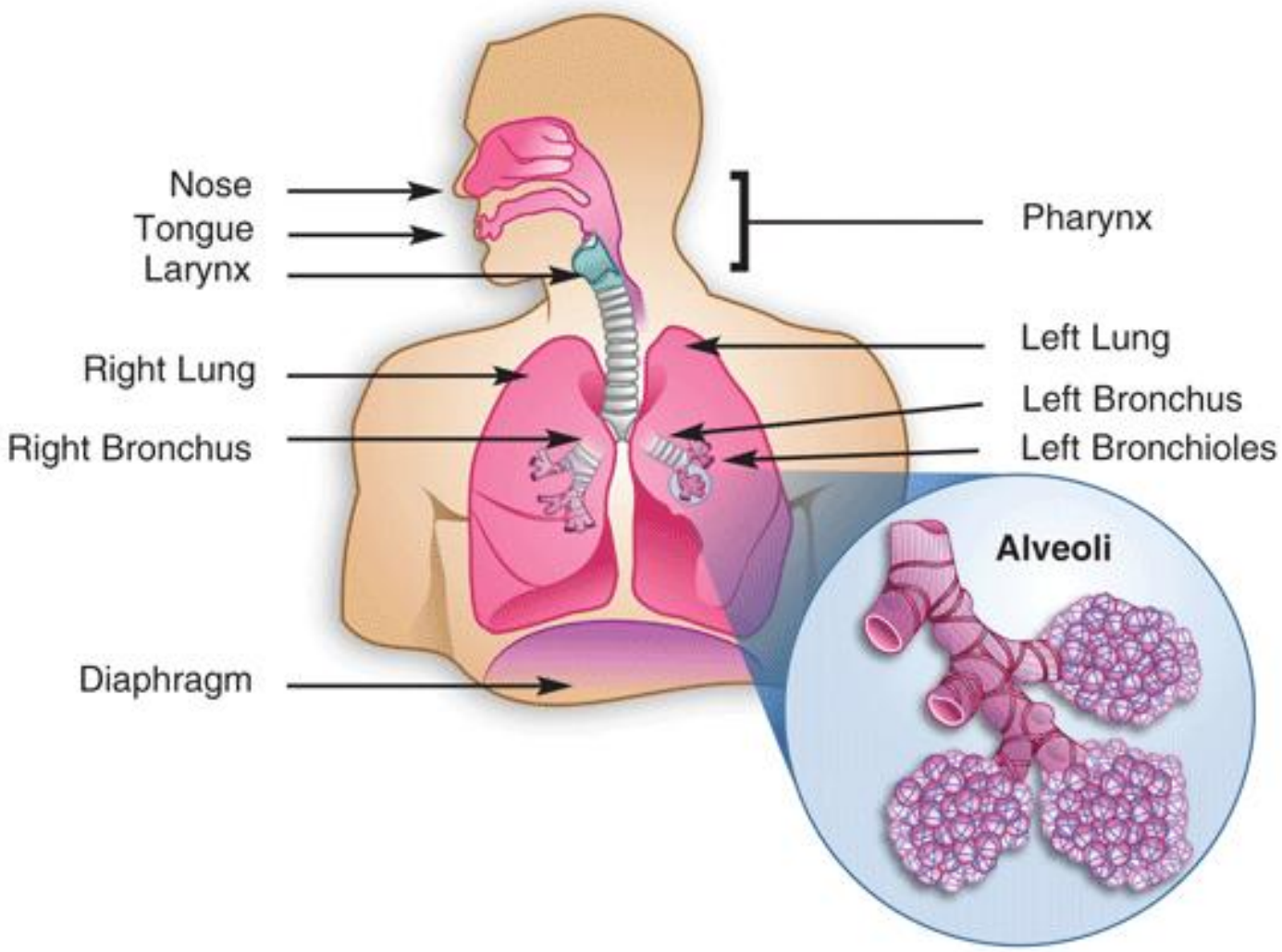
Human Respiratory System Infections

Ayda Basgul Martin, MD



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Learning Objectives Part 1 &2

After completing this chapter, the students should be able to,

- Explain the significant historical events regarding the respiratory tract infections
- Identify the major anatomical structures of the respiratory system and their roles in immune defense.
- Differentiate between upper and lower respiratory tract organs
- Describe normal microbiota of the respiratory system.
- Define the factors that can damage the respiratory system and promote infections.
- Define the terminology about inflammation and infection within the respiratory system.
- Identify common bacterial pathogens (e.g., Streptococcus pneumoniae, Hemophilus influenzae) and viral pathogens (e.g., influenza virus, respiratory syncytial virus) responsible for respiratory infections.
- Understand the role of fungi (e.g., Aspergillus, Histoplasma) and parasites (e.g., Toxoplasma gondii) in causing respiratory infections.
- Recognize the symptoms and signs associated with upper respiratory tract infections.
- Understand the laboratory diagnostic techniques used to identify respiratory pathogens, including cultures, PCR, serology, and imaging.
- Outline the treatment options for bacterial, viral, fungal, and parasitic respiratory infections.
- Discuss the role of vaccines in preventing common respiratory infections.
- Describe the public health measures to control the spread of respiratory infections.

Learning Objectives Part 3

- Identify common bacterial pathogens (e.g., *Streptococcus pneumoniae*, *Mycobacterium tuberculosis*, *Hemophilus influenzae*) and viral pathogens (e.g., influenza virus, respiratory syncytial virus) responsible for respiratory infections.
- Understand the role of fungi (e.g., *Aspergillus*, *Histoplasma*) and parasites (e.g., *Toxoplasma gondii*) in causing respiratory infections.
- Recognize the symptoms and signs associated with lower respiratory tract infections.
- Understand the laboratory diagnostic techniques used to identify respiratory pathogens, including cultures, PCR, serology, and imaging.
- Outline the treatment options for bacterial, viral, fungal, and parasitic respiratory infections.
- Discuss the role of vaccines in preventing common respiratory infections.
- Describe the public health measures to control the spread of respiratory infections.
- Discuss the role of vaccines in preventing common respiratory infections (e.g., influenza, pneumococcal disease, tuberculosis).
- Outline the treatment options for bacterial, viral, fungal, and parasitic respiratory infections.

Introduction

- The respiratory system serves as a vital gateway to the body's internal environment, facilitating the delivery of oxygen and the removal of carbon dioxide.
- In addition to its primary function in respiration, it also plays a key role in sound production and the detection of odors, contributing to both communication and sensory experiences.
- Infections of the respiratory system can significantly affect overall health, with consequences ranging from mild discomfort, such as sinusitis, to life-threatening conditions like pneumonia and COVID-19.

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History

Discoveries about the causes of respiratory infections:

- In ancient civilizations, respiratory infections were often attributed to bad air, the "miasma" theory, or divine punishment. Egyptians and Greeks used herbal remedies such as frankincense, myrrh, and prayers as treatment.
- The Greek physician Hippocrates (circa 400 BCE) described symptoms of pneumonia and other respiratory diseases, but understanding of infections was still limited.
- In 1720, for the first time, the infectious origin of tuberculosis (TB) was conjectured by the English physician Benjamin Marten, while the first successful remedy against TB was the introduction of the sanatorium cure.
- Louis Pasteur (1857–1860s) helped establish that microorganisms cause diseases with his work on the germ theory, including respiratory infections like tuberculosis and pneumonia.
- In 1882, Robert Koch isolated the Mycobacterium tuberculosis as the causative agent of tuberculosis. In the decades following this discovery, the Pirquet and Mantoux tuberculin skin tests, Albert Calmette and Camille Guérin BCG vaccine, Selman Waksman streptomycin, and other anti-tuberculous drugs were developed.

Milestones on the respiratory infections

- Before Gram's discovery, the identification of bacteria was primarily based on their shape and arrangement (cocci, bacilli, etc.). In 1884, Hans Christian Gram, who was working at the University of Copenhagen, developed the Gram stain, which helped to differentiate bacterial species This differentiation helped to classify bacteria based on their cell wall structure, influencing subsequent treatment of bacteria and research in microbiology, medicine, and immunology.
- Rebecca Langsfield classified and distinguished different serotypes of Streptococcus pyogenes based on the bacterial surface structures during the 1930s-40s.
- Identifying the influenza virus marked a breakthrough in understanding viral respiratory infections. In 1933, British researchers Wilson Smith, C.H. Andrewes, and P.P. Laidlaw made a breakthrough when they isolated and identified the influenza virus. Thomas Francis and Jonas Salk developed the first inactivated flu vaccine at the University of Michigan. The vaccine tested for safety and efficacy in the US military before being licensed for broader use in 1945(2).
- The coronavirus disease 2019 (COVID-19) started as an epidemic in Wuhan in 2019 and has become a pandemic. Groups from China identified and sequenced the virus as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (3). The first COVID-19 vaccine was discovered in 2020 and approved by the US Food and Drug Administration in 2021.

Milestones in Diagnosis and Treatment of Respiratory Infections

- The discovery of microscopy, X-Ray, polymerase chain reaction and ventilators helped in diagnosis and treatment of the respiratory infections.
- During the early 20th century, Alexander Fleming discovered penicillin in 1982, marking the beginning of the antibiotic era, and consecutively played an essential role in treating bacterial respiratory infections such as pneumonia and tuberculosis.
- Antiviral medications began to being developed in the 1940s and 1950s, but usage was limited.
- With the advent of the antibiotic rifampicin and other drugs, TB became treatable, although it remains a major global health issue, particularly in developing countries.

