Antibiotic/Anti-Infective Learning Program

Pneumonia With Concentration in Nosocomial Pneumonia Module

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Introduction

The main function of the respiratory system is to bring air into the lungs, allowing the transfer of oxygen and carbon dioxide between the air and the blood. However, this constantly exposes the lungs to potentially damaging molecules, such as dust and infectious agents.

Lower respiratory tract infections (LRTIs) are a group of diseases that are defined as acute illness (present for 21 days or less), usually with cough as the main symptom. LRTIs may be associated with other lower respiratory tract symptoms, such as sputum production, **dyspnea**, wheezing, or chest pain. LRTIs include pneumonia, acute bronchitis, and exacerbations of chronic lung disease.

Pneumonia is the most common lethal infectious disease worldwide. In the United States alone, it is estimated that community-acquired pneumonia (CAP) will be responsible for 1.5 million hospital admissions and 100,000 deaths each year.

In this module, we will learn about the pathogenesis, diagnosis, and treatment of pneumonia as well as the epidemiology of and risk factors for each type of pneumonia.

Learning Objectives

At the end of this module, you will be able to:

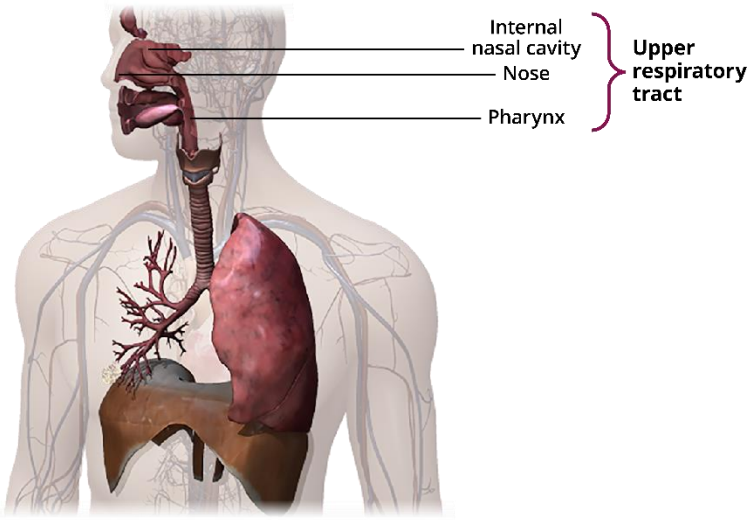
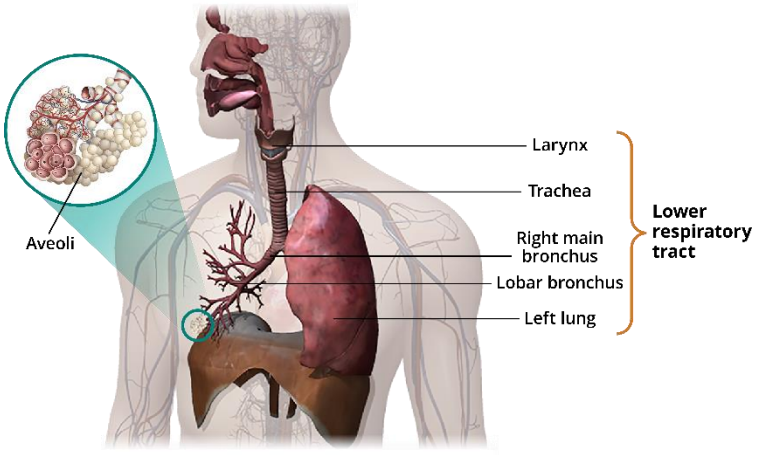
- Define pneumonia
- Differentiate between community-acquired and nosocomial pneumonia
- Outline the pathogenesis of pneumonia
- Identify the most common pathogens involved in pneumonia
- Outline the diagnosis of pneumonia
- List the recommended antibiotics for the treatment of pneumonia

Disease State Description

Structure and Function of the Respiratory System

As previously mentioned, the respiratory system functions to transfer oxygen and carbon dioxide between the external environment and the blood. The parts of the respiratory system can be divided according to either structure or function.

Structurally, the respiratory system consists of the upper respiratory tract and the lower respiratory tract.

Upper Respiratory Tract	
Lower Respiratory Tract	

Functionally, the respiratory system consists of 2 zones:

- The conducting zone: the passageways that filter, warm, and moisten air and direct it into the lungs. It is composed of the nose, nasal cavity, pharynx, larynx, trachea, bronchi, and bronchioles.
- The respiration zone: the site of gas exchange between the atmosphere and the blood. It is composed of respiratory bronchioles, alveolar ducts, alveolar sacs, and **alveoli** of the lungs.

