

## Viral respiratory tract infections

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List of the viruses that cause respiratory tract infections:

- Rhinoviruses A, B and C
- Coronaviruses HKU1, NL63, 229E and OC43
- Influenza A, B and C
- Parainfluenza viruses 1, 2, 3 and 4
- Respiratory syncytial viruses A and B
- Human metapneumovirus
- Adenoviruses
- Enteroviruses
- Human bocavirus
- EBV, CMV, other herpesviruses

# 1) Rhinovirus :

- Picornaviruses include two major groups of human pathogens: **enteroviruses** and **rhinoviruses**
- Human rhinovirus: 3 **species (A, B & C)** based on sequence analyses.
- **Nonenveloped, Icosahedral, +Sense single strand RNA virus.**
- Include more than 100 antigenic types (serotypes).
- Divided into major and minor receptor groups.
- Major group use **(ICAM-1)** as receptor & minor group bind(LDLR) family.
- Cause upper respiratory tract infections, common cold syndrome.
- Responsible for about half of asthma exacerbations.
- Most grow better at 33°C, which is similar to the temperature of the nasopharynx in humans.

## ❖ Pathogenesis:

- **Virus Entry and Replication:**
  - ✓ Rhinoviruses enter through the upper respiratory tract.
  - ✓ High titers of the virus in nasal secretions, detectable as early as 2–4 days after exposure, are associated with maximal illness.
  - ✓ Although viral titers decrease over time, the illness persists, and in some cases, the virus may remain detectable for up to 3 weeks.
  - ✓ There's a direct correlation between the amount of virus in secretions and the severity of illness.
- **Limited Replication Site:**
  - ✓ Replication occurs primarily in the surface epithelium of the nasal mucosa.
- **Histopathologic changes:**
  - ✓ are confined to the submucosa and surface epithelium, involving edema and mild cellular infiltration.

- ✓ Nasal secretions increase in both quantity and protein concentration.
- **Lower Respiratory Tract Impact:**
  - ✓ Rhinoviruses rarely cause lower respiratory tract disease in healthy individuals. However, they are commonly associated with acute asthma exacerbations.
- **Cold Myth and Experimental Evidence:**
  - ✓ Controlled experiments indicate that chilling, including wearing wet clothes, does not directly cause a cold or increase susceptibility to the rhinovirus.
  - ✓ Chilliness is an early symptom of the common cold, but it is not the direct cause.
- ❖ **Clinical Findings:**
  - **Incubation Period and Duration:**
    - ✓ The incubation period is brief, lasting from 2 to 4 days.
    - ✓ Acute illness typically persists for 7 days, with a nonproductive cough possibly lingering for 2–3 weeks.
  - **Frequency of Attacks:**
    - ✓ The average adult experiences one or two cold attacks each year.
  - **Symptoms in Adults:**
    - ✓ Common symptoms in adults include sneezing, nasal obstruction, nasal discharge, and sore throat.
    - ✓ Additional symptoms may comprise headache, mild cough, malaise, and a chilly sensation.
    - ✓ There is generally little or no fever.
  - **Mucosal Changes:**
    - ✓ The nasal and nasopharyngeal mucosa exhibit redness and swelling.
  - **Diagnosis Challenges:**

- ✓ There are no distinctive clinical findings that allow for an etiologic diagnosis distinguishing rhinovirus-induced colds from those caused by other viruses.
- **Secondary Bacterial Infections:**
  - ✓ Secondary bacterial infections may arise, leading to conditions such as acute otitis media, sinusitis, bronchitis, or pneumonitis, especially in children.

## 2) Coronavirus:

- Family: Coronaviridae
- Virus: Coronavirus
- Characteristics: enveloped, +ss RNA, helical capsid • Transmission: direct contact & aerosols
- Diseases: common cold, SARS, COVID19, MERS
- Diagnosis: RT-PCR
- Treatment: supportive
- Prevention: avoid contact
- The Coronaviridae contain six genera (Alphacoronavirus, Betacoronavirus, Gammacoronavirus, Deltacoronavirus, Bafinivirus, and Torovirus) .
- There are six coronaviruses that can infect humans
- The alpha coronaviruses: 229E and NL63
- The beta coronaviruses : OC43, HKU1, SARS-CoV1, SARS-CoV2 and MERS-CoV.
- Coronaviruses :229E, NL63, OC43 and HKU1 cause **URTIs**
- • SARS-CoV2 receptor is ACEII receptors, causing COVID19 disease.

