Medical Virology for MD students

Paramyxoviridae & Togaviridae

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Paramyxoviridae

- The paramyxoviruses include the most important agents of **respiratory infections** of **infants and young children,** as well as the causative agents of two of the common contagious diseases of childhood (**mumps** and **measles**).
- All members of the *Paramyxoviridae* family **initiate** infection **via the respiratory tract**.
- The paramyxoviruses are enveloped **-ss RNA viruses** with non-segmented genome.

Acute respiratory infections and pneumonia are responsible for the deaths of 4 million children younger than 5 years of age worldwide.

Togaviridae

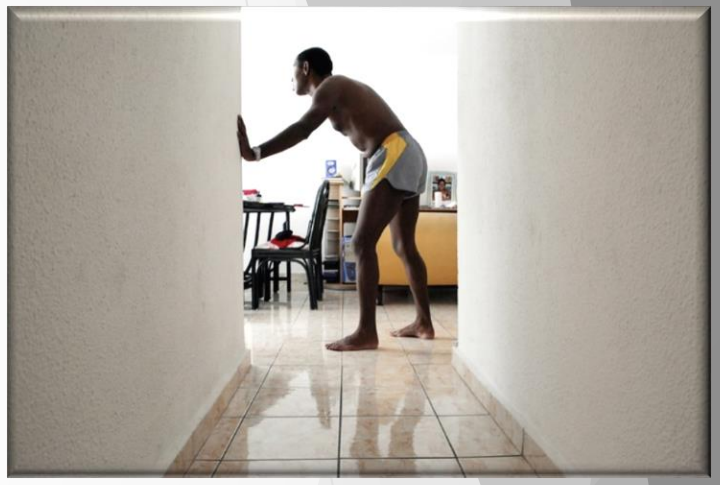
- The togaviruses are **enveloped** +ss RNA viruses that contribute significantly to human disease.

- *Togaviridae* is divided into two genera: Alphavirus and Rubivirus.

Alphavirus

- The alphaviruses are **ar**thropod-**bo**rne viruses (**arbo**viruses), which are transmitted to humans and domestic animals by **mosquitoes**.

- ***The majority of infections are subclinical***, however, several clinical syndromes are associated with alphavirus infections of humans. These include: **acute encephalitis** (equine encephalitis viruses); **acute arthropathy** (**Chikungunya virus**) and a febrile illness with **a flulike syndrome**.



Rubella virus

- Rubella (German measles; 3-day measles) is an acute febrile illness characterized by a rash and lymphadenopathy that affects children and young adults.
- **In 20–50% of cases, the primary infection is subclinical**. It is the mildest of common viral exanthems. However, infection during early pregnancy may result in serious abnormalities of the fetus including congenital malformations and mental retardation.
- The consequences of rubella in utero are referred to as the **congenital rubella syndrome**.

Rubella (German Measles)

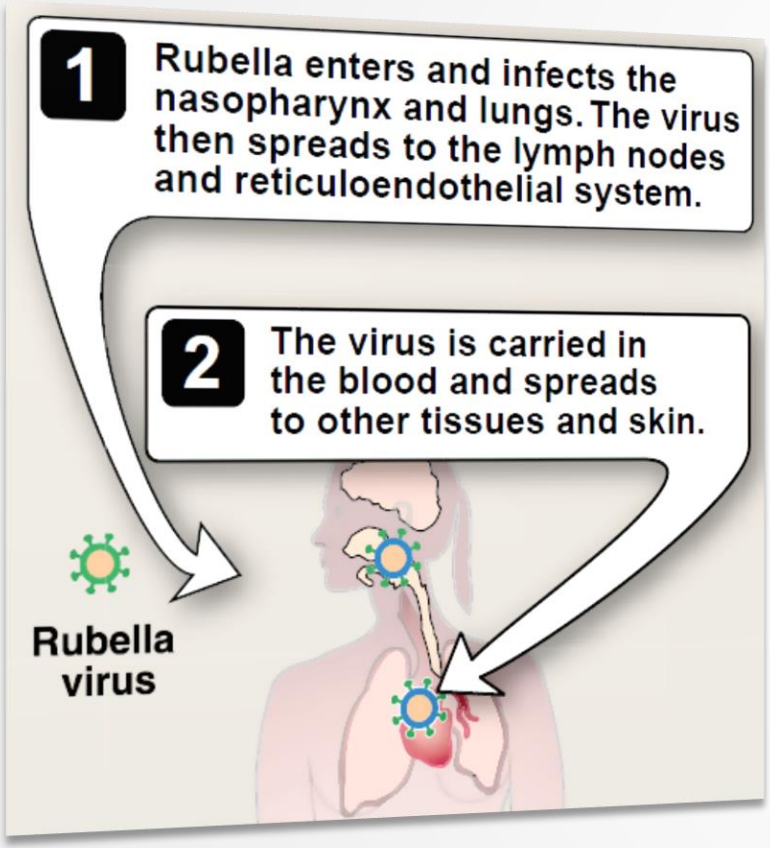
- Rubella usually begins with malaise, low-grade fever, and a **morbilliform (red macules) rash** appearing on the same day. The rash starts on the face, extends over the trunk and extremities, **and rarely lasts more than 3 days**. No feature of the rash is pathognomonic for rubella.

