Medical Virology for MD students

Paramyxoviridae & Togaviridae

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Examples :
Parainfluenza/ syncytial virus

Paramyxoviridae

Respiratory syncytial virus is the the most serious virus of these respiratory viruses in infants but it can be treated so it's important to seek for medical attention + to isolate the infant to prevent the spread of the disease

- 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** النكاف and **measles**). الحصبة

- All members of the *Paramyxoviridae* family **initiate** infection **via the respiratory tract**.

- The paramyxoviruses are enveloped **-ss RNA viruses** with non-segmented genome.

Orthomyxovirusrs : segmented / paramyxoviruses : non segmented

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.

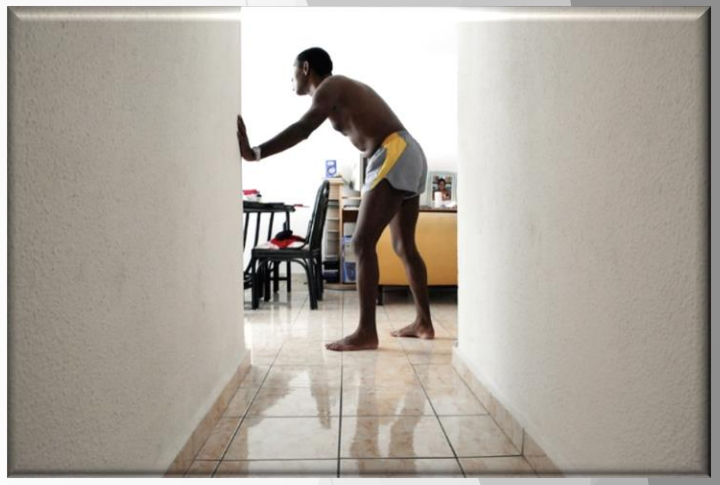
- *Togaviridae* is divided into two genera: Alphavirus and Rubivirus. Rubella (German measles)

  One kind of arboviruses (transmitted by arthropod vectors)

Alphavirus

Other members of the flaviviridea family are arthropod borne viruses : e.g : yellow fever , Zika , dengue viruses

- 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**.

Severe joints pain + fever

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. + fever

In comparison to hard measles : less severe , less duration , less complications , lower mortality rate

- **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.

Viral infections that cause both rash and fever

- 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.

Flat , 1 cm in diameter skin lesions

In children , rublella infections are self limited , resolve completely, withh almost none to few problems and gives them life long immunity

Anti vaccination campaigns led to several outbreaks of measles and German measles during the past few years (some scientifically incorrect articles linked vaccination to autism development)

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

coxsackievirus , echovirus

Rubella (German Measles)

Joints pain Joints infection

- 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.