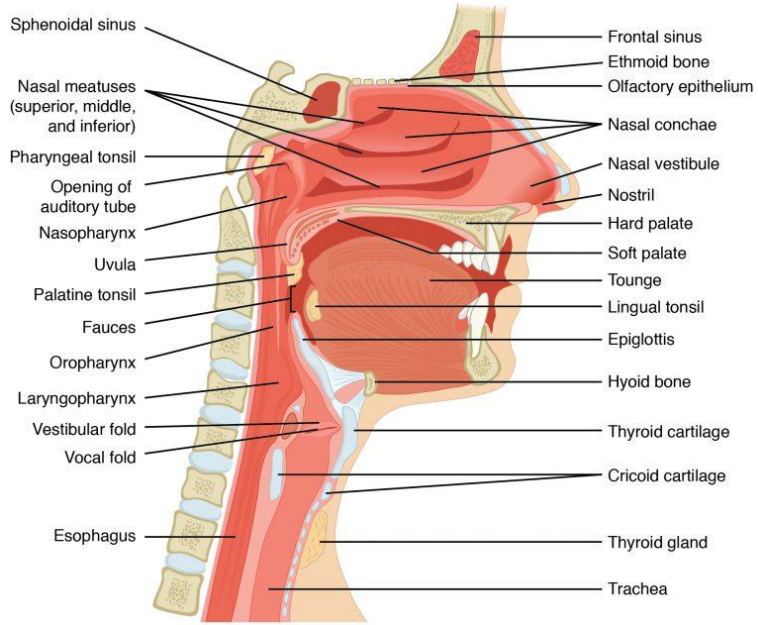
https://www.manualslib.com/manual/2003976/Penlon-Eso-2.html

Overview of Human Respiratory System Anatomy and Physiology

Anatomically, the respiratory system is studied in two parts: the upper and lower respiratory tract.

1. Upper Respiratory Tract (URT):

- ***The Organs:*** Nose, nasal cavities, paranasal sinuses, tonsils (lymphoid tissues), pharynx(throat), and larynx (voice box)
- ***Functions:*** URT organs filter, warm, moisten the air, and allow sound production.
- ***Defense mechanisms:***
  - Mucous membranes line the nose, nasal cavities, pharynx, larynx, and sinuses. The mucosa of the respiratory system contains goblet cells, which produce mucus to create a protective barrier and trap foreign particles and goblet cells.
  - The respiratory epithelium contains cilia that propels the mucus toward the gastrointestinal system so that an acidic stomach can eliminate trapped particles in the mucus. This system is called the mucociliary clearance or escalator because it propels mucus and traps particles away from the lungs.
  - Tonsils are lymphoid tissues that act as a first line of defense, preventing harmful pathogens (like bacteria and viruses) that enter the body through the mouth or nose.



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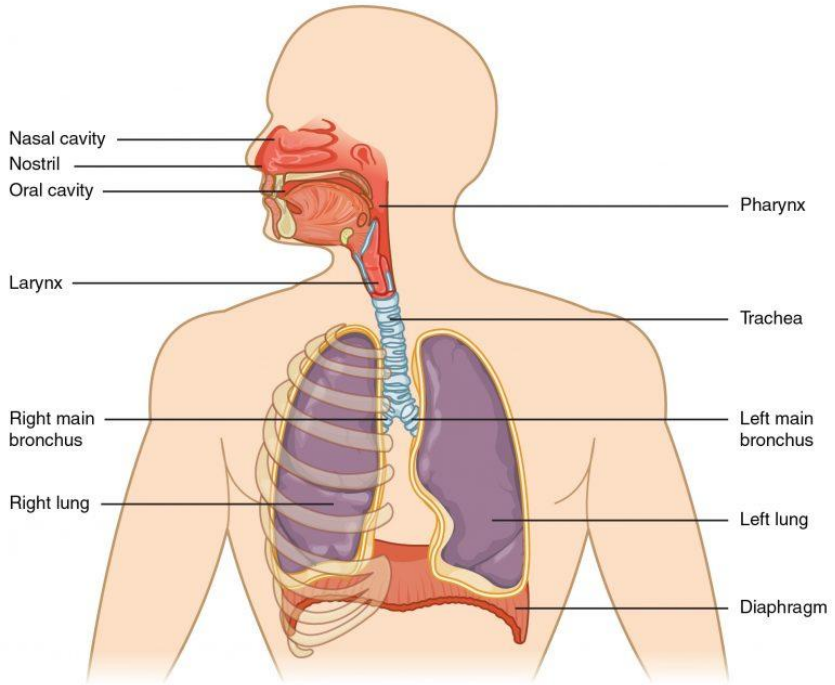
Overview of Human Respiratory System Anatomy and Physiology

2. Lower Respiratory Tract (LRT):

- ***The Organs:*** Trachea, bronchi, bronchioles, alveoli of the lung
- ***Functions:*** LRT organs continue filtering and humidifying the air, gas transport, oxygen exchange, and carbon dioxide removal.
- ***The Defense mechanisms*** of our body against lower respiratory tract infections are
  - Mucociliary clearance and
  - Immune responses (e.g., phagocytosis by macrophages).



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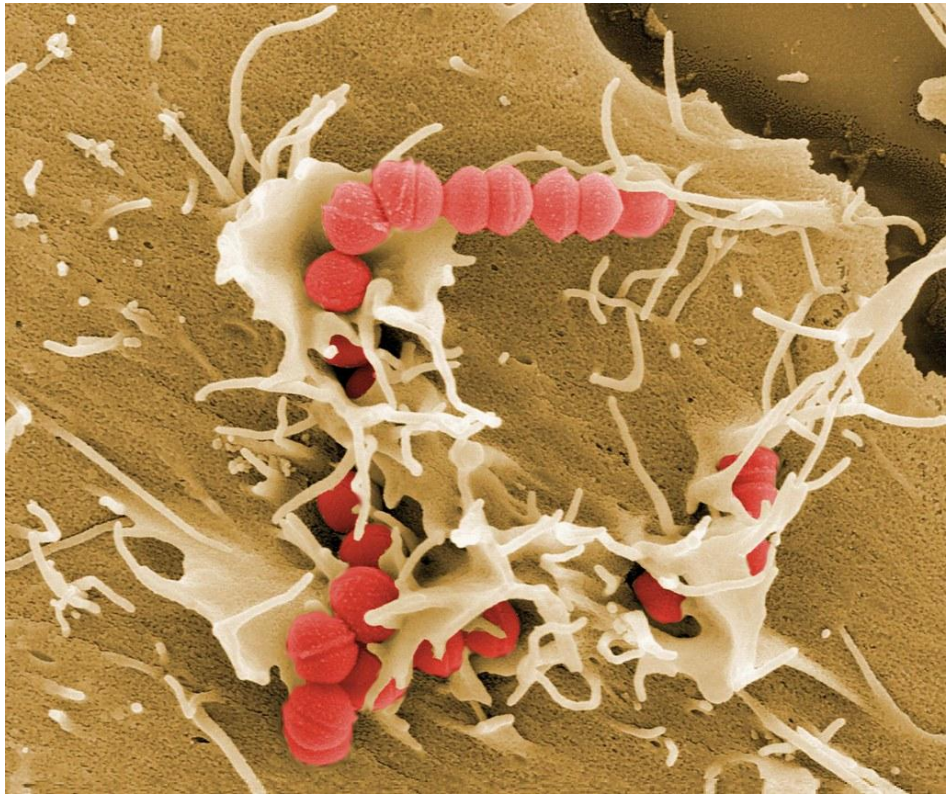
Terminology about inflammation and infection within the respiratory system.

- ***Rhinitis:*** Inflammation and/or infections of the nose
- ***Tonsillitis:*** Inflammation and/or infections of tonsils
- ***Sinusitis:*** Inflammation and/or infections of sinuses.
- ***Pharyngitis:*** Inflammation and/or infections of the pharynx (throat).
- ***Laryngitis:*** Inflammation and/or larynx infections (voice box).
- ***Epiglottitis***: Inflammation and/or infections of epiglottis.
- ***Tracheitis:*** *Inflammation and/or infections of the trachea*
- ***Bronchitis:*** Inflammation and/or infections of bronchi.
- ***Bronchiolitis***: Inflammation and/or infections of bronchioles
- ***Pneumonia:*** Infections of the lungs, particularly the alveoli, fill with fluids.
  - *Conjunctivitis: Inflammation and/or infection of conjunctiva
  - *Otitis media: Inflammation and /or infection of the middle ear.
  - *Although they are not anatomically part of the respiratory system, they are also involved when there are respiratory infections due to their location nearby.

Bacterial Infections of Upper Respiratory Tract:

- The most common bacteria that cause infections in the organs of the URT are Streptococcus pyogenes, Streptococcus *pneumoniae*, Hemophilus *influenzae*, Moraxella *catarrhalis*, and Klebsiella *pneumoniae*.
- Proper diagnosis and treatment with appropriate antibiotics are crucial to managing these infections and preventing complications
- To cause an infectious disease, the bacteria need to colonize, and the acquisition and elimination of species change the balance of certain bacteria. It is strongly related to the host's immune strength and the environmental factors



Invasion of Streptococcus pyogenes into human epithelial cell

Group A Streptococcus (GAS), Streptococcus pyogenes

- The pathogen is the "Group A Streptococcus (GAS), known as Streptococcus *pyogenes."* They cause a disease known as Streptococcal Pharyngitis ("Strep Throat")
- Streptococcus pyogenes is a Gram-positive bacterium and grows in chains.
- It causes β-hemolysis on the blood agar (a clear area forms due to complete lysis)
- According to Lancefield grouping, it is a Group A Streptococcus (GAS), and different strains of the GAS can be distinguished by M protein.

Streptococcus pyogenes (Lancefield Group A) on Columbia Horse Blood Agar
https://commons.wikimedia.org/wiki/File:Streptococcus_pyogenes_%28Lancefield_Group_A%29_on_Columbia_Horse_Blood_Agar.jpg

Group A Streptococcus (GAS), Streptococcus pyogenes

- Streptococcus pyogenes secretes enzymes, such as hyaluronidase and streptokinase, that break down tissues and help the bacteria invade deeper mucosa layers. Streptolysins O and S make holes in the membranes of erythrocytes and leukocytes, yield β-hemolysis, and inhibit the immune system.
- GAS produces several virulence factors (the ability of a microorganism to cause damage to its host). Factors that help it evade the host's immune defenses. These include:
  - M protein: This protein helps the bacteria avoid being engulfed by phagocytes (immune cells) and prevents the activation of the complement system.
  - C5a peptidase: This enzyme degrades C5a, a molecule involved in the immune response, reducing the recruitment of immune cells to the site of infection.
  - Capsule: The bacterial capsule, made of hyaluronic acid, is like human tissue, allowing the bacteria to avoid recognition by the immune system

Diagnosis and Treatment of Streptococcus *pyogenes*

- Diagnosing strep throat involves a combination of clinical evaluation and laboratory tests. Examination findings that may suggest strep throat include erythema (redness) and swelling of the throat and tonsils, exudate (pus) on the tonsils, petechiae (small red spots) on the roof of the mouth (in some cases).
- *The rapid antigen test* (the rapid strep test) is a commonly used diagnostic tool. It works by detecting the presence of Group A Streptococcus antigen in a throat swab sample. The procedure is relatively quick and can provide results in about 15-20 minutes.