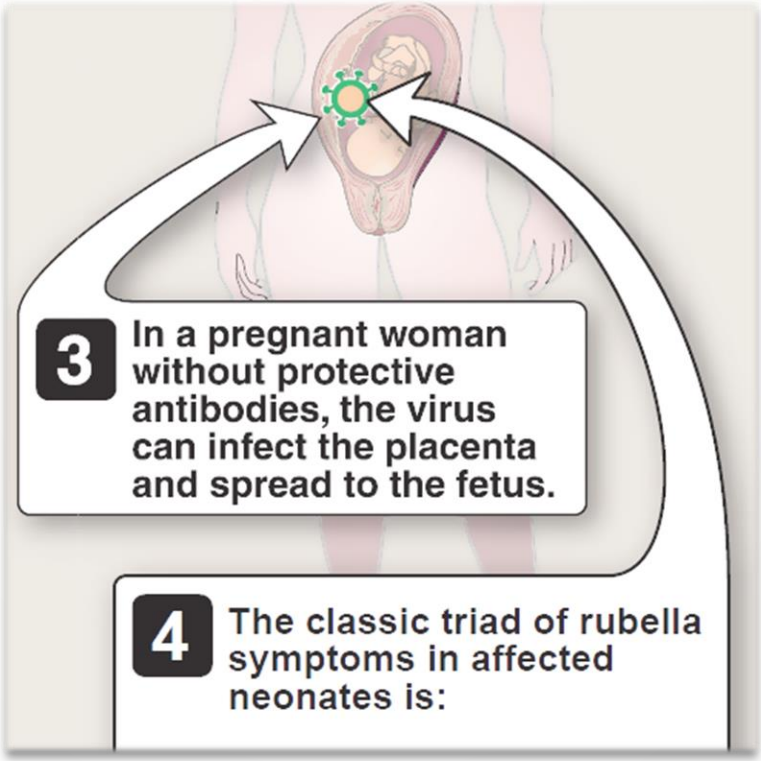
- Unless an epidemic occurs, the disease is difficult to diagnose clinically because the rash caused by other viruses (e.g. enteroviruses) is similar.

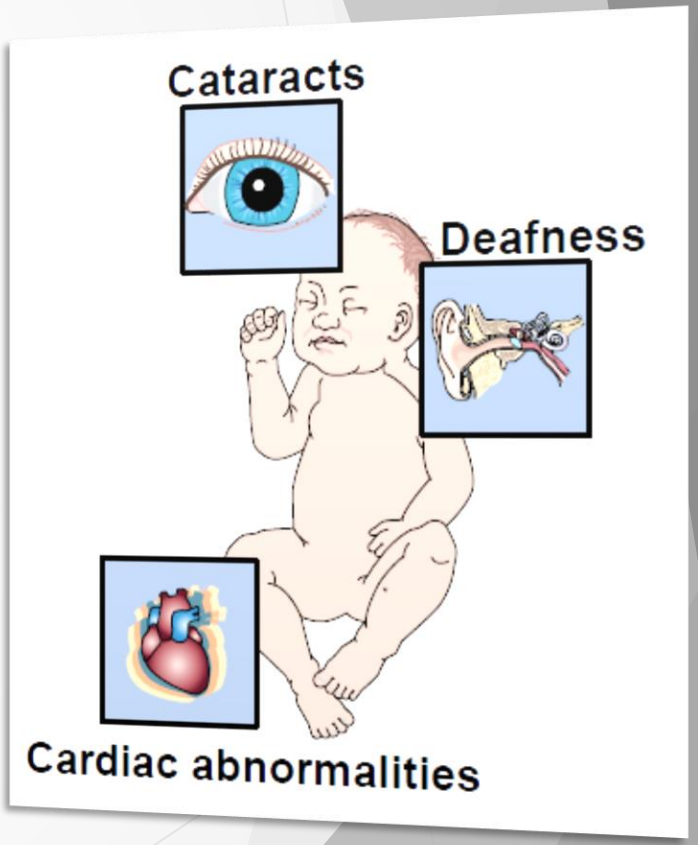
Rubella (German Measles)

