoxicillin with clavulanic acid, oral cephalosporins, macrolides, or doxycycline should be used. In case of allergy, respiratory fluoroquinolones, e.g., levofloxacin, apply (Martin-Loeches et al., 2023).

If COVID-19 infection is suspected, with exposure in history or in the case of a high number of infections in each region, one of the available tests should be performed. Protective vaccination plays a very large role in prevention. Among antiviral drugs, remdesivir has the highest documented effectiveness in treating an infection of this etiology (Bhimraj et al., 2024).

Treatment for influenza virus infection depends on the severity of the disease course. In the case of a severe course, administration of oseltamivir is recommended. In a moderate course, antiviral treatment is not necessary; only in the case of a high risk of clinical progression may the administration of baloxavir be indicated (Uyeki et al., 2019).

Treatment of hospital-acquired pneumonia should be conducted based on the results of a culture from the upper respiratory tract along with an antibiogram. Empirical treatment conducted before antibiogram results are available depends on the local bacterial flora and its antibiotic resistance. Appropriate antibiotics for this indication include piperacillin with tazobactam, cephalosporins e.g., cefepime, fluoroquinolones e.g., levofloxacin, or carbapenems e.g., meropenem (Kalil et al., 2016).

After receiving the results of bacteriological tests, the treatment should be corrected based on the antibiogram results, in correlation with the patient's clinical condition. Treatment for uncomplicated pneumonia should last 7 days. During treatment, a gradual resolution of symptoms should be observed. If complications occur in the form of an abscess, bacteremia, or others, longer treatment is indicated according to the complication specification (Pugh et al., 2015).

In the prevention of lower respiratory tract infections, protective vaccinations play a very large role. The most important of them include preparations directed against S. pneumoniae and H. influenzae type b - bacteria that are frequent causes of lower respiratory tract infections (Fally et al., 2021).

The patient's age is key to choosing the right treatment. Among children up to 5 years of age, the prevention and treatment of infections caused by the RSV virus have a very important share. In 2023, the monoclonal antibody Nirsevimab was introduced, whose effectiveness was studied in a group of newborns born after 35 weeks of pregnancy. The use of this monoclonal antibody allows for a significant reduction in the number of cases of lower respiratory tract infection caused by the RSV virus (Hammitt et al., 2022). Palivizumab is another monoclonal antibody used in the prophylaxis of RSV virus infections. Such prophylaxis is recommended in the first year of life for infants born before 29 weeks of pregnancy. The use of such prophylaxis is also justified in the first and second years of life in the case of children born after 28 weeks of pregnancy, but only in patients with additional burdens such as chronic lung disease or heart defects. Palivizumab is effective only in prophylaxis; it is not effective in treating developed disease ("Updated guidance for palivizumab prophylaxis among infants and young children at increased risk of hospitalization for respiratory syncytial virus infection," 2014).

Summary:

The analysis of lower respiratory tract infection topics indicates the dominant role of viruses in milder forms of disease, e.g., acute bronchitis, and the key importance of bacteria such as *S. pneumoniae* or *H. influenzae* during pneumonia. Proper diagnosis plays an important role, with particular emphasis on the characteristic clinical picture and microbiological tests in the case of hospital infections. Analysis of the epidemiological situation and pathogen resistance profile allows for selecting optimal empirical treatment. The results of microbiological tests allow for the correction of treatment if necessary. The role of optimally selected treatment also translates into preventing the emergence of microbial antibiotic resistance and reducing the risk of developing complications. Protective vaccinations against influenza, pneumococci, and COVID-19 play a special role in the prevention of lower respiratory tract infections.

Conclusions:

1. The etiology of lower respiratory tract infections is diverse and depends on the age and comorbidities of the patient. The dominance of viral infections in bronchitis excludes the routine use of antibiotics in this group of patients.
2. Rapid differential diagnosis is essential to limit the phenomenon of antibiotic resistance. The decision to include antibacterial treatment should be based on objective clinical criteria and auxiliary tests.
3. Amoxicillin remains the first-line treatment in community-acquired pneumonia unless there are risk factors for infection with resistant or atypical microbes.
4. Patient education in the field of protective vaccinations is the most effective method of reducing the number of hospitalizations due to severe lower respiratory tract infections.

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