- Antibiotics (typically penicillin or amoxicillin) are effective in treating streptococcal pharyngitis, reducing symptoms, preventing complications, and shortening the duration of the illness.
- Due to cross-reactive antibodies (M-protein), complications may develop after streptococcal infections. If left untreated or ineffectively treated, streptococcal pharyngitis can lead to serious complications, such as:
- Rheumatic fever: An autoimmune condition that can affect the heart, joints, skin, and nervous system, occurring due to cross-reactivity between antibodies against the bacteria and host tissues.
- Post-streptococcal glomerulonephritis: Damage to kidneys from immune complexes.
- Peritonsillar abscess: Forms a collection of pus near the tonsils that can cause severe pain and difficulty swallowing.

Corynebacterium *diphtheriae*

- Corynebacterium diphtheriae, a pleomorphic, gram-positive rod that has caused diphtheria since ancient times
- The bacterium is an aerobic, gram-positive bacillus with club-shape that grows side by side in "palisades" or attached on one end in a "V" formation. It produces a toxin. Diphtheria toxin causes cell death - may be released into the bloodstream, causing organ damage.
- Diphtheria primarily affects the throat and upper respiratory tract; It may form a pseudo membrane in the throat from dead cells and may obstruct airways.

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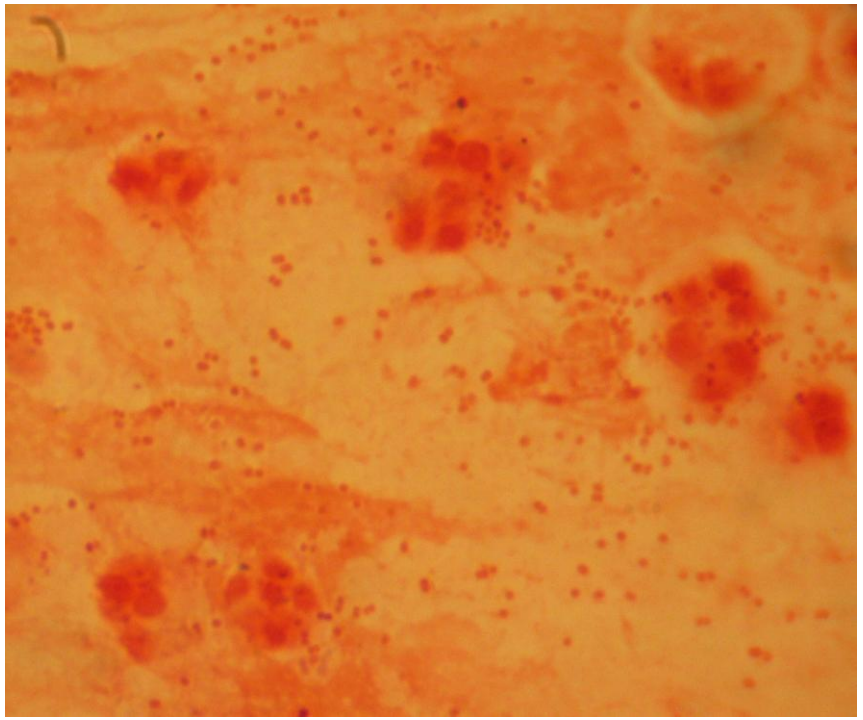
Hemophilus influenzae

- H. influenzae is a gram-negative, facultatively anaerobic coccobacillus.
- There are six types of H. influenzae. H. influenzae, type b (Hib) usually causes the most severe disease and is the only type that is preventable by the vaccine.
- Hemophilus influenzae (H. influenzae) is a group of bacteria that can cause different types of infections but most often cause ear, eye, or sinus infections. They also cause pneumonia. People spread H. influenzae to others by coughing or sneezing, which creates tiny respiratory droplets that contain the bacteria.



https://commons.wikimedia.org/wiki/File:Haemophilus_influenzae_Gram.JPG

Streptococcus *pneumoniae*

- Streptococcus pneumoniae is a gram-positive, lancet-shaped, facultative anaerobic organism typically occurring in pairs or short chains (Dion). Streptococcus pneumoniae (the pneumococcus) is the leading cause of otitis media, community-acquired pneumonia, and bacterial meningitis

- **Causes**: Sinusitis, otitis media, pneumonia. It can also affect the lower respiratory tract and cause bacterial bronchitis and pneumonia.
- **Symptoms**: Nasal congestion, cough, ear pain, fever, and sometimes difficulty breathing.
- **Treatment**: Antibiotics, including amoxicillin, penicillin, or other broad-spectrum antibiotics.

Bacterial infections of URT

- **Moraxella *catarrhalis***
- Moraxella *catarrhalis* is a gram-negative diplococcus. In humans, it most commonly involves the upper respiratory tract and the middle ear (Embers).
- **Causes**: Otitis media, sinusitis, and sometimes bronchitis in children and adults.
- **Symptoms**: Nasal congestion, sore throat, ear pain, and cough.
- **Treatment**: Often treated with amoxicillin-clavulanate or other antibiotics, though some strains are resistant to common antibiotics.

- **Neisseria *gonorrhoeae*** are gram-negative diplococci with hair-like appendages, pili, covering the bacterial surface. Pili allows adhesion to the epithelial lining.
- It is an obligatory human pathogen and sexually transmitted disease. It can also infect the upper respiratory tract, causing a condition called "gonococcal pharyngitis," Typically transmitted through oral receptive sex. N. gonorrhoeae is currently the second most common cause of sexually transmitted bacterial infections worldwide

Viral Infections of Upper Respiratory Tract

The most common viruses responsible for upper respiratory infections include:

1. Rhinovirus

- Rhinovirus is a single-stranded RNA virus that belongs to the Picornaviridae family of viruses. There are over 100 serologic virus types. Rhinoviruses are the most common viral infective agents in humans, and the main cause of the common cold. (Crowe) https://www.sciencedirect.com/science/article/pii/B9780128012383026003
- More than 30-50% of the time causative agents of common cold are Rhinoviruses. Adenoviruses (5-10% of the common cold) and coronavirus (10-15 % of common cold) also produce cold sign and symptoms.
- Symptoms are runny nose, nasal congestion, sneezing, sore throat, cough, mild headache, and mild fever.
- Common cold spread through respiratory droplets, direct contact with infected surfaces, or close contact with an infected person. Rhinovirus infections are most common in fall and spring.

Viral Infections of Upper Respiratory Tract

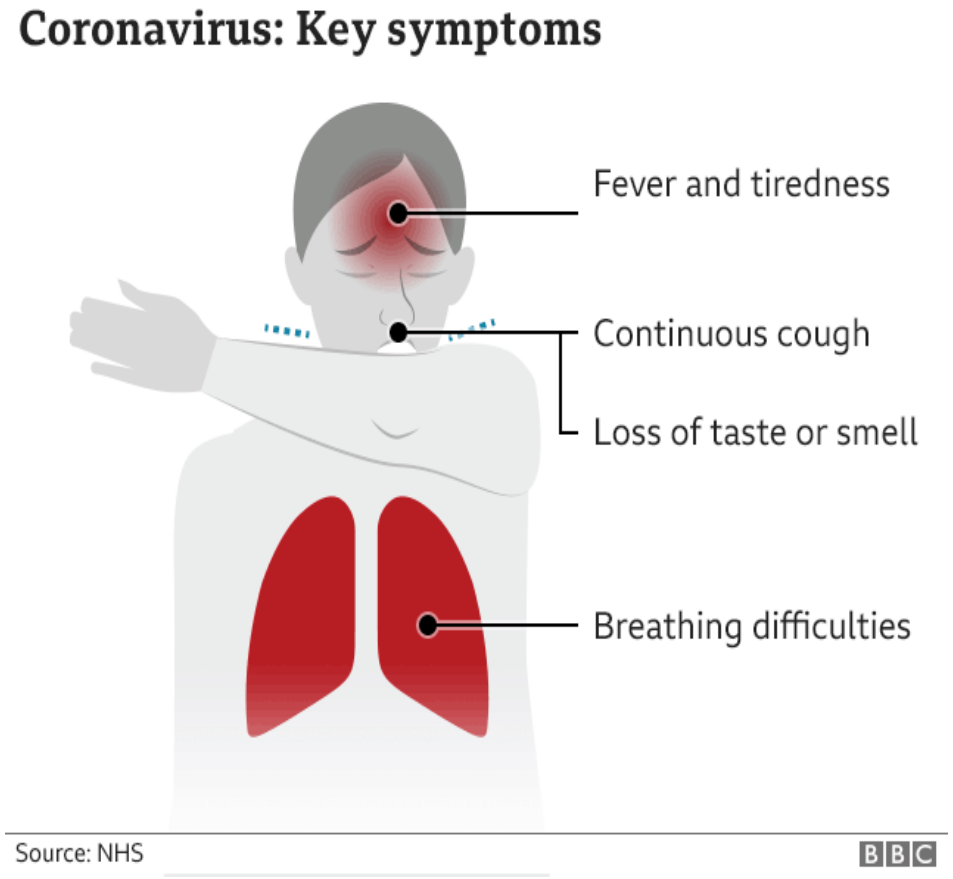
2. Influenza Virus

- Influenza virus is an RNA type of virus.
- There are four types of influenza viruses: A, B, C, and D. Influenza A and B viruses cause seasonal epidemics of disease in people (known as flu season) almost every winter in the United States. Influenza C virus infections generally cause mild illness and are not thought to cause human epidemics. Influenza D viruses primarily affect cattle with spillovers to other animals but are not known to infect people to cause illness.
- Influenza A viruses are divided into subtypes based on two proteins on the surface of the virus: hemagglutinin (H) and neuraminidase (N). There are 18 different hemagglutinin subtypes and 11 different neuraminidase subtypes

Viral Infections of Upper Respiratory Tract

3. Coronavirus

- Coronaviruses are a group of related RNA viruses. Coronaviruses can cause upper respiratory infections, which affect the nose, sinuses, and throat. Symptoms include sneezing, sore throat, and cough. COVID-19 can also affect the lower respiratory system, causing more severe symptoms like chest tightness and shortness of breath.
- The Symptoms of common cold caused by coronaviruses runny nose, sore throat, cough, and sometimes mild fever. For COVID-19, symptoms can be more severe, including high fever, cough, shortness of breath, loss of taste/smell, and fatigue.
- Spread through respiratory droplets, close contact, or contaminated surfaces. COVID-19 is highly contagious, especially via airborne particles.