- Transient arthralgia and arthritis are commonly seen in adults, especially women.
- Rubella antibodies appear in the serum of patients as the rash fades.
- One attack of the disease confers **lifelong immunity** because only one antigenic type of the virus exists.
- A rubella vaccine is available.

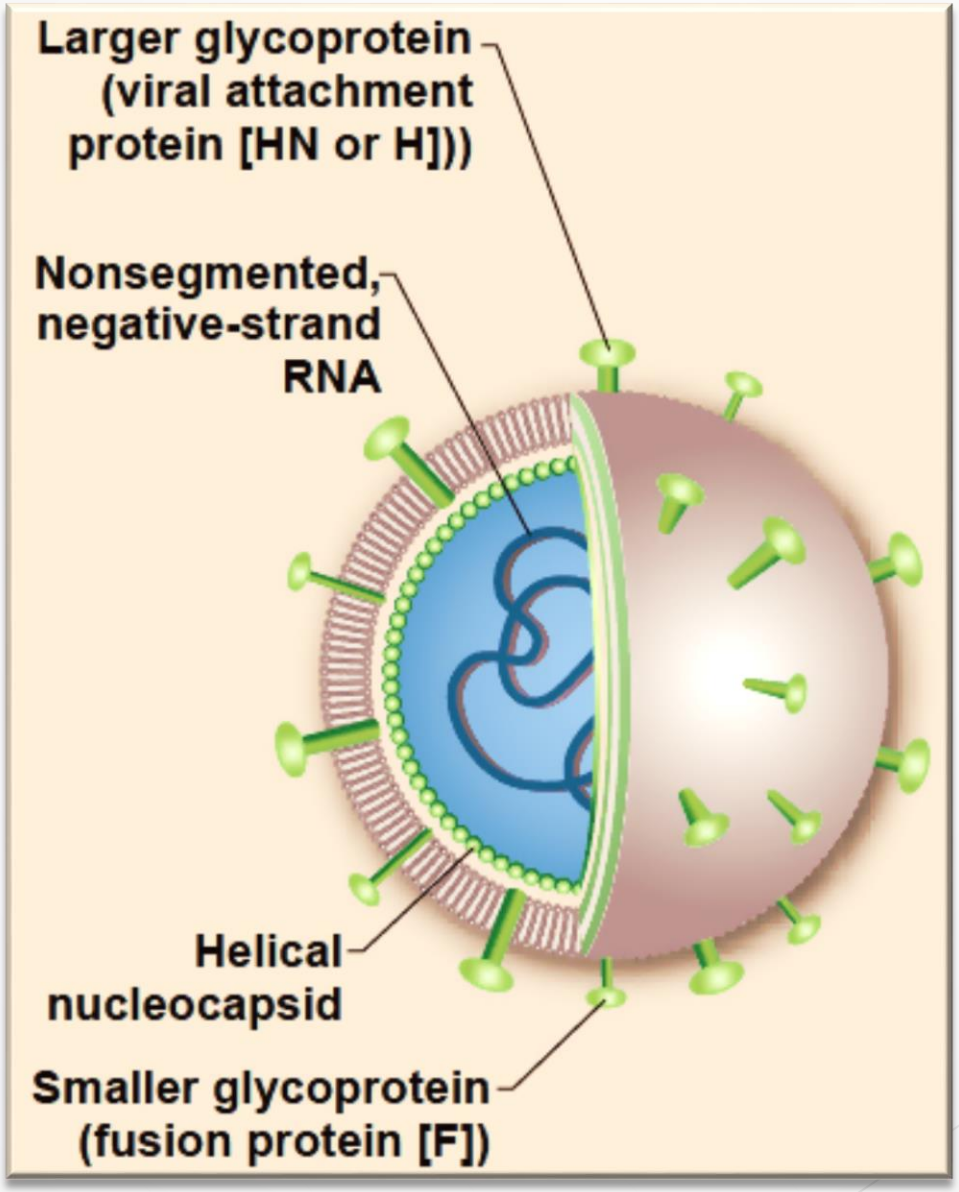
Congenital rubella syndrome







Paramyxoviridae

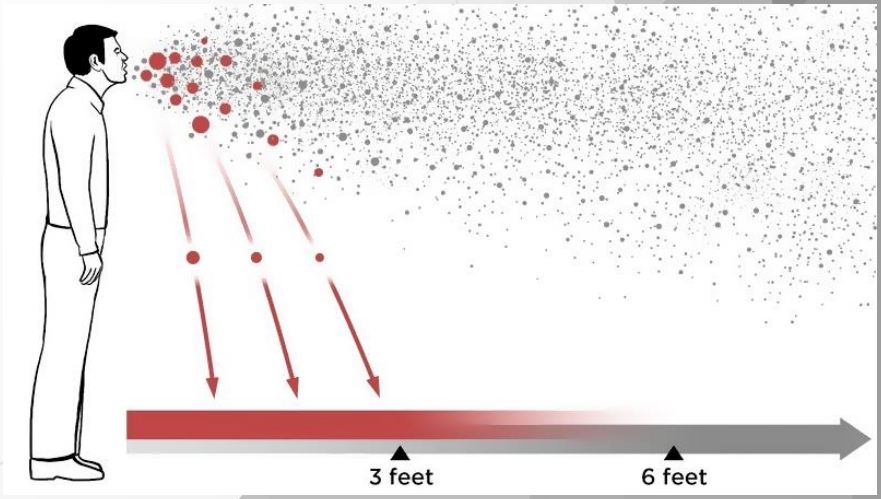


Classification of *Paramyxoviridae*

Subfamily	*Paramyxovirinae*				*Pneumovirinae*	
Genus	Respivirus	Rubulavirus	Morbillivirus	Henipavirus	Pneumovirus	Metapneumovirus
Species	PIV-1, PIV-3	Mumps, PIV-2, PIV-4	Measles	Hendra, Nipah	RSV	Metapneumovirus

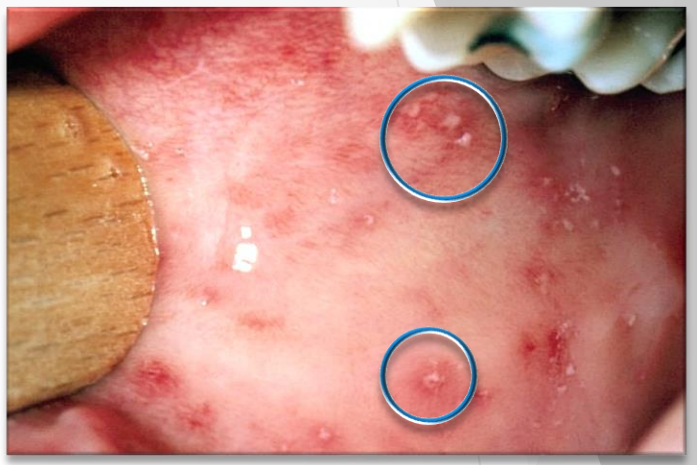
Measles virus

- The cellular receptor for measles virus is **CD46**.
- Measles virus is transmitted by sneeze- or cough-produced **respiratory droplets**.
- The virus is **extremely infectious**, and almost all infected individuals develop a clinical illness.
- Measles virus replicates initially in the respiratory epithelium and then in various lymphoid organs.



Measles (Rubeola, First Disease)

- Measles begins with a prodrome of fever, upper respiratory tract symptoms, and conjunctivitis.



- A few days later, specific signs develop; first, **Koplik spots** (small white spots on bright red mucous membranes of the mouth and throat) and then a **generalized macular rash**, beginning at the head and traveling slowly to the lower extremities.

Measles (Hard Measles, 10-day measles)

- Soon after the rash appears, the patient is no longer infectious.
- The major morbidity and mortality caused by measles are associated with various complications of infection, especially **pneumonia** and **encephalitis**.
- The most important of these is **postinfectious encephalomyelitis**, which is estimated to affect 1 of 1,000 cases of measles, usually occurring within two weeks after the onset of the rash. This is an **autoimmune disease** associated with an immune response to **myelin basic protein**.