Part of the MMR vaccine : measles mumps rubella

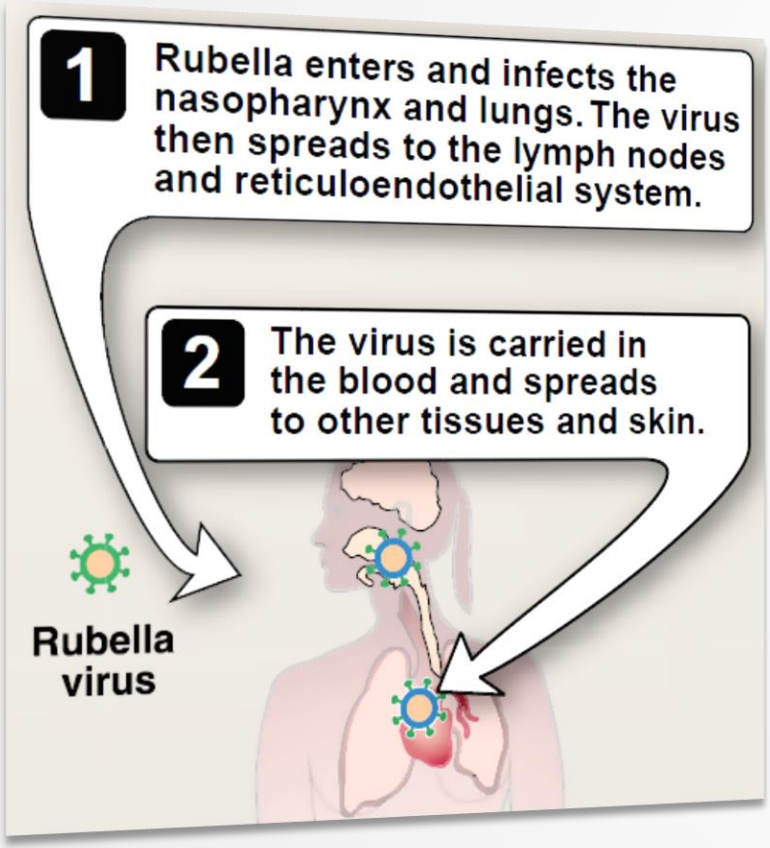
Two doses must be given

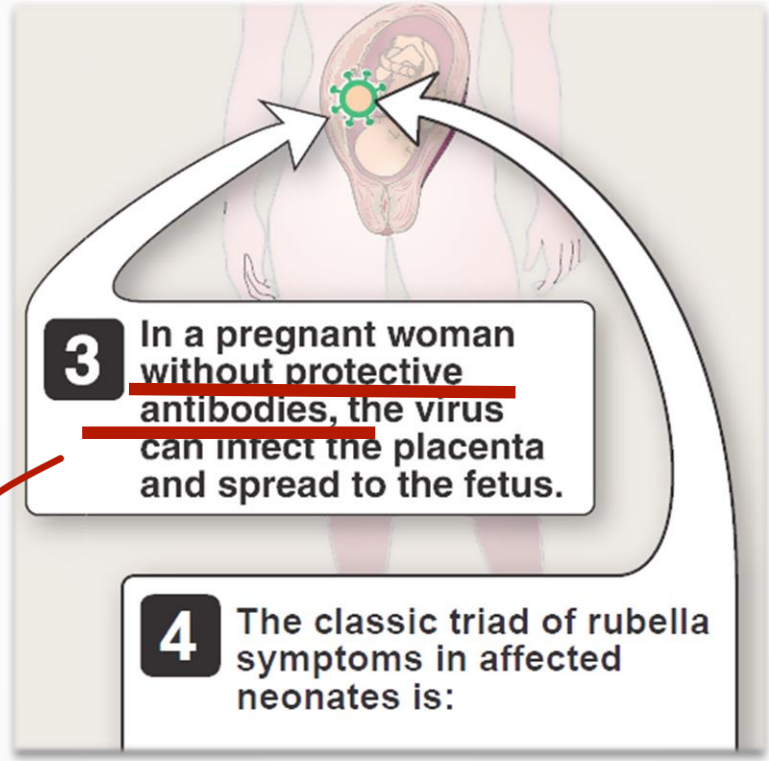
It's a live attenuated vaccine (the most efficient type of vaccines)