Viral Infections of Upper Respiratory Tract

4. Adenovirus

- Adenoviruses are a type of DNA virus that commonly causes upper and lower respiratory infections, often presenting as symptoms similar to a common cold and may cause pharyngitis, tonsillitis, common cold, and conjunctivitis (pink eye). It may progress to viral pneumonia or acute respiratory disease (ARD) in military recruits (vaccine available).
- Symptoms are sore throat, fever, cough, nasal congestion, conjunctivitis, headache and sometimes gastrointestinal symptoms like diarrhea.
- Spread through respiratory droplets, direct contact, or contaminated surfaces (like swimming pools). Adenoviruses circulate year-round but are more common in colder months.

5. Parainfluenza viruses (PIV)

- The human parainfluenza virus (HPIV) is an enveloped, single-stranded RNA virus that belongs to the family of Paramyxovirus. Parainfluenza viruses (PIV) can cause upper respiratory tract infections (URTIs
- They are a common cause of URTIs in children and are also a major cause of respiratory infections in the elderly and immuno-compromised adults. They are particularly associated with croups, in children, accounting for up to 80% of cases. It is one of the major causes of morbidity and mortality in infants worldwide.
- Symptoms are runny or stuffy nose, sore throat, fever, cough (which may be barky in the case of croup), shortness of breath or wheezing.

Fungal Infections of the Upper Respiratory Tract

- Healthy people rarely get fungal infections but may cause severe infections for the individuals who have another health condition (such as cystic fibrosis), suppressed immune system due to taking medication that suppresses their immune system (such as treatments for cancer or rheumatoid arthritis) or the diseases who causes weakened immune system such as AIDS.
- Most common causes of fungal infections of upper respiratory tracts are the candidiasis and aspergillus.
- Candida ranks as one of the most prevalent causes of health care–associated infections in North America
- Aspergillus is a mold found widely in the environment. Given the ubiquitous nature of fungi, exposure is unavoidable yet can cause a condition called aspergillosis primarily in the individuals with weakened immune conditions or underlying chronic conditions

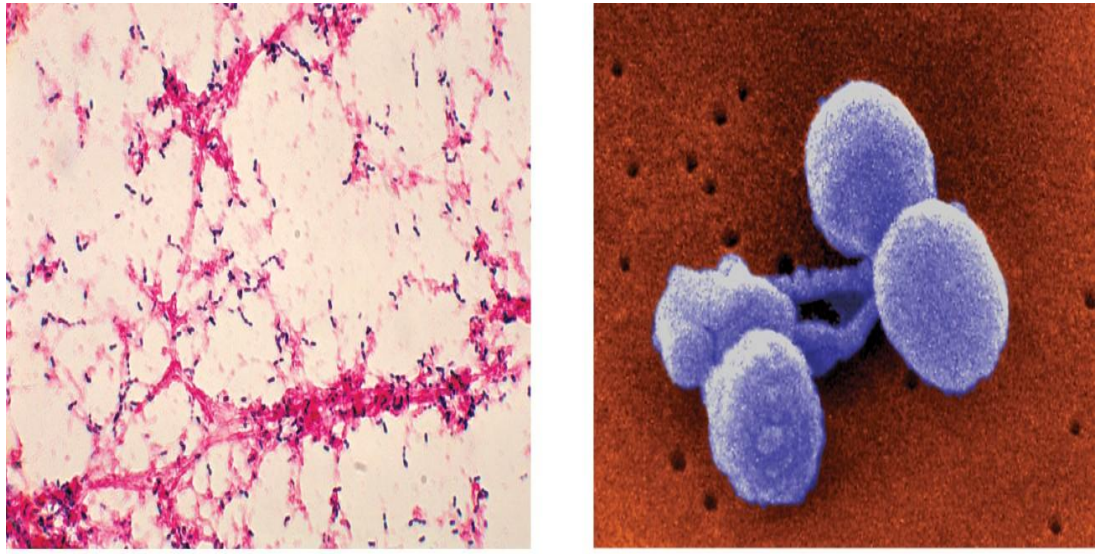
Infections of The Lower Respiratory Tract (LRI)
A. Bacterial Infections of the Lower Respiratory Tract Infections

- Typical Community Acquired Pneumonia (CAP)s are most commonly caused by pathogens, such as Streptococcus *pneumoniae* and Haemophilus *influenzae.*
- They primarily present more acute symptoms, such as a high fever, productive cough and localized chest pain.
- These infections are typically associated with radiographical findings of lobar consolidation and respond well to β-lactam antibiotics, which target the bacterial cell wall.

Bacterial Infections of the Lower Respiratory Tract Infections

1. Pneumococcal pneumonia:

- The most common type of bacterial pneumonia is called pneumococcal pneumonia and caused by the Streptococcus pneumoniae bacteria that normally lives in the upper respiratory tract. It infects over 900,000 Americans every year.
- With childhood conjugate vaccination for Streptococcus pneumoniae, the colonization frequency has decreased.
- Pneumococcal infections are present throughout the world and are most common during the winter and early spring months.
- Bacterial pneumonia can occur on its own or develop after people have a virus like the cold, flu, COVID-19 or RSV. Bacterial pneumonia often affects just one part, or lobe of a lung. When this happens, the condition is called lobar pneumonia.



(a) (b)

(a) This micrograph of Streptococcus pneumoniae grown from a blood culture shows the characteristic lancet-shaped diplococcal morphology. (b) A colorized scanning electron micrograph of S. pneumoniae. (credit a: modification of work by Centers for Disease Control and Prevention; credit b: modification of work by Janice Carr, Centers for Disease Control and Prevention)

Bacterial Infections of the Lower Respiratory Tract Infections

2. Haemophilus i*nfluenzae*

- Haemophilus *influenza* is a small, facultatively anaerobic, pleomorphic, and capnophilic gram-negative coccobacillus.
- It can cause infections in children and sometimes in adults. One type, Haemophilus influenzae type b (Hib), is more likely to cause serious infections. H. influenzae can cause many different types of infections. These infections range from mild, like ear infections, to serious, like bloodstream infections such as bronchitis, pneumonia and meningitis. Bronchitis is a common result of a bacterial infection caused by Haemophilus influenzae.
- Infection is spread by sneezing, coughing, or touching infected people.
- Washing hands often and not having close contact with people who are sick helps prevent H. influenzae disease. The best way to prevent Hib disease is to get vaccinated. CDC recommends Hib vaccines for all children younger than 5 years old.
- The approach to treating H. influenzae infections mainly involves antibiotics and conservative measures. The initial antibiotic choice is a third-generation cephalosporin while waiting for the culture and sensitivity results. Antibiotic resistance is the issue of concern, and it is essential to monitor the response to treatment and alter the antibiotic accordingly

Bacteria Cause Atypical Pneumonia

- If a patient presents with pneumonia, and in addition there are extrapulmonary findings, the patient has an atypical pneumonia.
- The most common atypical pneumonias are caused by three zoonotic pathogens, *Chlamydia psittaci* (psittacosis), *Francisella tularensis* (tularemia), and *Coxiella burnetii* (Q fever), and three non-zoonotic pathogens, *Chlamydia pneumoniae, Mycoplasma pneumoniae, and Legionella.* (Cunha)
- Atypical pulmonary pathogens causing pneumonia may also cause outbreaks of nursing home-acquired pneumonia (NHAP) or nosocomial pneumonia (NP). Legionella is an important cause of severe community acquired pneumonia (CAP) in hospitalized patients.

Mycoplasma pneumoniae

- Mycoplasma pneumoniae, a tiny wide-spread bacterium that usually infects people younger than 40 years old, especially those living and working in crowded conditions. The illness is often mild enough to go undetected and is sometimes referred to as walking pneumonia.
- People who have pneumonia caused by M. pneumoniae often have milder illnesses than you would think for someone with a lung infection. They started calling this type of infection “walking pneumonia” because people did not stay home and in bed due to the mild symptoms. You should stay home when you are sick. Like other respiratory infections, it is spread through respiratory droplets when an infected person sneezes or coughs.
- These bacteria are referred to as "atypical" because pneumonia caused by these organisms might have slightly different symptoms, appear different on a chest X-ray, or respond to different antibiotics than the typical bacteria that cause pneumonia. Even though these infections are called "atypical," they are not uncommon. (ALA)
- Mycoplasma pneumoniae tightly binds to the host epithelial cells through its unique attachment organelle, which are considered the primary factor and prerequisite for the pathogenicity of M. pneumoniae.

Hospital-Acquired Bacterial (HAP) or Nosocomial Infections.