Pneumonia

Definition

Pneumonia is an infection of the lung **parenchyma**, the site of gas exchange in the lungs.

Although pneumonia causes significant morbidity and mortality, it is often misdiagnosed, mistreated, and underestimated.

The Challenge of Pneumonia
The diagnosis and management of pneumonia has become more challenging due to: • Growing number of aged and comorbid, debilitated, institutionalized, and immunocompromised individuals • Diverse array of causative microbes • Increasing antimicrobial resistance

Patients with pneumonia may present with:

- Cough
- Sputum production
- Dyspnea
- Chest pain
- Fever

Examination of the chest, either physically or radiologically, may reveal evidence of **consolidation** within the lung.

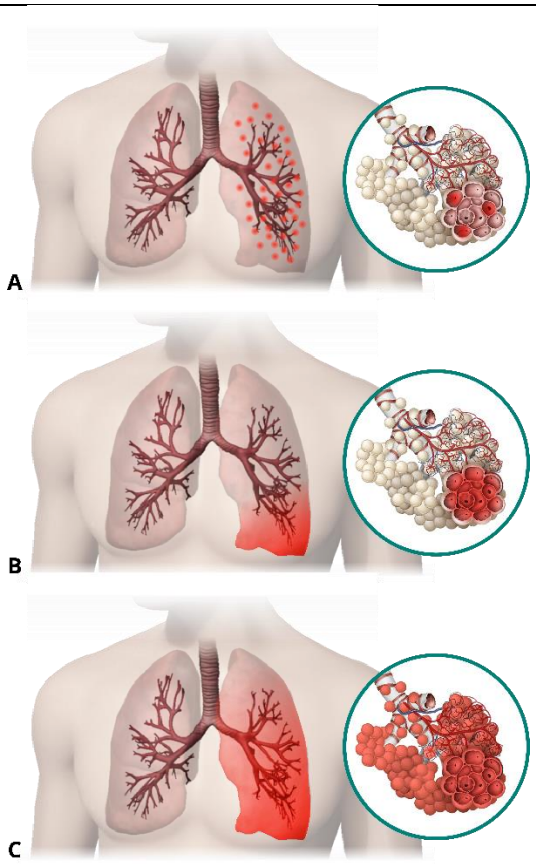
Nonrespiratory symptoms may also be present, including fatigue, **tachycardia**, sweats, headache, nausea, muscle pain, and occasionally diarrhea and abdominal pain.

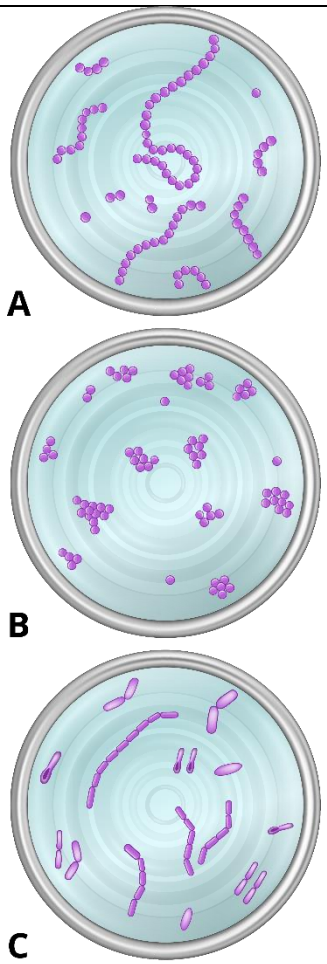
Classification

Pneumonia can be classified in several ways, such as by:

- Environment in which the infection is acquired
- Anatomic site affected
- Etiology

Environment in Which the Infection Is Acquired Pneumonia can be acquired in the community or in the hospital (nosocomial pneumonia).	 
Anatomic Site Affected Pneumonia can be classified as: (A) *Bronchopneumonia* is characterized by a patchy pattern of infection that is limited to the segmental bronchi and surrounding lung parenchyma. It often involves both lungs. (B) *Lobar pneumonia* is characterized by diffuse or widespread alveolar inflammation and consolidation. (C) *Interstitial pneumonia* is usually diffuse and often bilateral inflammation that primarily involves the alveolar septa and **interstitium**. It is commonly associated with infections of *Mycoplasma pneumonia* or	

viruses.	
Etiology Pneumonia can be classified based on the causative pathogen. For example: (A) *Streptococcus* is responsible for streptococcal pneumonia. (B) *Staphylococcus* is the causative agent of staphylococcal pneumonia. (C) Bacilli, such as *Haemophilus influenzae*, may also cause pneumonia. Although predominantly caused by bacteria, pneumonia may also result from infection with other pathogens, such as viruses, fungi, and protozoa.	