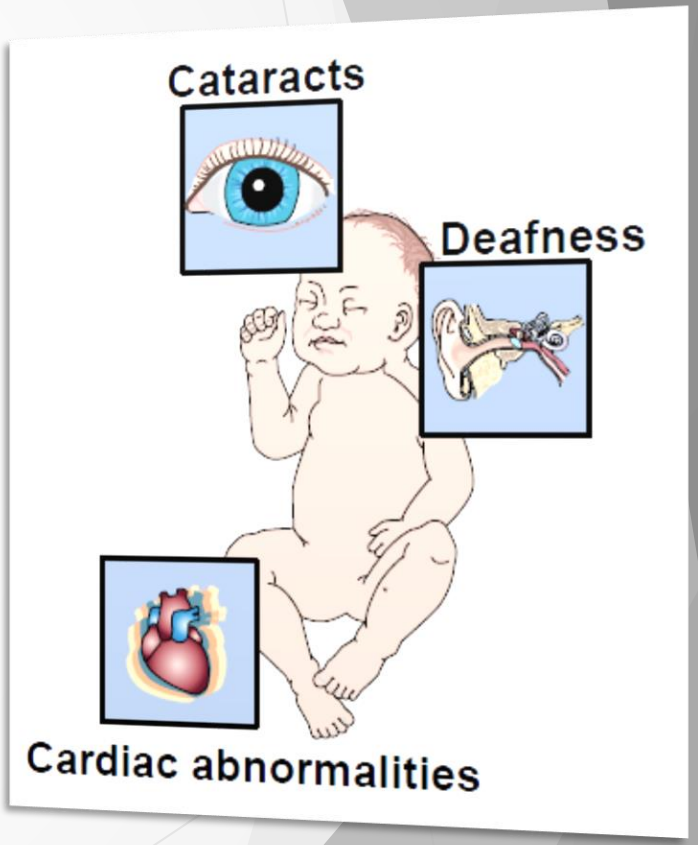
Can't be given to immunocompromised individuals nor pregnant women

Because it resembles the live fully active virus , replicates , and mounts both humoral & cell mediated immune responses