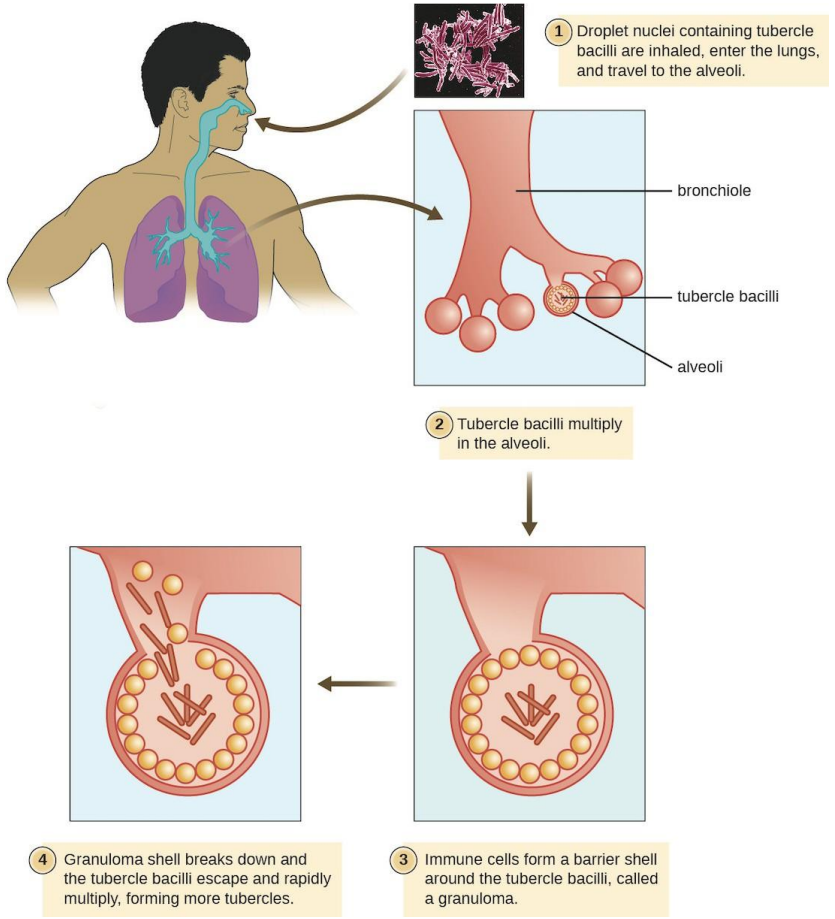
- HAP refers to any pneumonia contracted by a patient in a hospital at least 48–72 hours after being admitted. It is thus distinguished from community-acquired pneumonia. It is usually caused by a bacterial infection, rather than a virus.
- Common pathogens of HAP and Ventilator associated pneumonia (VAP) include aerobic gram-negative bacilli (e.g. *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter* spp, *Acinetobacter* spp) and gram-positive cocci (e.g., *Staphylococcus aureus*, which includes methicillin-resistant S. aureus, *Streptococcus* spp). Differences in host factors and in the hospital flora of an institution affect the patterns of the causative pathogens.
- HAP occurs at a rate of 5 to 10 per 1000 hospital admissions and is considered the most common cause of hospital-acquired infection in Europe and the United States. Over 90% of pneumonia episodes developing in ICUs occur in patients who are intubated and mechanically ventilated. Symptoms may include cough, expectoration, a rise in body temperature, chest pain, or dyspnea. Signs include fever, tachypnea, consolidations, or crackles.

Mycobacterium tuberculosis

- **Tuberculosis (TB)** is an infectious disease caused by the bacterium Mycobacterium *tuberculosis*. It primarily affects the lungs but can also spread to other organs. TB is spread through the air when a person with active TB disease coughs, sneezes, or talks. Common symptoms of active tuberculosis include cough, chest pain, and coughing up blood.
- *M. tuberculosis* causes a chronic granulomatous disease that can infect any area of the body, although it is typically associated with the lungs. *M. tuberculosis* is spread by inhalation of respiratory droplets or aerosols from an infected person. The infectious dose of *M. tuberculosis* is only 10 cells. After inhalation, the bacteria enter the alveoli and are engulfed by macrophages but are not destroyed because of the mycolic acid in bacterial cell walls.
- The infection progresses and causes immune reactions to form small round lesions called tubercles. Bacteria are still alive and released into the center of the tubercles and the chronic immune response results in tissue damage and induction of apoptosis (programmed host-cell death) in a process called liquefaction. This creates a caseous center, or air pocket, where the aerobic *M. tuberculosis* can grow and multiply. Tubercles may eventually rupture, and bacterial cells can invade pulmonary capillaries; from there, bacteria can spread through the bloodstream to other organs, a condition known as **miliary tuberculosis**. The rupture of tubercles also facilitates transmission of the bacteria to other individuals via droplet aerosols that exit the body in coughs. Because these droplets can be very small and stay aloft for a long time, special precautions are necessary when caring for patients with TB, such as the use of face masks and negative-pressure ventilation and filtering systems.

Mycobacterium tuberculosis

- Eventually, most lesions heal to form calcified **Ghon complexes**. These structures are visible on chest radiographs and are a useful diagnostic feature. But even after the disease has apparently ended, viable bacteria remain sequestered in these locations. Release of these organisms at a later time can produce **reactivation tuberculosis** (or secondary TB). This is mainly observed in people with alcoholism, the elderly, or in otherwise immunocompromised individuals.
- Diagnostic tests are the chest X-ray, Tuberculin skin test (Mantoux test), and blood test (Interferon-gamma release assay).



Mycobacterium tuberculosis

- It can be prevented by vaccination with the BCG vaccine, avoiding contact with people with active TB disease, practicing good hygiene, such as covering your mouth and nose when coughing or sneezing. (OER)
- Because TB is a chronic disease, chemotherapeutic treatments often continue for months or years. Multidrug resistant (MDR-TB) and extensively drug-resistant (XDR-TB) strains of *M. tuberculosis* are a growing clinical concern. These strains can arise due to misuse or mismanagement of antibiotic therapies. Therefore, it is imperative that proper multidrug protocols are used to treat these infections. Common antibiotics included in these mixtures are isoniazid, rifampin, ethambutol, and pyrazinamide. (OER)
- TB is treated with a combination of antibiotics for several months. The specific treatment plan depends on the severity of the disease and the patient's overall health.

Viral Infections of the LRT Infections

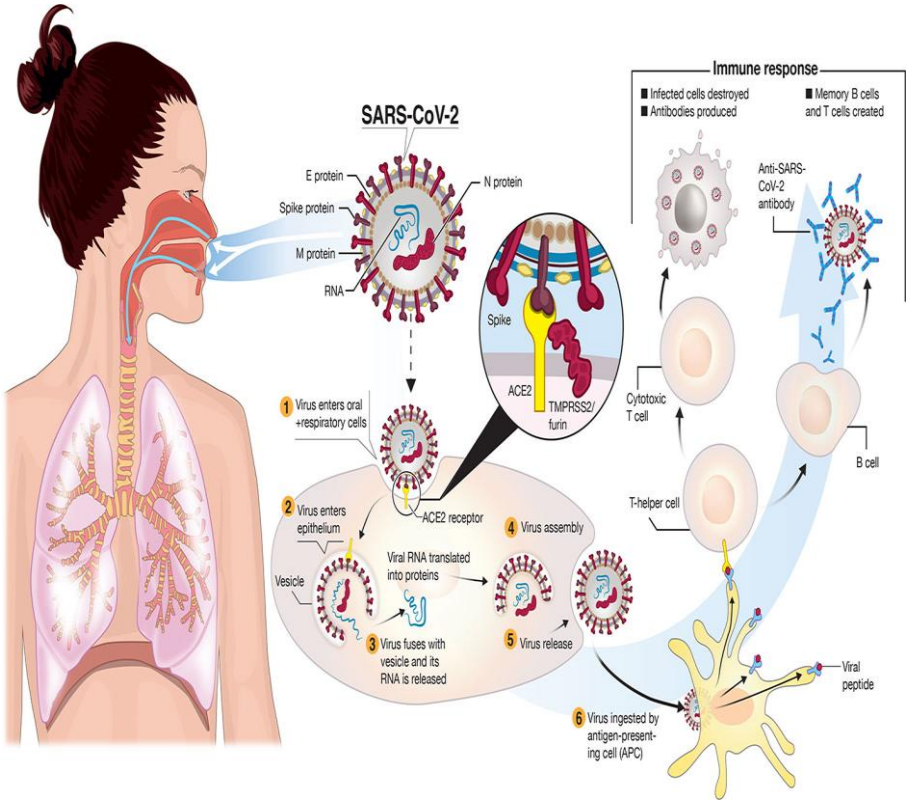
- Pneumonia, bronchiolitis and other lower respiratory tract infections (LRTI) continue to be a major cause of morbidity and mortality worldwide disproportionately affecting adults ≥ 70 years and children < 5 years old.
- 60% or more of LRIs are primarily viral.
- Viruses that infect the upper respiratory tract may also cause pneumonia. SARS-CoV-2, the virus that causes COVID-19, and the influenza virus are the most common causes of viral pneumonia in adults. Respiratory syncytial virus (RSV) is the most common cause of viral pneumonia in young children. Most viral pneumonias are not serious and last a shorter time than bacterial pneumonia.
- COVID-19 pneumonia can be severe, causing low levels of oxygen in the blood and lead to respiratory failure and in many cases a condition called acute respiratory distress syndrome (ARDS). Viral pneumonia caused by the SARS-CoV-2 virus generally occurs in both lungs. As the lungs fill with fluids, oxygen exchange becomes more difficult and results in breathing difficulties. Recovery may take months before symptoms ease.