Given that the distinction between bronchopneumonia and lobar pneumonia is often indistinct and that pathogens and outcomes tend to be similar in patients in similar clinical settings, it is often preferable to classify pneumonia by the environment in which the infection is acquired.

Community-Acquired Pneumonia

Pneumonia that develops in people with limited or no contact with a hospital or extended-care facility is called CAP. Patients may be treated at home or admitted to hospital for treatment.

Nosocomial Pneumonia

Nosocomial pneumonia, also referred to as hospital-acquired pneumonia (HAP), is a pneumonia that occurs more than 48 hours after hospital admission.

The nosocomial pneumonia category includes ventilator-associated pneumonia (VAP). VAP develops in intensive care units (ICUs) and is defined as pneumonia that occurs more than 48 to 72 hours after tracheal intubation. The definition of VAP does not include patients with

nosocomial pneumonia who require mechanical ventilation during their treatment after the onset of infection.

Other Terms

Health care-associated pneumonia (HCAP) is a term used to describe disease in nonhospitalized patients under certain conditions. For example:

- Patients previously hospitalized for at least 2 days within the 90 days before infection
- Patients from nursing homes
- Patients from **hemodialysis** centers

However, the etiology of HCAP is believed to be similar to that of CAP, so the distinction is not used in management guidelines.

Pneumonia

Epidemiology

Community-Acquired Pneumonia

CAP is the leading infectious cause of death in the United States. It affects 5 to 6 million people each year and leads to an estimated 1.5 million hospital admissions. Of those admitted to the hospital with CAP, approximately 10% to 20% will require care in the ICU, where mortality rate may be as high as 50%.

Despite these estimates, the true incidence of CAP is not certain, because pneumonia is not a reportable disease, and only 20% to 50% of patients require hospitalization.

Reportable Diseases
The Centers for Disease Control and Prevention (CDC), through the National Notifiable Diseases Surveillance System (NNDSS), works closely with state and local health departments to collect public health data in an effort to monitor, control, and prevent diseases of interest. As part of the NNDSS, reportable diseases are mandatorily reported to state or territorial jurisdictions when identified by a health care provider, hospital, or laboratory. The list of reportable diseases is generated at the state level and may vary among states/territories over time.

CAP is associated with a mortality rate of less than 5% among outpatients. However, among hospitalized patients, the mortality rate ranges from ~12% to 40%.

Determining the site of care of patients with CAP is an important initial decision that health care providers need to make. It has been estimated that the cost of treating uncomplicated pneumonia in the hospital is 25-fold more expensive than treating it in the outpatient setting.

Nosocomial pneumonia

Nosocomial pneumonia is the second most common nosocomial infection, and it is estimated that 3.5% of patients hospitalized for 3 or more days will develop the disease. Approximately one-third of all nosocomial pneumonia cases are acquired in the ICU.

Nosocomial pneumonia has been shown to increase health care costs and extend hospital stays by 7 to 9 days. Additionally, it is estimated that:

- VAP increases the duration of mechanical ventilation and intensive care by 4 to 6 days
- Over the years, mean hospital charges per patient with VAP have increased by approximately $40,000

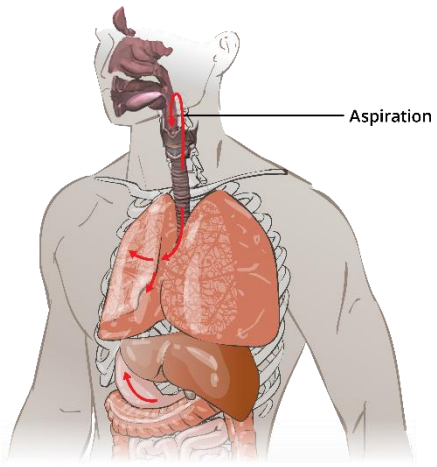
- VAP increases mortality of the underlying disease by 30%