Congenital rubella syndrome



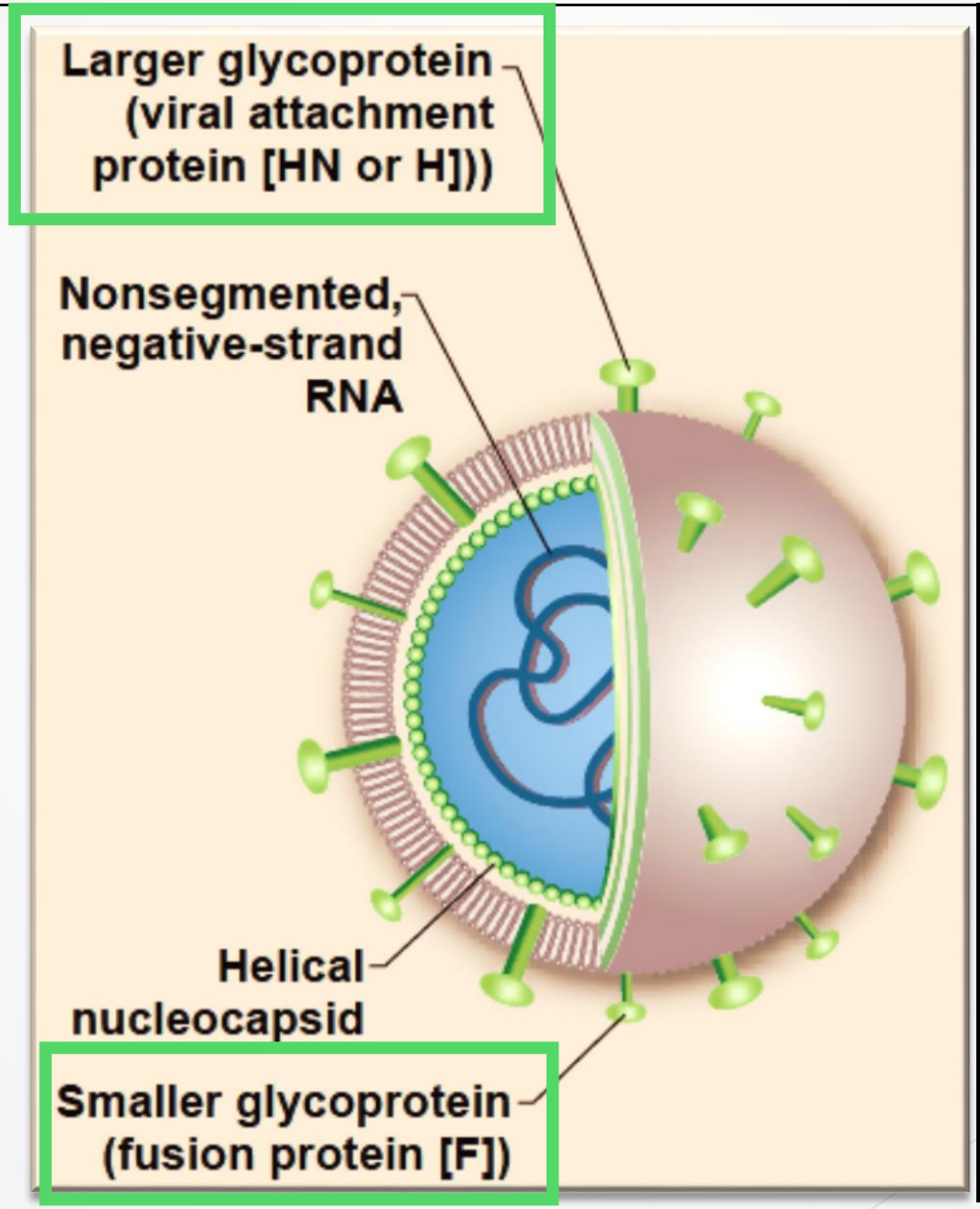




Wasn't infected before and didn't take the vaccine

Paramyxoviridae

Non segmented ssRNA :
no genetic reassortment



Zoonotic infections

Hendra : respiratory infection / lower mortality rate in comparison with nipah / origin : Australia (people who dealt with horses) / limited / one outbreak

Nipah : encephalitis (along with possible fever , dizziness, headaches) / high mortality rate (~ 50%) / origin : Malaysia (people who dealt with pigs) / reached other countries (not limited) / multiple consequent outbreaks

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

Parainfluenza 1 , 3 , 2 , 4

Animal reservoir:

pteropus - flying foxes (one kind of bats)

Measles virus

Remember the complement system

- The cellular receptor for measles virus is **CD46**.

- Measles virus is transmitted by sneeze- or cough-produced **respiratory droplets**.

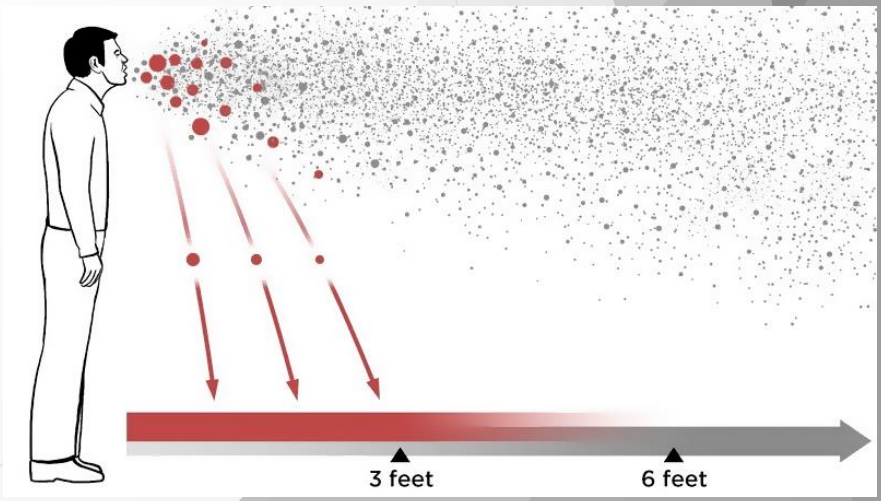
  Similar to chickenpox (almost all cases are symptomatic)

- 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.