Coronaviruses

Coronaviruses are a large family of viruses that usually cause mild to moderate upper-respiratory tract illnesses in humans. However, three coronaviruses have caused more serious and fatal disease in people:

- SARS coronavirus (SARS-CoV), which emerged in November 2002 and causes severe acute respiratory syndrome (SARS);
- MERS coronavirus (MERS-CoV), which emerged in 2012 and causes Middle East respiratory syndrome (MERS); and
- SARS-CoV-2, which emerged in 2019 and causes coronavirus disease 2019 (COVID-19)

CDC recommends that all people use core prevention strategies. These are important steps you can take to protect yourself and others: Stay up to date with immunizations, practice good hygiene (practices that improve cleanliness), take steps for cleaner air, when you may have a respiratory virus: use precautions to prevent spread, seek health care promptly for testing and/or treatment if you have risk factors for severe illness; treatment may help lower your risk of severe illness

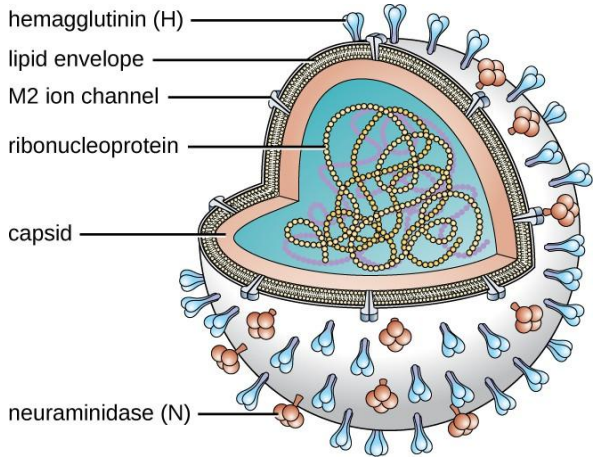


Respiratory Syncytial Virus (RSV)

- RSV is an RNA virus and may cause bronchiolitis and pneumonia (more common in infants (children under 1 year of age) and young children, but it can affect adults too.
- It may cause cold-like symptoms, including runny nose, sore throat, cough, fever, and wheezing.
- It spread through respiratory droplets, direct contact, or contact with contaminated surfaces. RSV infections are most common in the winter and early spring.
- Because the immune response to RSV does not protect against reinfection, the attack rate is approximately 40% for all exposed people. However, antibody to RSV decreases illness severity. (Bhatia).
- Usually, a specific viral diagnosis is clinically unnecessary but may help distinguish a parainfluenza virus infection from a bacterial infection in patients with severe lower respiratory tract disease. The virus can be detected by polymerase chain reaction.
- Treatment of parainfluenza virus infection is symptomatic.

Influenza A and B Virus

- Influenza viruses are single-strand RNA viruses.
- Influenza A viruses primarily target and infect airway and alveolar epithelial cells, which contain the SA glycans as receptors, thus causing alveolar epithelial injury and eventually failure of gas exchange Hence, human IAV infection may lead to acute respiratory distress syndrome (ARDS) and even death.
- Influenza is a type of self-limiting disease characterized by acute onset of fever, sore throat, malaise, and respiratory symptoms. In healthy people, the disease is resolved without any complications. However, considerable excess mortality is observed in elderly and comorbid patients1. Although influenza combined with pneumonia can lead to death, mortality is often caused by the aggravation of a preexisting disease such as bronchial asthma, chronic obstructive airways disease, and cardiovascular diseases.
- There have been at least 31 influenza pandemics since 1510.



Influenza A and B Virus

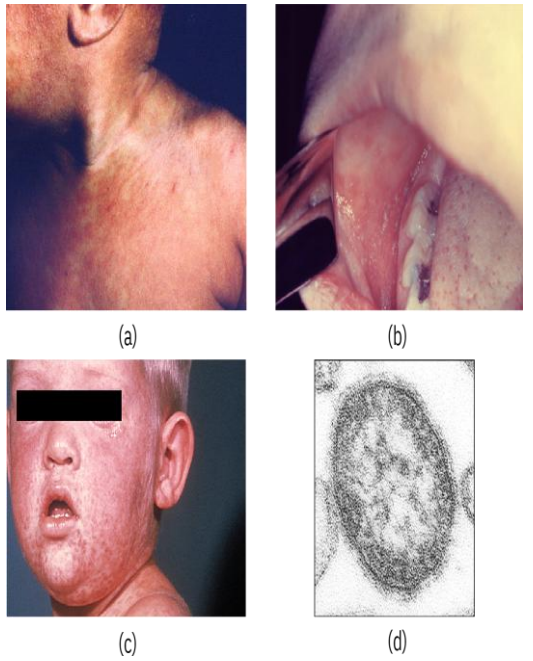
- Influenza contains two types of spikes. Hemagglutin (H) helps the virion attach and penetrate host cells. Neuraminidase (N) helps release virions from the host cell after replication and assembly. Each year a slightly different seasonal flu strain evolves and requires development of a new vaccine – a mixture of the most common type A and B subtypes
- Influenza A strikes every year and causes most epidemics. Influenza B also strikes every year but is less common than type A. Influenza C causes mild respiratory illness but not epidemics.
- Complications are Guillain-Barre syndrome damages nerves and Reye syndrome which develops on the kids using aspirin
- The best way to prevent the flu is to get vaccinated annually. Other ways to prevent the spread of the flu include avoiding people who are sick, washing your hands, and covering your cough.
- Antiviral medications such as oseltamivir or zanamivir can treat and prevent the flu. Rest and fluids are self-care remedies that can help with flu symptoms.

Parainfluenza Virus

- Human parainfluenza viruses (HPIV) cause respiratory illnesses commonly in infants and young children, but anyone can become ill once they are infected. There are four types of HPIVs (HPIV-1, HPIV-2, HPIV-3, and HPIV-4). HPIV-1 and -2 are commonly associated with cold-like symptoms. HPIV-3 is often associated with pneumonia. HPIV-4 usually causes mild to severe illness. (Olakino)
- HPIV causes croup, laryngitis, and bronchitis (mostly in children but can affect adults).
- Symptoms develop 2-7 days after the infection and are cough, fever, sneezing, sore throat, and stridor (a high-pitched wheezing sound when breathing in, characteristic of croup) and wheezing.
- It spreads via respiratory droplets or direct contact. RSV infections are more common in the fall and early winter months.
- HPIV infections can be diagnosed with confirmatory tests by polymerase chain reaction (PCR), detection of viral antigens in respiratory secretions, viral culture, and HPIV-specific antibody detection.
- There is no specific treatment for HPIV illness. Treatments for symptom relief include taking over-the-counter medication for fever, cough and sore throat, drinking plenty of fluids, and resting.

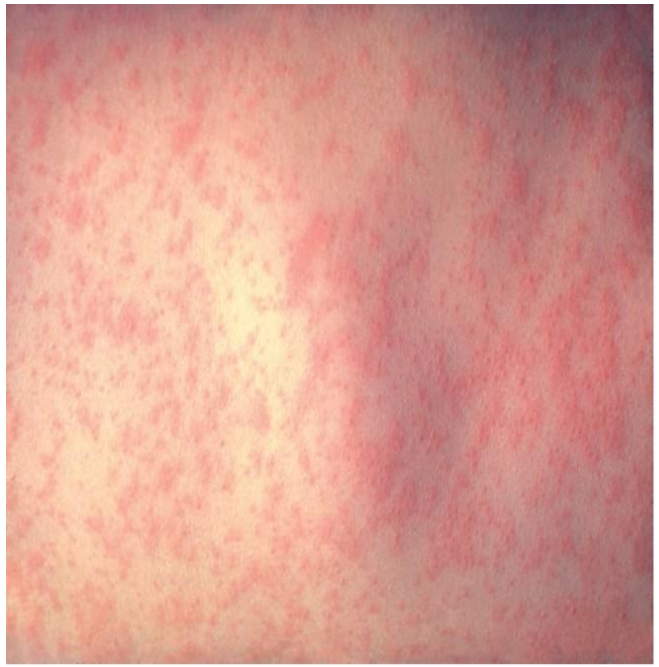
Viruses may spread through respiratory system - Rubeola

- It is highly contagious virus causes Measles. The virus lives in the nose or throat of an infected person and spreads through the mucus or saliva of the infected person. The infected droplets spread into the air through sneezing and coughing and may fall on surfaces; this can remain active for several hours.
- The symptoms usually begin 7 to 14 days after infection. Measles can be dangerous, especially for babies and young children and can lead to serious complications. Measles typically begins with high fever (may spike to more than 104°), cough, runny nose (coryza) and conjunctivitis. Koplik spots are small, bluish-white spots on the inner lining of the mouth (buccal mucosa) in people with measles. They are a characteristic sign of the disease and typically appear 1-2 days before the onset of the measles rash.
- Measles affects multiple systems, including the respiratory system, with pneumonia being one of the most lethal complications. Management involves best supportive care, correction of dehydration and nutritional deficiencies, treatment of secondary bacterial infections and provision of vitamin A.



Viruses may spread through respiratory system-Rubella

- Rubella, or the German measles, is a relatively mild viral disease that produces a rash somewhat like that caused by the measles, even though the two diseases are unrelated.
- The rubella virus is an enveloped RNA virus that can be found in the respiratory tract.
- It is transmitted from person to person in aerosols produced by coughing or sneezing. Nearly half of all infected people remain asymptomatic.



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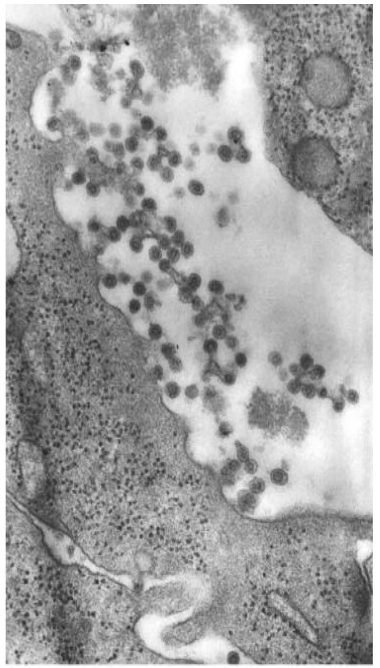


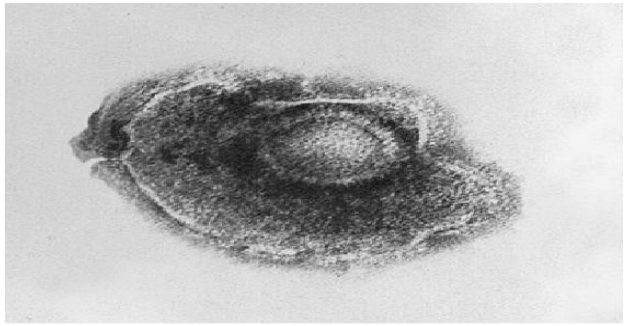
(b)

Viruses may spread through respiratory system- Varicella Zoster

- Varicella-zoster virus (VZV), the cause of chickenpox and shingles, primarily spreads through the respiratory route, with initial infection occurring in the upper respiratory tract, followed by potential complications like varicella pneumonia.
- Once infected, most individuals acquire a lifetime immunity to future chickenpox outbreaks. For this reason, parents once held “chickenpox parties” for their children. At these events, uninfected children were intentionally exposed to an infected individual so they would contract the disease earlier in life, when the incidence of complications is very low, rather than risk a more severe infection later. After the initial viral exposure, chickenpox has an incubation period of about 2 weeks.
- The initial infection of the respiratory tract leads to viremia and eventually produces fever and chills. A pustular rash then develops on the face, progresses to the trunk, and then the extremities, although most form on the trunk. Eventually, the lesions burst and form a crusty scab. Individuals with chickenpox are infectious from about 2 days before the outbreak of the rash until all the lesions have scabbed over.