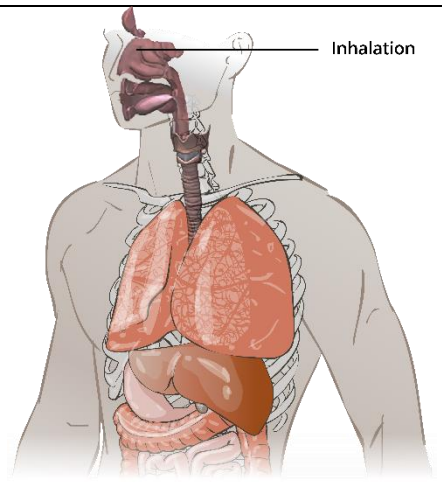
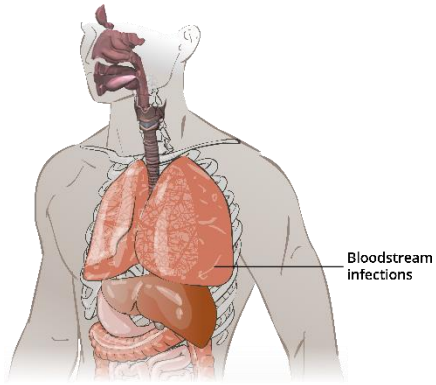
There are different estimates for the mortality rate associated with nosocomial pneumonia. In non-ICU nosocomial pneumonia, the mortality rates range from 26% to 53%. However, mortality may be as high as 70%, particularly in VAP. Nosocomial pneumonia is the leading cause of death from nosocomial infections in critically ill patients.

Pathogenesis

Pneumonia results from the inflammatory response engendered in the alveoli when pulmonary defenses cannot efficiently kill pathogens. The mechanisms by which pathogens may enter the lungs include:

- **Aspiration** of oropharyngeal contents
- **Inhalation** of contaminated droplets
- Bloodstream infections

Aspiration of Oropharyngeal Contents The most common mechanism of contamination of the lower airways is aspiration of oropharyngeal contents. Small-volume aspiration occurs frequently during sleep, especially in the elderly, and in patients with decreased levels of consciousness. In this manner, pathogenic organisms that colonize the oropharynx gain access to and infect the lung. Aspiration is a major cause of anaerobic lung infections. In mechanically ventilated patients, the endotracheal tube provides a focus for infection. Aspiration is enhanced by the supine position and feeding through a nasogastric tube.	
Inhalation of Contaminated Droplets The second mechanism consists in the inhalation from the environment of suspended, aerosolized droplets that may contain pathogens. Inhalation pneumonia is often due to microorganisms that are able to survive suspended in the air for prolonged	

periods. Such bacteria include *Mycoplasma pneumoniae*, *Legionella*, and *Mycobacterium tuberculosis*.	
Bloodstream Infections Rarely, pathogens can access the lung via the bloodstream, eg, from an infection of the heart valve or **pleural** space.	

Microbiology

Community-Acquired Pneumonia

Bacterial pathogens are identified in 20% to 50% of CAP cases. *Streptococcus pneumoniae* is the most common infectious bacteria, responsible for approximately 27% of CAP cases. Other common bacteria include *Haemophilus influenzae*, *Moraxella catarrhalis*, and *Staphylococcus aureus*. Atypical pathogens include *Mycoplasma pneumoniae*, *Legionella pneumophila*, and *Chlamydophila species*.

Nosocomial Pneumonia

In contrast to their prominent role in CAP, *S pneumoniae* and *H influenzae* cause less than 15% of nosocomial pneumonia cases. Approximately 50% to 60% of nosocomial pneumonia cases are caused by aerobic gram-negative bacteria.

However, the microbiology of nosocomial pneumonia varies considerably depending on:

- Duration of hospitalization before pneumonia
- Severity of illness
- Comorbid conditions
- Reason for admission
- Prior antibiotic exposures

The predominant risk factors for pneumonia caused by microorganisms with decreased susceptibility are:

- Prolonged hospitalization
- Recent broad-spectrum antimicrobial exposure
- Hemodialysis
- Poor functional status
- Severe pneumonia

It is estimated that 13% to 40% of cases of nosocomial pneumonia are caused by *S aureus.* The risk of *S aureus* being methicillin resistant increases progressively with duration of hospitalization. There is a correlation between the severity of pneumonia and the responsible pathogen. For example, methicillin-resistant *S aureus* (MRSA) is more likely to be the causative pathogen in patients requiring intubation.

Late Onset Nosocomial Pneumonia
Late onset nosocomial pneumonia (ie, pneumonia that develops after 5 days of hospitalization) is more likely to be caused by multidrug-resistant (MDR) pathogens and is associated with increased morbidity and mortality.

A substantial proportion of VAP cases are polymicrobial, with additional colonizing species. Viruses can account for up to one-third of severe pneumonias, particularly in immunocompromised hosts.

Risk Factors

Several risk factors for the development of pneumonia have been identified. Some of these include:

- Alcoholism
- Asthma
- Immunosuppression

- Institutionalization
- Smoking
- Chronic obstructive pulmonary disease (COPD)
- Age ≥70 years

Additional risk factors in the elderly include decreased cough and gag reflexes, dementia, seizure disorders, heart failure, and cardiovascular disease.