Measles Dx and Prevention

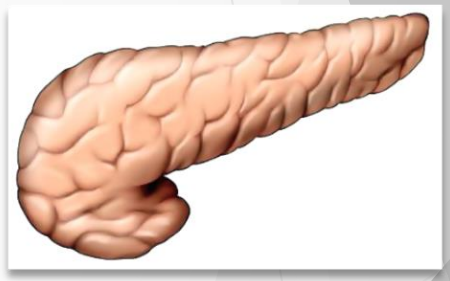
- In most cases, diagnosis can be achieved **clinically**, especially in an epidemic situation.
- The presence of **Koplik spots** provides a definitive diagnosis.
- Measles is usually a disease of childhood, and is followed by life-long immunity (single serotype).
- A live attenuated measles vaccine is available.

Mumps virus

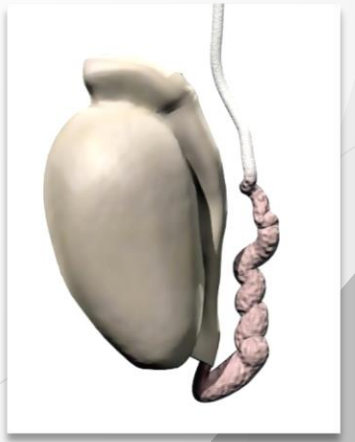
- Mumps is an acute contagious disease characterized by enlargement of one or both salivary glands.
- Mumps virus mostly causes a mild childhood disease, but in adults complications including meningitis and orchitis are fairly common.
- More than one-third of all mumps infections are **asymptomatic**.

Mumps

- The virus is spread by **respiratory droplets.** The classic clinical presentation and diagnosis revolve around infection and swelling of the salivary glands, primarily the parotid glands.



- However, infection is widespread in the body and may involve not only the salivary glands but also the **pancreas**, **CNS**, and **testes**. **Orchitis** (inflammation of the testis) caused by mumps virus may cause sterility.