(a)

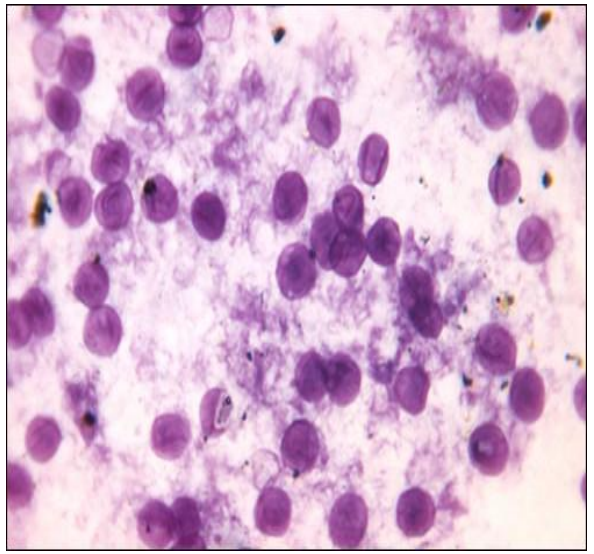
(b)



(c)

Fungal Infections of the Lower Respiratory Tract

- The most common fungal causes of pneumonia are Aspergillus, Cryptococcus, and Pneumocystis. These fungi can be found in the air, soil, and hospitals.
- Geographically restricted fungal diseases, commonly referred to as endemic, namely, blastomycosis, coccidioidomycosis, and histoplasmosis, present a growing public health concern.
- Fungal pneumonia is most common in people with chronic health problems or weakened immune systems, and in people who are exposed to large doses of certain fungi from contaminated soil or bird droppings.



Pneumocystis pneumonia

- Disease: Pneumocystis pneumonia (PCP). Pneumocystis is a leading cause of pneumonia in patients with acquired immunodeficiency syndrome (AIDS) and can be seen in other compromised patients and premature infants.
- Pathogen: *Pneumocystis jirovecii.* It occurs in people who have weak immune systems due to HIV/AIDS or the long-term use of medicines that suppress their immune systems, such as those used to treat cancer or manage organ transplants.

Pneumocystis pneumonia

- Sign and symptoms: fever, cough, and shortness of breath.
- Diagnostic tests: The organism is typically identified by microscopic examination of tissue and fluid samples from the lungs, PCR-based test.
- Pulmonary aspergilloma, a fungal infection, occurs when Aspergillus fungus colonizes pre-existing lung cavities, forming a "fungus ball" or mycetoma, which can cause hemoptysis and other respiratory issues.
- Primary prophylaxis against Pneumocystis pneumonia in HIV-infected adults, including pregnant women and those receiving highly active antiretroviral treatment (HAART), should begin when CD4+ counts less than 200 cells/μl or if there is a history of oropharyngeal candidiasis.
- Antimicrobial treatment: combination drug trimethoprim-sulfamethoxazole (TMP/SMZ). These sulfa drugs often have adverse effects, but the benefits outweigh these risks. Left untreated, PCP infections are often fatal.
- All immunosuppressed patients with documented Pneumocystis pneumonia require treatment. Despite newer agents, trimethoprim–sulfamethoxazole remains the most effective regimen for treating severe Pneumocystis pneumonia. Adjunctive corticosteroids, given in addition to antibiotics, are of substantial benefit to HIV-infected patients with moderate to severe Pneumocystis pneumonia with hypoxemia

Fungal Infections of the Lower Respiratory Tract

Coccidioidomycosis

- Disease: Coccidiomycosis (Valley Fever). It is endemic to the San Joaquin Valley of California; the disease is sometimes referred to as Valley fever. A related species that causes similar infections is found in semi-arid and arid regions of the southwestern United States, Mexico, and Central and South America
- Pathogen: Dimorphic fungus Coccidioides immitis or Coccidioides posadasii. People become infected by inhaling spores from disturbed soil in areas where the fungus is present, typically in the southwestern United States and parts of Mexico.
- Sign and symptoms: Most C. immitis infections are asymptomatic and self-limiting. However, the infection can be very serious for immunocompromised patients. Most people who inhale spores do not develop symptoms. However, those who do may experience: Fever, cough, shortness of breath, chest pain, fatigue, night sweats, joint pain, and skin rash.
- The endospores may be transported in the blood, disseminating the infection and leading to the formation of granulomatous lesions on the face and nose. In severe cases, other major organs can become infected, leading to serious complications such as fatal meningitis.
- Diagnostic tests: can be diagnosed by culturing clinical samples. C. immitis readily grows on laboratory fungal media, such as Sabouraud's dextrose agar, at 35 °C (95 °F). Serologic tests to detect IgM and IgG antibodies are the most common diagnostics.
- Antimicrobial treatment: Although mild cases generally do not require intervention, disseminated infections can be treated with intravenous antifungal drugs like amphotericin B and fluconazole

Histoplasmosis

- Disease: Histoplasmosis
- Pathogen: Histoplasma capsulatum is a dimorphic fungus. This microbe grows as a filamentous mold in the environment but occurs as a budding yeast during human infections. The primary reservoir for this pathogen is soil, particularly in locations rich in bat or bird feces. It is found in the Ohio and Mississippi River Valleys. (
- In immunocompromised patients, histoplasmosis can become disseminated and lead to considerable morbidity and mortality.
- Signs and symptoms: Symptomatic illness is primarily caused by intense exposure (e.g., cleaning an attic or a chicken coop), and the severity of disease is related to the number of spores inhaled. It may cause fever, cough, fatigue, chills, headache, and weakness with some chest discomfort.
- Diagnostic tests: The initial diagnosis is often based on chest radiographs as granulomatous inflammation and cultures grown on fungal selective media like Sabouraud's dextrose agar. Direct fluorescence antibody staining and Giemsa staining can also be used to detect this pathogen. In addition, serological tests including a complement fixation assay and histoplasmin sensitivity can be used to confirm the diagnosis.
- Antimicrobial treatment: In most cases, these infections are self-limiting, and antifungal therapy is not required. Acute pulmonary infections, with symptoms less than four weeks do not need treatment. If the symptoms persist beyond this period, a three-month course of itraconazole is recommended. (Akram)
- The antifungal agents, amphotericin B and ketoconazole are effective; itraconazole may be effective in immunocompromised patients, in whom the disease can be more serious.

Fungal Infections of the Lower Respiratory Tract

Cryptococcus

- Disease: Cryptococcosis. Cryptococcal infections are more common in immunocompromised people, such as those with AIDS. These patients typically require life-long suppressive therapy to control this fungal infection.
- Pathogen: encapsulated yeast Cryptococcus neoformans is an invasive fungus and found throughout the United States in bird droppings and soil contaminated with bird droppings.
- Cryptococcosis is a serious fungal infection caused by breathing in fungal spores in the environment. Cryptococcus neoformans and Cryptococcus gattii cause most infections. Most infections occur in people with weakened immune systems, particularly people with HIV/AIDS. Cryptococcus usually infects the lungs or brain (cryptococcal meningitis).

Aspergillosis

- Pathogen: Aspergillus fumigatus, leading to a condition known as "aspergillosis," which can manifest in various forms depending on the severity and individual's immune system, ranging from mild allergic reactions to serious invasive infections, particularly in people with weakened immunity or pre-existing lung conditions; symptoms may include coughing, wheezing, shortness of breath, and sinus pain. (lumen learning)
- Sign and symptoms: Inhalation of spores can lead to asthma-like allergic reactions resulting in allergic bronchopulmonary aspergillosis (ABPA) and allergic fungal rhinosinusitis The symptoms commonly include shortness of breath, wheezing, coughing, runny nose, and headaches. Fungal balls, or aspergilloma, can form when hyphal colonies collect in the lungs. The fungal hyphae can invade the host tissues, leading to pulmonary hemorrhage and a bloody cough. In severe cases, the disease may progress to a disseminated form that is often fatal. Death most often results from pneumonia or brain hemorrhages.
- Diagnostic tests: chest radiographs and a microscopic examination of tissue and respiratory fluid samples. Serological tests are available to identify Aspergillus antigens. In addition, a skin test can be performed to determine if the patient has been exposed to the fungus. Aspergilloma, commonly referred to as “fungus ball,” occurs in preexisting pulmonary cavities that were caused by tuberculosis, sarcoidosis, or other bullous lung disorders and in chronically obstructed paranasal sinuses.
- Antimicrobial treatment: Allergic bronchopulmonary aspergillosis (ABPA) is treated with a combination of corticosteroids and antifungal medications. The goal of treatment is to reduce inflammation and prevent lung damage. Corticosteroids remain the main drug therapy used for ABPA regardless of classification. At present, only itraconazole and voriconazole are used in the treatment against ABPA and only for patients who are unable to taper oral prednisolone or have an ABPA exacerbation.