Risk factors for nosocomial pneumonia include any factor that enhances the risk of aspiration. A more complete list of risk factors for nosocomial pneumonia and VAP is shown in Table 1.

Table 1: Risk Factors for Nosocomial Pneumonia

Risk Category	Risk Factors
Mental status	Central nervous system disease Reduced consciousness Sedation
Bacterial burden	Increased hospital stay Prolonged antibiotic exposure Use of proton pump inhibitors
Patient factors	Age Pre-existing lung disease Severity of illness
Hospital factors	Staffing levels Transportation out of ICU
Intubation	As an emergency Reintubation Duration Supine position Enteral feeding Use of paralytic agents Underinflation of endotracheal tube cuff

Diagnosis

Diagnosis of pneumonia can be challenging. Clinical examination often needs to be confirmed by a variety of tests.

Diagnostic testing has 2 purposes: to determine whether the symptoms are attributable to pneumonia and to identify the responsible pathogen, which helps decide the best treatment option.

Nosocomial Pneumonia

The diagnosis of nosocomial pneumonia, including VAP, is still a matter of controversy, particularly with regard to the role of quantitative cultures and bronchoscopic sampling. However, to diagnose and guide treatment, the US guidelines recommend noninvasive sampling (endotracheal aspiration) with semiquantitative cultures over invasive techniques.

Accurate diagnosis of VAP is improved by a combination of clinical criteria with laboratory criteria and radiological features.

Treatment

Nosocomial Pneumonia

Treating nosocomial pneumonia is a delicate balancing act between factors that favor additional antibiotics (eg, delay may impair outcomes, MDR pathogens are likely) and those that favor fewer antibiotics (eg, accurate diagnosis is difficult, inappropriate treatment may drive antibiotic resistance). Continual reevaluation of the patient and the treatment can help minimize antibiotic exposure.

The IDSA/ATS guidelines recommend the following regarding the initial empiric treatment of nosocomial pneumonia:

- Empiric treatment should be informed by local data on pathogens and antibiotic resistance
- Include coverage for *S aureus*, *P aeruginosa*, and other gram-negative bacilli
- If coverage for MRSA is indicated: treatment with vancomycin or linezolid is recommended

Summary

- Pneumonia is an infection of the lung parenchyma, the site of gas exchange in the lungs.
- Patients with pneumonia may present with cough, sputum production, dyspnea, chest pain, and fever.
- Pneumonia can be classified according to the environment in which the infection is acquired, the anatomic site affected, or the etiology.
- CAP is pneumonia that develops in people with limited or no contact with a hospital or extended-care facility.
- Nosocomial pneumonia or hospital-acquired pneumonia (HAP) is pneumonia that occurs 48 hours or more after hospital admission.
- Nosocomial pneumonia is the second most common nosocomial infection, and it is estimated that 3.5% of patients hospitalized for 3 or more days will develop the disease.
- Pneumonia results from the inflammatory response engendered in the alveoli when pulmonary defenses cannot efficiently kill pathogens.
- The mechanisms by which pathogens may enter the lungs include aspiration of oropharyngeal contents, inhalation of contaminated droplets, and bloodstream infections.
- Approximately 50% to 60% of nosocomial pneumonia cases are caused by aerobic gram-negative bacteria.
- There are numerous risk factors for pneumonia, including advanced age, underlying diseases, and lifestyle factors.
- Diagnosis of pneumonia can be challenging. Clinical examination often needs to be confirmed by a variety of tests.
- Antibiotic treatment of nosocomial pneumonia is initially empirical and refined on the basis of culture results, taking account of potentially MDR pathogens.

Glossary

Term	Definition (referenced)
alveoli	Pleural of alveolus; alveolus: an air sac of the lungs.
aspiration	The inhalation of fluid or solid objects into the lower airways or lungs.
consolidation	The process of becoming solid.
dyspnea	Dys-: prefix meaning bad, difficult, painful; –pnea: to breathe, breathing; difficult breathing.
hemodialysis	The use of an artificial kidney to clear urea, metabolic waste products, toxins, and excess fluid from the blood.
inhalation	The act of drawing breath, vapor, or gas into the lungs.
interstitium	Space consisting of the walls of the alveoli and the spaces around blood vessels and small airways.
parenchyma	The essential parts of an organ that are concerned with its function in contradistinction to its framework.
pleural	Concerning the pleura; pleura: a serous membrane that enfolds both lungs and is reflected upon the walls of the thorax and diaphragm.
tachycardia	An abnormally elevated heart rate.

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