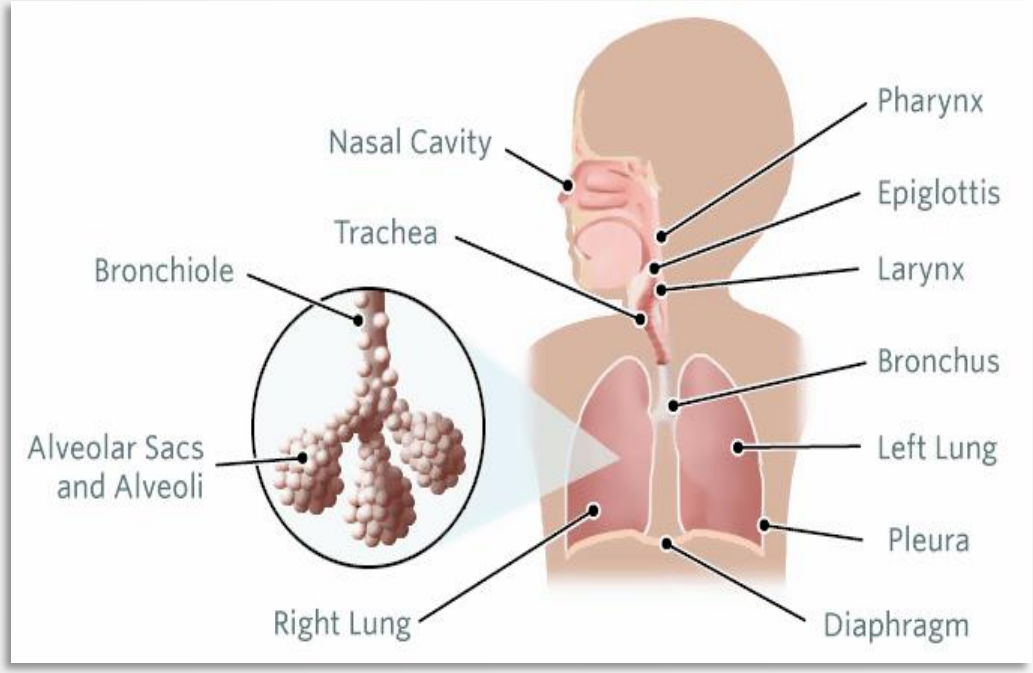


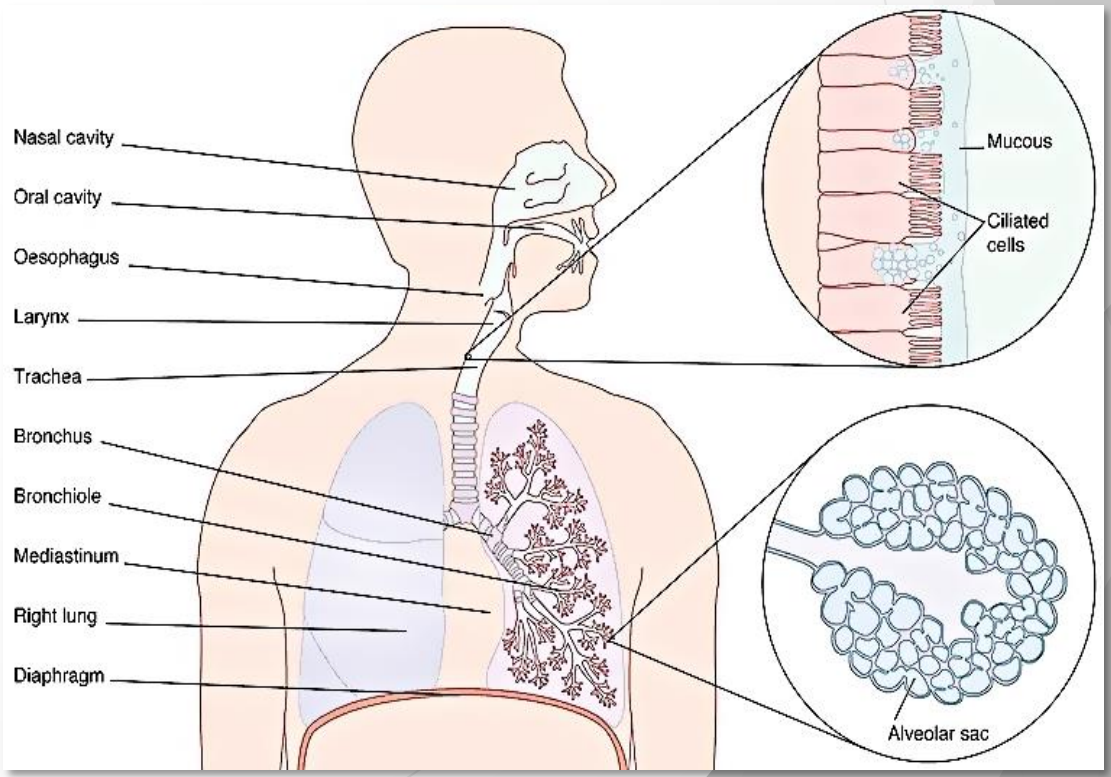
Mumps

- The diagnosis of typical cases usually can be made on the basis of **clinical** findings.
- Immunity is permanent after a single infection.
- An effective attenuated live-virus vaccine is available.
- Mumps vaccine is available in combination with measles and rubella (**MMR**) live-virus vaccines. **Two doses of MMR vaccine are recommended** for school entry.

Parainfluenza viruses (PIVs 1-4)