❖ Pathogenesis:

- **Specificity:**
  - ✓ Often displaying tropism for epithelial cells in the respiratory or gastrointestinal tract.
  - ✓ Most known animal coronaviruses infect respiratory or gastrointestinal epithelial cells.
- **In Vivo Infections:**
  - ✓ In vivo, coronavirus infections can either be disseminated, as seen with mouse, hepatitis virus, or localized.
  - ✓ In humans, coronavirus infections typically, though not always, remain limited to the upper respiratory tract.
- **SARS-CoV Outbreak (2003):**
  - ✓ The outbreak of (SARS-CoV) in 2003 resulted in severe respiratory illness, including pneumonia and progressive respiratory failure.
  - ✓ The virus was detected not only in the respiratory tract but also in other organs such as the kidney, liver, small intestine, and stool.
- **SARS-CoV Outbreak (2003):**
  - ✓ The likely origin was in a nonhuman host, probably bats, amplified in palm civets, and transmitted to humans in live animal markets.
  - ✓ Chinese horseshoe bats serve as natural reservoirs of SARS-like coronaviruses.
  - ✓ Conditions in rural southern China, where the outbreak originated, such as close living proximity of people, pigs, domestic fowl, and the use of wild species for food and traditional medicine, promote the emergence of new viral strains.
- **MERS-CoV Outbreak (2012):**
  - ✓ (MERS-CoV) outbreak starting in 2012 was characterized by pneumonia and respiratory failure, with most fatalities occurring in patients with medical comorbidities.
  - ✓ MERS-CoV likely originated in bats and became widespread in camels, as evidenced by seropositivity in animals in the region.
  - ✓ Initial human infections are likely through contact with bats or camels, with subsequent person-to-person transmission.

- SARS-CoV-2 and COVID-19:
  - **Virus characteristics:**
    - ✓ SARS-CoV-2 is a novel single-stranded RNA ( $\oplus$  ssRNA) coronavirus responsible for the COVID-19 pandemic.
  - **Clinical Presentation:**
    - ✓ Clinical course varies, with some individuals being asymptomatic.
    - ✓ Common symptoms include fever, dry cough, shortness of breath, and fatigue.
    - ✓ More specific symptoms involve anosmia (loss of smell) and dysgeusia (altered taste).
  - **Complications:**
    - ✓ include acute respiratory distress syndrome (ARDS), hypercoagulability leading to thrombotic complications (including cryptogenic and/or ischemic stroke), shock, organ failure, and death.
  - **Risk Factors:**
    - ✓ for severe illness or death include increasing age (**strongest** risk factor), obesity, diabetes, hypertension, and chronic kidney disease, as well as severe cardiopulmonary illness.
  - **Diagnosis:**
    - ✓ Diagnosed by nucleic acid amplification test (NAAT), most commonly reverse transcription-polymerase chain reaction (RT-PCR).
    - ✓ Tests detecting viral antigen are less sensitive than NAATs but are rapid and more accessible.
  - **Transmission:**
    - ✓ Spreads through respiratory droplets and aerosols.
    - ✓ Host cell entry occurs through the attachment of the viral spike protein to the ACE2 receptor on cell membranes.
  - **Immunity and Vaccination:**
    - ✓ Anti-spike protein antibodies confer immunity.

- ✓ Vaccination induces both humoral and cellular immunity, reducing the risk of contracting or transmitting the virus and preventing more severe disease, hospitalization, and death.
- **Therapeutic Approaches:**
  - ✓ Supplemental oxygen and supportive care are the mainstay of therapy for hospitalized
  - ✓ Dexamethasone, remdesivir, and IL-6 pathway inhibitors may benefit some severely ill patients.