Droplets : can travel short distances

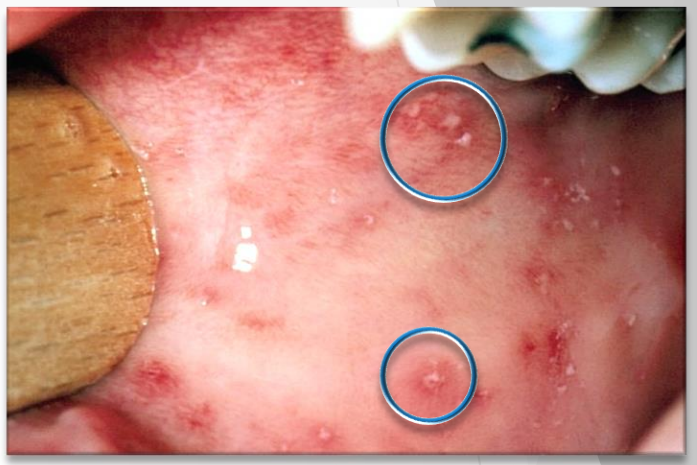
Aerosols.:can travel relatively long distances



Remember: parvo (fifth disease) / sixth disease : rosella

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.

Pathognomonic , definitive sign (used for diagnosis)

Measles (Hard Measles, 10-day measles)

In some Cases measles might lead to Subacute sclerosing panencephalitis (explained in the last slide)

- Soon after the rash appears, the patient is no longer infectious.

The most common complication : otitis media ~ 10%

- The major morbidity and mortality caused by measles are associated with various complications of infection, especially **pneumonia** and **encephalitis**.

50% of measles cases electroencephalogram readings are abnormal

5% : Viral pneumonia/ secondary bacterial pneumonia

- 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**.

30 % out of post infectious encephalomyelitis cases die (the ones who live might deal with neurological disturbances)/Symptoms : seizures ,lethragia , coma

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. MMR

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.

Testicular infection

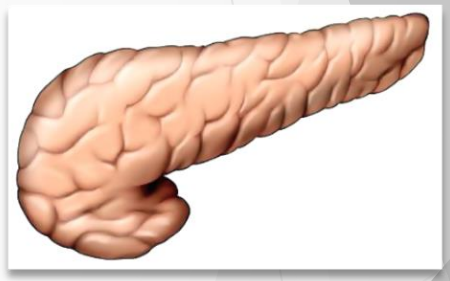
- More than one-third of all mumps infections are **asymptomatic**.

German measles : 20-50% sub clinical

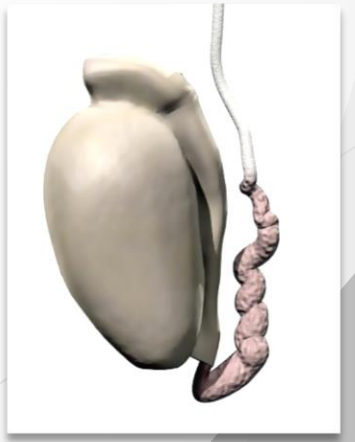
Almost all measles cases are symptomatic