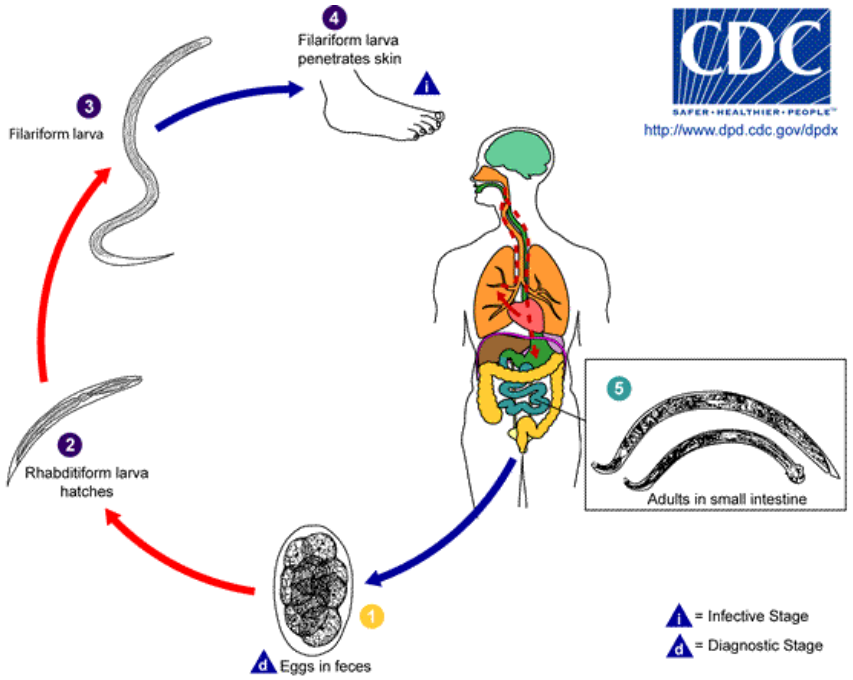
Parasitic Infestations of Lower Respiratory Tract

- Although most parasites that affect the lungs are endemic to tropical and subtropical regions, immigration and travel practices have resulted in the transfer of these diseases to other areas. Parasitic infestations of the lungs occur worldwide among both immunocompetent and immunocompromised patients and may affect the respiratory system in a variety of ways.
- Parasitic infection can be categorized into helminthic and protozoal infections. The diagnosis of parasitic diseases of the respiratory system is relatively difficult because clinical manifestations and radiologic findings are non-specific. Therefore, high index of suspicion, travel history, and detailed interrogation of personal hygiene are crucial for diagnosis of parasitic lung diseases.

- ***Protozoal infections:***
- **Entamoeba histolytica amebiasis** occur worldwide. Humans become infected via feco-oral route by ingestion of mature E. *histolytica* cyst. Trophozoites invade the intestinal mucosa and enter the bloodstream which results in systemic infection. Invasive amebiasis is an emerging parasitic disease in human immunodeficiency virus (HIV)-infected patients. Pleuropulmonary amebiasis occurs mainly by local extension from the amoebic liver abscess. Patients usually present with fever, right upper quadrant abdominal pain, chest pain, and cough.
- A combination of serologic tests with detection of the parasite by antigen detection by polymerase chain reaction (PCR) is the preferred approach to diagnosis. Metronidazole is a treatment of choice for invasive amoebiasis

Parasitic Infestations of Lower Respiratory Tract

- **Pulmonary Leishmaniasis.** Leishmania *donovani* is transmitted by various species of the sand fly and causes visceral leishmaniasis. The endemic areas of leishmaniasis are Asia, Africa, Central and South America. Pulmonary manifestations include pneumonitis, pleural effusion, and mediastinal lymphadenopathy. The treatment of choices includes pentavalent antimonials and liposomal amphotericin B
- **Pulmonary Toxoplasmosis** is caused by the protozoan parasite, Toxoplasma *gondii.* Cats are primary hosts of T. *gondii*. Humans become infected by ingestion of parasitic cyst-contaminated undercooked food.
- The symptoms of toxoplasmosis are myalgia and generalized lymphadenopathy.
- Diagnosis of toxoplasmosis is based on the detection of the bradyzoites of T. gondii in body tissue. A real-time PCR-based assay in BAL fluid has been reported in HIV-positive patients.
- Pulmonary toxoplasmosis has been reported with increasing frequency in HIV-infected patients. Pulmonary manifestations include interstitial pneumonia, diffuse alveolar damage, or necrotizing pneumonia. Toxoplasmosis can be treated with a combination of pyrimethamine and sulfadiazine for 3–4 weeks.



Hookworm LifeCycle

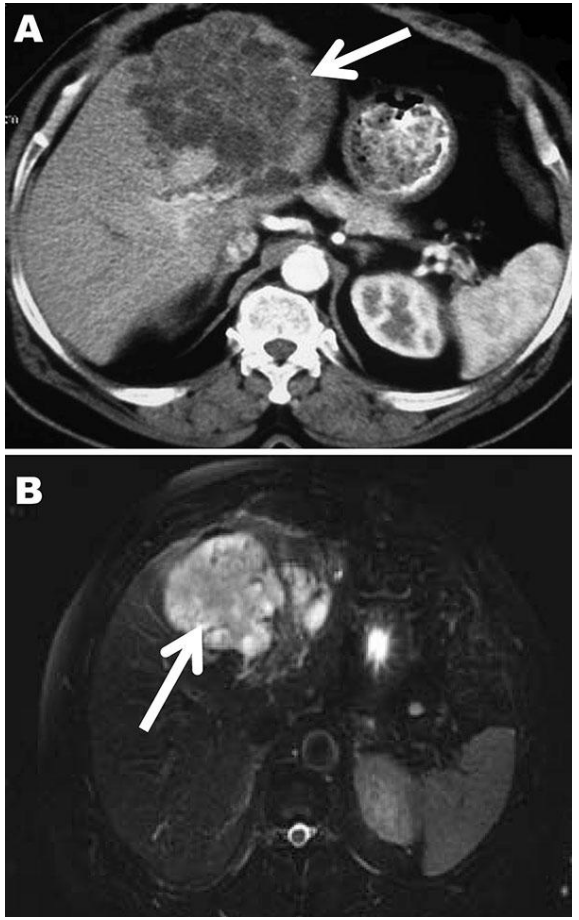
Helminthic Parasites

- **Ascariasis** is caused by a nematode (round warm) called Ascaris *lumbricoides* one of the most common parasitic infestations, affecting over a billion of the world's population causing more than thousand deaths annually. A. lumbricoides transmitted through the feco-oral route. Ascaris larvae migrate to the lungs via either the venules of the portal system or the lymphatic drainage.
- Larval ascariasis causes Löffler's syndrome, consisting of wheezing, pulmonary infiltrations, and a moderate eosinophilia.
- Mechanical removal of ascaris through bronchoscopy is the management of choice. Mebendazole and albendazole are the most effective agents against ascariasis.
- **Ancylostomiasis (Hookworm Disease):** The common hookworms are Ancylostoma duodenale and Necator americanus. The latter is found in parts of southern USA. Hookworm larvae enter human hosts via the skinand travels to lungs through the bloodstream.
- It is characterized by nausea, vomiting, dyspnea, cough, throat irritation, hoarseness, and eosinophilia. (Hotez).
- Patients can become profoundly anemic and malnourished. Anti-parasitic agents for hookworm are mebendazole and albendazole

- **Trichinellosis**. Trichinella spiralis is the most common Trichinella species that infects humans. Trichinella is a food-borne disease from undercooked pork containing larval trichinellae. In addition to pork meat, wild animals such as bear meat may also contain T. spiralis. Cooking meat to safe temperatures prevents trichinellosis.
- Trichinellosis symptoms can be mistaken for flu symptoms. The dyspnea may develop due to parasitic invasion of the diaphragm and the accessory respiratory muscles. The diagnosis is confirmed by muscle biopsy, which may demonstrate T. spiralis larvae. An ELISA using anti-Trichinella IgG antibodies can confirm the diagnosis in humans.
- Recommended treatment is the two-week course of mebendazole with analgesics and corticosteroids.

Helminthic Parasites

- **Echinococcosis**. Echinococcus granulosus and E. multilocularis are the parasite species that cause hydatid disease in humans. E. granulosus is endemic in sheep-herding areas of the Mediterranean, Eastern Europe, the Middle East, and Australia
- Two different presentations of echinococcosis are as follows: (a) cystic hydatidosis and (b) alveolar echinococcosis.
- In most cases, lung hydatidosis is a single cyst (72–82 %). An echinococcal infection becomes symptomatic after 5–15 years, secondary to local compression or dysfunction of the affected organ.
- Pulmonary symptoms from the intact cyst include cough, fever, dyspnea, and chest pain. The cyst may rupture into a bronchus and cause hemoptysis and/or expectoration of cystic fluid containing parasitic components (hydatoptysis) which is considered a pathognomonic finding of cyst rupture.
- Cystic hydatidosis is diagnosed by chest radiography which demonstrates a well-defined homogenous fluid-filled round opacity.
- Cystic hydatid disease generally requires surgical treatment, whereas almost all other parasitic lung conditions can be treated medically.



Respiratory infections can be classified based on the affected area of the respiratory tract and the causative agent.

- In general, diagnosing respiratory infections typically involve:
- **Clinical Evaluation:** Patient history, physical examination (e.g., lung auscultation for abnormal breath sounds).
- **Laboratory Tests:**
  - **PCR (Polymerase Chain Reaction):** Detects viral and bacterial DNA/RNA.
  - **Blood Tests:** To check for markers of infection like elevated white blood cells.
  - **Chest X-ray:** Used to identify pneumonia or tuberculosis.
  - **Sputum Culture:** Identifies specific pathogens.

- The management of respiratory infections depends on the causative organism and severity:
  - **Viral Infections:**
    - **Supportive care:** Rest, hydration, pain relievers (e.g., acetaminophen).
    - **Antiviral drugs:** For specific viruses (e.g., oseltamivir for influenza).
    - **Vaccination:** Flu and COVID-19 vaccines can reduce the severity of infections.
  - **Bacterial Infections:**
    - **Antibiotics:** Empiric antibiotics are often prescribed until specific pathogens are identified (e.g., amoxicillin for streptococcal pharyngitis).
    - **Hospitalization:** For severe cases like bacterial pneumonia or tuberculosis.
  - **Fungal Infections:**
    - **Antifungal agents:** E.g., itraconazole, amphotericin B.
    - **Monitoring and supportive care:** Especially in immunocompromised patients.
- **Preventive Measures:**
  - **Vaccines:** Flu vaccines, pneumococcal vaccines, and COVID-19 vaccines.
  - **Hygiene:** Handwashing, wearing masks, and avoiding close contact with sick individuals.
  - **Smoking cessation:** Smoking weakens the respiratory system's defenses.