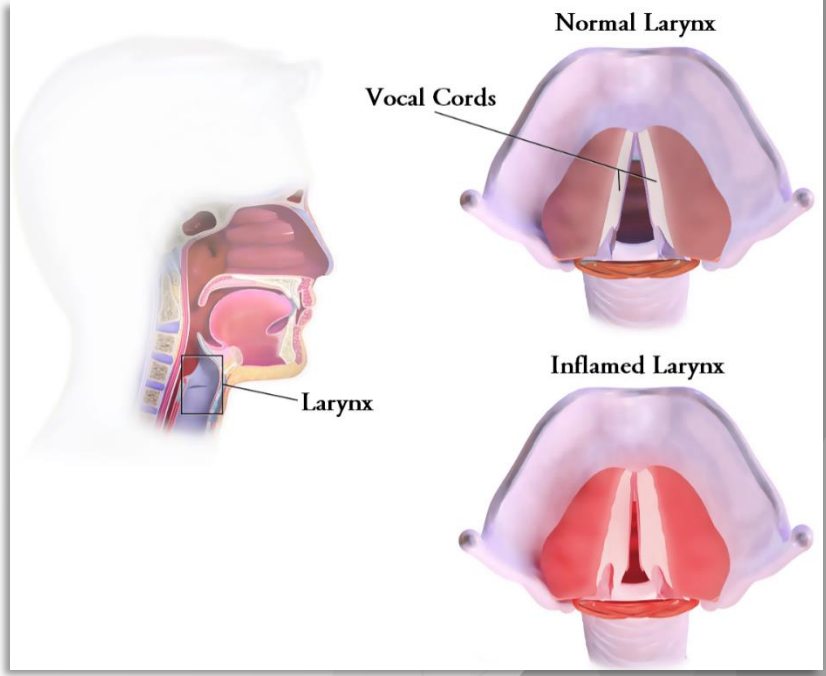
Parainfluenza viruses are ubiquitous and cause common respiratory illnesses in persons of all ages. They are major pathogens of **severe** respiratory tract disease **in infants and young children**.





Parainfluenza viruses (PIVs 1-4)

- Parainfluenza virus replication in the immunocompetent host appears to be **limited to respiratory epithelia**.
- The infection may involve only the nose and throat, resulting in a harmless "**common cold**" syndrome.
- Infection may be more extensive and, especially with types 1 and 2, may involve the larynx and upper trachea, resulting in **croup** (**laryngotracheobronchitis**).



Parainfluenza viruses (PIVs 1-4)

- Factors that determine the severity of PIVs disease are unclear but include **both viral and host properties**, such as immune status of the patient, and airway hyperreactivity.
- Primary infection usually results in **rhinitis** and **pharyngitis**, often with **fever**. However, primary infections caused by PIV type 1, 2, or 3 can be serious ranging from **croup** (particularly with types 1 and 2) to **bronchiolitis** and **pneumonia** (particularly with type 3).
- **PIV type 4 does not cause serious disease**.
- The most common complication of PIVs infection is **otitis media**.

Respiratory Syncytial Virus (RSV)

- **RSV is the most important cause of lower respiratory tract illness in infants** and young children, usually outranking all other microbial pathogens as the cause of bronchiolitis and pneumonia in infants.

- Although the airways of very young infants are narrow and more readily obstructed by inflammation and edema, only a subset of young babies develops severe RSV disease.

- It has been reported that susceptibility to **bronchiolitis** is genetically linked to polymorphisms in innate immunity genes.

Respiratory Syncytial Virus (RSV)

- Children who have had RSV bronchiolitis and pneumonia as infants often exhibit recurrent episodes of wheezing illness for many years.

- RSV is an important cause of **otitis media**. It is estimated that 30–50% of wintertime episodes in infants may be caused by RSV infection.

Respiratory Syncytial Virus (RSV)

- Presumptive diagnosis of RSV infection in infants can often be made on the basis of the clinical syndrome combined with the time of year and other epidemiologic features.
- Radiographic findings are common but relatively nonspecific.
- Rapid detection is desirable to guide the use of appropriate infection-control measures and to potentially limit unnecessary antibiotic use.
- DFA and RT-PCR can be used for laboratory diagnosis.

Respiratory Syncytial Virus (RSV) Rx

- Treatment of serious RSV infections depends primarily on **supportive care** (e.g. removal of secretions, administration of oxygen).
- The antiviral drug **ribavirin** is approved for treatment of lower respiratory tract disease caused by RSV, especially in infants at high risk for severe disease.
- The drug is administered in an **aerosol** for 3–6 days.
- Monoclonal Ab (palivizumab) against RSV has been shown to reduce viral shedding.

Metapneumovirus infections

A newly discovered human pneumovirus isolated from young children with respiratory tract disease

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Metapneumovirus infections

- Human metapneumoviruses are associated with a variety of symptoms of the respiratory tract. These symptoms cannot be distinguished from those induced by RSV.
- Populations at risk besides children include elderly adults and immunocompromised individuals.
- Healthy adults tend to develop cold and flu-like symptoms in response to metapneumovirus infection. Asymptomatic infections are more common than for influenza virus or RSV in this population.
- There is no specific therapy for human metapneumovirus infections, and no vaccine is available.

Thanks for Listening