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. العقم



Mumps

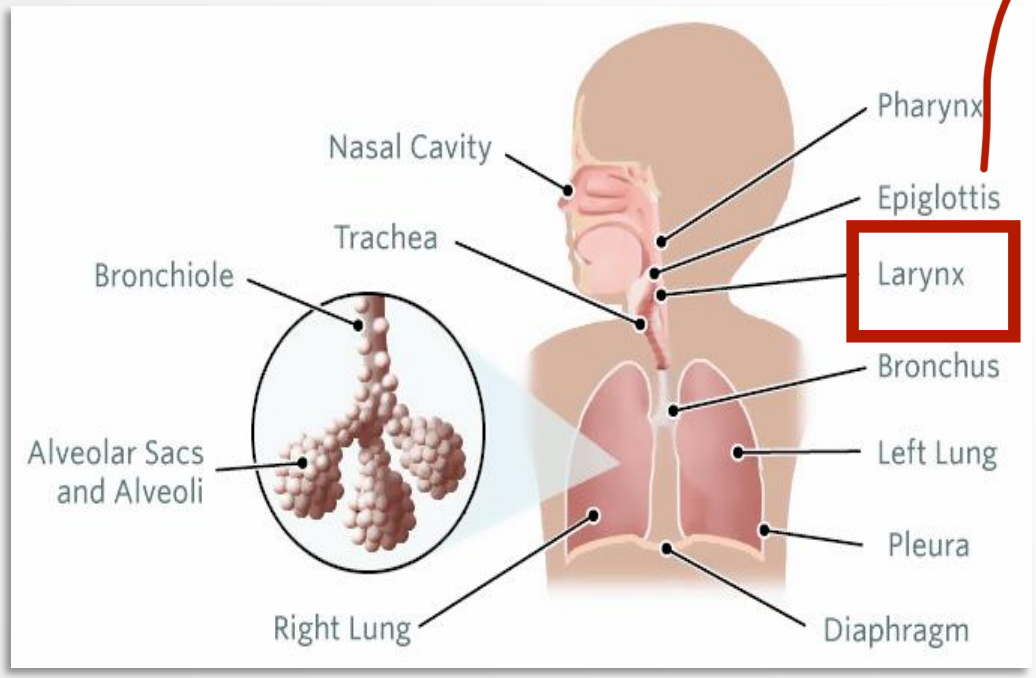
- The diagnosis of typical cases usually can be made on the basis of **clinical** findings.
- Immunity is permanent after a single infection.
- An effective attenuated live-virus vaccine is available.
- Mumps vaccine is available in combination with measles and rubella (**MMR**) live-virus vaccines.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

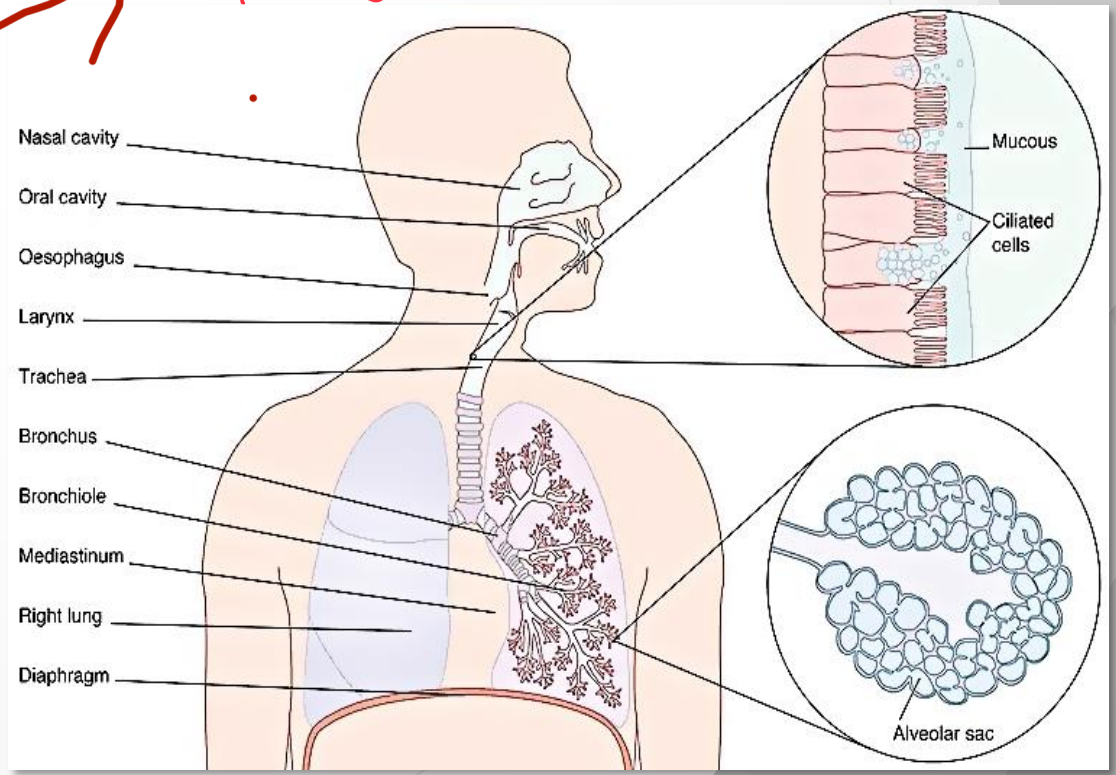
Parainfluenza viruses (PIVs 1-4)

Found everywhere

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**.