### 3) Adenovirus:

Family	<i>Adenoviridae</i>
Common name	Adenovirus
Virus	Adenovirus
Characteristics	Double-stranded deoxyribonucleic acid (DNA) genome; icosahedral capsid, no envelope; approximately 50 human serotypes
Transmission	Respiratory, fecal-oral, and direct contact (eye)
Site of latency	Replication in oropharynx
Disease	Pharyngitis, pharyngoconjunctival fever, keratoconjunctivitis, pneumonia, hemorrhagic cystitis, disseminated disease, and gastroenteritis in children
Diagnosis	Cell culture (HEp-2 and other continuous human epithelial lines), enzyme immunoassay (EIA) for gastroenteritis serotypes 40-41
Treatment	Supportive
Prevention	Vaccine (adenovirus serotypes 4 and 7) for military recruits

## Respiratory Diseases

- **Typical Symptoms:**
  - ✓ Common symptoms of respiratory diseases caused by adenoviruses include cough, nasal congestion, fever, and sore throat.
  - ✓ This syndrome is most prevalent in infants and children.
- **Viral Types and Age Distribution:**
  - ✓ Group C viruses, especially types 1, 2, and 5, are often associated with respiratory diseases in infants and children.
  - ✓ Infections with types 3, 4, and 7 are more frequent in adolescents and adults.
- **Pneumonia and Adenoviruses:**
  - ✓ Adenoviruses, particularly types 3, 7, and 21, are implicated in approximately 10–20% of childhood pneumonias.
  - ✓ Adenoviral pneumonia, especially in the very young, has been associated with a mortality rate of up to 10%.
- **Military Recruit Respiratory Syndrome:**
  - ✓ Adenoviruses are the causative agents
  - ✓ This syndrome is characterized by fever, sore throat, nasal congestion, cough, and malaise, with the potential to progress to pneumonia.
  - ✓ Epidemics of this syndrome often occur among young military recruits, particularly under conditions of fatigue, stress, and crowding.
- **Adenovirus Types in Military Recruit Syndrome:**
  - Types 4 and 7 are primarily responsible
  - Occasionally, type 3 may also contribute to the syndrome.



## 4) Parainfluenza:

Family	<i>Paramyxoviridae</i>
Common name	Paramyxoviruses
Characteristics	Single-stranded, ribonucleic acid (RNA) genome; helical capsid with envelope; no segmented genome (e.g., orthomyxoviruses)
Virus	Parainfluenza virus
Transmission	Contact with respiratory secretions
Disease	Adults: upper respiratory disease, rarely pneumonia Children: respiratory including croup, bronchiolitis, and pneumonia
Detection	Cell culture (PMK), shell vial culture, and FA stain
Epidemiology	Four serotypes, disease occurs year-round
Treatment	Supportive
Prevention	Avoid contact with virus.

- Human parainfluenza viruses have five serotypes:
  - Types 1 and 3 belong to the genus *Respirovirus*
  - Types 2, 4 a and 4b belong to the genus *Rubulavirus*

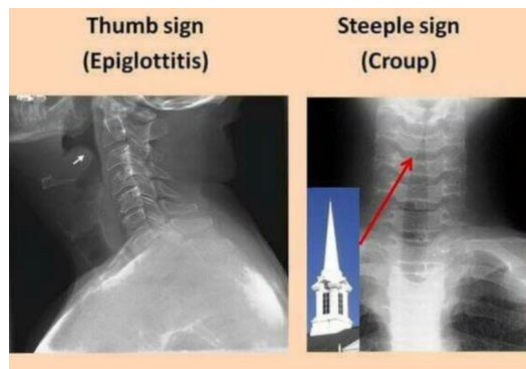
### ❖ Overview:

- Common pathogens causing respiratory illnesses in individuals of all ages.
- They are particularly significant as severe respiratory tract disease agents in infants and young children.
- Reinfections with parainfluenza viruses are common.

### ❖ Pathogenesis:

- **Host Tropism and Replication:**
  - ✓ Parainfluenza virus replication in immunocompetent hosts is primarily limited to respiratory epithelia.
  - ✓ Viremia is uncommon, with infection often involving the nose and throat, resulting in a "common cold" syndrome.
- **Variability in Infection Extent:**

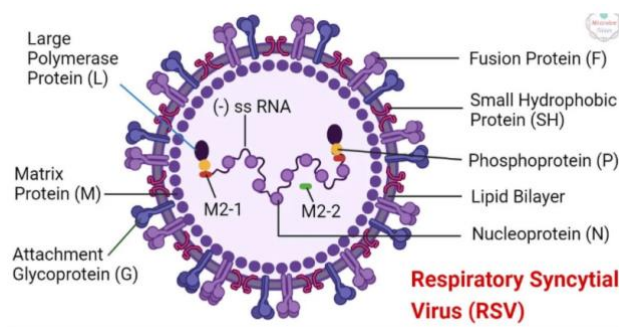
- ✓ Infection may become more extensive, especially with types 1 and 2, involving the larynx and upper trachea, leading to **croup** (laryngotracheobronchitis).
- **Croup**: is characterized by respiratory obstruction due to swelling of the larynx and related structures producing steeple sign on anterior neck x-ray.



- **Potential for Lower Respiratory Involvement:**
    - ✓ Deeper spread to the lower trachea and bronchi, causing pneumonia or bronchiolitis, is more common with type 3, albeit at a lower frequency than observed with RSV.
  - **Viral Shedding Duration:**
    - ✓ Parainfluenza virus shedding typically lasts about 1 week after the onset of illness.
    - ✓ Type 3 may be excreted for up to 4 weeks after the onset of primary illness, facilitating the spread of infection.
  - **IgE Antibodies and Inflammation:**
    - ✓ Production of virus-specific IgE antibodies during primary infections is associated with disease severity.
    - ✓ The mechanism may involve the release of inflammatory mediators altering airway function.
- ❖ Clinical Findings of Parainfluenza Viruses
- **Primary Infections in Young Children:**

- ✓ Typically manifest as rhinitis and pharyngitis, often accompanied by fever and some bronchitis.
- ✓ Severe illness may occur with primary infections caused by parainfluenza virus types 1, 2, or 3,
- ✓ Ranging from laryngotracheitis and croup (especially with types 1 and 2) to bronchiolitis and pneumonia (especially with type 3).
- **Primary Infections in Young Children:**
  - ✓ Severe illness associated with type 3 is more prevalent in infants under 6 months,
  - ✓ while croup or laryngotracheobronchitis is more likely in children aged 6 months to 18 months.
  - ✓ Over half of initial infections with types 1, 2, or 3 result in febrile illness, with an estimated 2–3% progressing to croup.
  - ✓ Parainfluenza virus type 4 typically does not cause serious disease, even during the first infection.
- **Common Complication:**
  - ✓ The most common complication of parainfluenza virus infection is **otitis media**.
- **Susceptibility in Immunocompromised Individuals:**
- Immunocompromised children and adults are particularly susceptible to severe parainfluenza virus infections.
  - Mortality rates after parainfluenza infection in bone marrow transplant recipients range from 10% to 20%.

## 5) RESPIRATORY SYNCYTIAL VIRUS (RSV)



Family	<i>Paramyxoviridae</i>
Common name	Paramyxoviruses
Characteristics	Single-stranded, ribonucleic acid (RNA) genome; helical capsid with envelope; no segmented genome (e.g., orthomyxoviruses)
Virus	Respiratory syncytial virus (RSV)
Transmission	Person-to-person by hand and respiratory contact
Disease	Primarily in infants and children. Infants: bronchiolitis, pneumonia, and croup Children: upper respiratory disease
Detection	Cell culture (HEp-2), EIA, and FA stain
Epidemiology	Disease occurs annually late fall through early spring; nosocomial transmission can occur readily.
Treatment	Supportive; treat severe disease in compromised infants with ribavirin.
Prevention	Avoid contact with virus; immune globulin for infants with underlying lung disease; prevent nosocomial transmission with isolation and cohorting.

### ➤ Overview

- ✓ leading cause of lower respiratory tract illness in infants and young children,
- ✓ particularly responsible for bronchiolitis and pneumonia in those under 1 year.
- ✓ It accounts for approximately 25% of pediatric hospitalizations due to respiratory disease.

### ❖ Pathogenesis

#### ○ **Initial Replication Site:**

- ✓ RSV replication begins in epithelial cells of the nasopharynx.
- ✓ The virus may spread to the lower respiratory tract, leading to bronchiolitis and pneumonia.

#### ○ **Viral Detection:**

- ✓ Viral antigens can be identified in the upper respiratory tract and in shedding epithelial cells.
- ✓ Viremia is rare, occurring infrequently if at all.

#### ○ **Incubation Period and Shedding:**

- ✓ The incubation period between exposure and illness onset is 3–5 days.
- ✓ Viral shedding can persist for 1–3 weeks in **infants and young children**, while **adults** typically shed the virus for only 1–2 days.
- **Inoculum Size and Infection Success:**
  - ✓ Inoculum size is a crucial determinant of successful infection, particularly in adults and possibly in children.
- **Role of Immune System:**
  - ✓ An intact immune system is crucial for resolving RSV infections.
  - ✓ Patients with impaired cell-mediated immunity **may** become persistently infected with RSV, shedding the virus for extended periods, even months.
- **Susceptibility Factors:**
  - ✓ Only a subset of young babies develops severe RSV disease.
  - ✓ Genetic susceptibility to bronchiolitis is linked to polymorphisms in innate immunity genes.
- ❖ Clinical Findings of (RSV)
  - **Spectrum of Respiratory Illness:**
    - ✓ RSV causes a spectrum of respiratory illnesses, ranging from inapparent infections or the common cold to pneumonia in infants and bronchiolitis in very young babies.
    - ✓ Bronchiolitis is a distinct clinical syndrome associated with RSV.

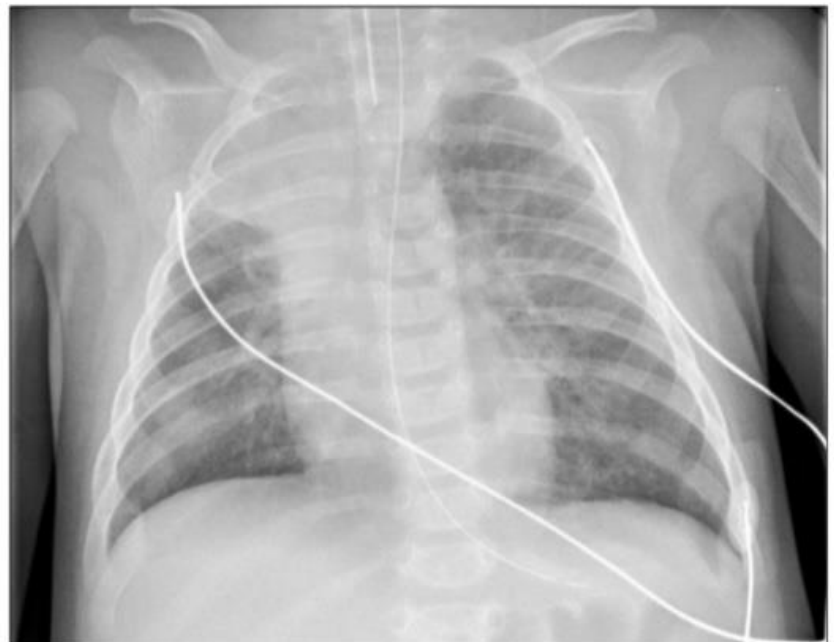
RSV SYMPTOMS		
Infants	Children	Adults
<ul style="list-style-type: none"> <li>• Irritability</li> <li>• Poor feeding</li> <li>• Lethargy</li> <li>• Apnea (pauses in breathing)</li> <li>• Fever (not always present)</li> </ul>	<ul style="list-style-type: none"> <li>• Runny nose</li> <li>• Decreased appetite</li> <li>• Cough</li> <li>• Sneezing</li> <li>• Fever</li> </ul>	<ul style="list-style-type: none"> <li>• Runny nose</li> <li>• Sore throat</li> <li>• Cough</li> <li>• Headache</li> <li>• Fatigue</li> </ul>

- **Severity and Hospitalization:**
  - ✓ About one-third of primary RSV infections involve the lower respiratory tract severely enough to necessitate medical attention.
  - ✓ Almost 2% of infected babies require hospitalization, with the peak occurrence at 2–3 months of age.

- ✓ Higher viral loads in respiratory secretions are predictors of longer hospitalizations.
- **Rapid Progression and Mortality:**
  - ✓ Progression of symptoms may be rapid, potentially culminating in death. Mortality rate in normal infants is low (approximately 1% of hospitalized patients).
  - ✓ In the presence of preexisting diseases like congenital heart disease, mortality rates may be high.
- **Reinfection and Symptomatic Episodes:**
  - ✓ Reinfection is common in both children and adults.
  - ✓ Symptomatic reinfections usually involve the upper respiratory tract, resembling a cold in healthy individuals.
- **RSV in Immunocompromised Patients:**
  - ✓ RSV infections account for about one-third of respiratory infections in bone marrow transplant patients.
  - ✓ Pneumonia develops in approximately half of infected immunocompromised children and adults, especially in the early post-transplant period.
  - ✓ Reported mortality rates range from 20% to 80%.
- **RSV in Elderly Adults:**
  - ✓ Infections in elderly adults may present symptoms similar to influenza, with the potential development of pneumonia.
  - ✓ Prevalence in long-term care facilities includes infection rates of 5–10%, pneumonia in 10–20% of those infected, and mortality rates of 2–5%.
- **Long-Term Effects in Children:**
  - ✓ Children who had RSV bronchiolitis and pneumonia as infants may experience recurrent wheezing episodes for many years.
  - ✓ However, no causal relationship has been established between RSV infections and long-term abnormalities.
- **RSV and Otitis Media:**
  - ✓ RSV is a significant cause of otitis media, with an estimated 30–50% of wintertime episodes in infants attributed to RSV infection.



Chest radiograph of a 14-month-old girl admitted to hospital with RSV-positive ALRTI. There is hyperinflation of the lungs and presence of bronchial wall cuffing (arrows), without evidence of consolidation or effusion.



**Chest radiograph of a 3-month-old infant with severe RSV bronchiolitis**

demonstrating a collapsed right upper lobe, hyperinflated left lung and bilateral perihilar, peribronchial thickening. The patient is intubated and has a nasogastric tube in situ.



❖ Treatment

○ **Supportive Care:**

- ✓ The primary approach to serious RSV infections involves supportive care.
- ✓ Supportive measures include the removal of secretions and the administration of oxygen.

○ **Antiviral Medication - Ribavirin:**

- ✓ Ribavirin, an antiviral drug, is approved for the treatment of lower respiratory tract disease caused by RSV, especially in infants at high risk for severe disease.
- ✓ Administration is done in aerosol form over 3–6 days.
- ✓ Oral ribavirin is not considered effective.

○ **Immune Globulin and Monoclonal Antibodies:**

- ✓ Immune globulin with high-titer antibodies against RSV has marginal benefits.
- ✓ Humanized antiviral monoclonal antibodies (palivizumab) are available as a treatment option.

❖ Prevention

○ **Vaccine Development Challenges:**

- ✓ Developing an RSV vaccine has been challenging.
- ✓ An experimental formalin-inactivated RSV vaccine in the late 1960s resulted in recipients developing nonneutralizing serum antibodies.
- ✓ Immunized children faced more severe lower respiratory tract illness upon subsequent wild-type RSV infection.

○ **Unique Challenges for RSV Vaccine Development:**

- ✓ RSV poses specific challenges for vaccine development, especially because the target group is newborns.
- ✓ Eliciting a protective immune response at this early age is difficult due to the presence of maternal antibodies.

○ **Maternal Immunization Strategy:**

- ✓ A strategy being tested involves maternal immunization with a vaccine.
- ✓ The goal is to ensure the transfer of protective levels of virus-specific neutralizing antibodies to infants, persisting for 3–5 months, the period of greatest vulnerability for newborns to severe RSV disease.

○ **Current Vaccine Status:**

- ✓ RSV vaccine is available for pregnant ladies. (may, 2023)

○ **Control Measures during Nosocomial Outbreaks:**



- ✓ Control measures during nosocomial outbreaks are similar to those for parainfluenza viruses.
- ✓ Measures include contact isolation, handwashing, and visitor restriction.

## 6) Metapneumovirus

- Respiratory pathogen first described in 2001.
- Detected using a molecular approach on clinical samples from children with respiratory illnesses but with negative test results for known respiratory viruses.
- Cause a wide range of respiratory illnesses from mild upper to severe lower respiratory tract disease in all age groups.
- In general, symptoms are similar to those caused by RSV.

○ ارجعوا للسلايدات عشان الأسئلة

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