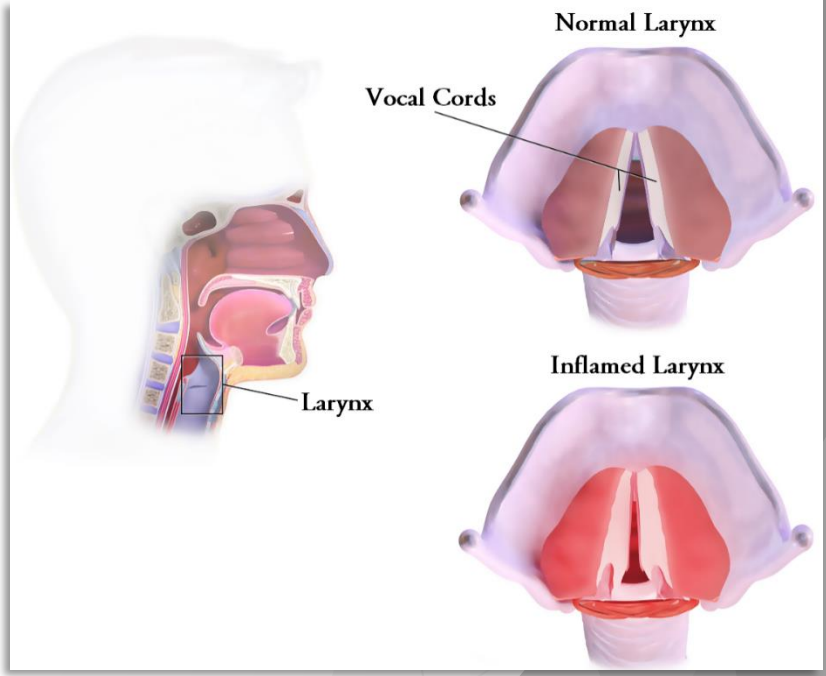
Especially affected





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.

Important

- 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).

Notice the involvement of the lower respiratory tract

- **PIV type 4 does not cause serious disease**.

- The most common complication of PIVs infection is **otitis media**.

Ear infection

Respiratory Syncytial Virus (RSV)

+ most common

- **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)

Can cause mortality especially in infants

- 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. Late autumn , winter , early spring
- 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. Isolation for example

  Immunofluorescence , Real time PCR , antigenic tests all can be used for its diagnosis
- DFA and RT-PCR can be used for laboratory diagnosis.

  Reverse transcriptase PCR is the definitive diagnostic test

Respiratory Syncytial Virus (RSV) Rx

- Treatment of serious RSV infections depends primarily on **supportive care** (e.g. removal of secretions, administration of oxygen).

Clinical trials showed that ribavirin isn't significantly efficient

- 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.

Targets fusion proteins of RSV ; given to kids with chronic respiratory infections or immunocompromised individuals to prevent the infection (IM once monthly)

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.

In almost all respiratory tract infections differentiation is difficult that's why real time PCR is used for diagnosis and differentiation (molecular detection)

- 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.

subacute sclerosing panencephalitis (progressive disease)

A late , very rare complication of measles results from the persistence of the virus in the CNS . Although it's rare , but once it's established in the body it leads to death (even if not immediate) along with the permanent persistence of the measles virus in the CNS (the virus won't leave the body) . A patient with this complication might die within months , or can live up to 5 years after diagnosis. During the remaining years of the patient's life he / she deals with personality disturbances, loss of intellectuality, and motor disturbances (involuntary movements)

It's hard and almost impossible to make sure of the diagnosis (to ensure the presence of the measles virus in the CNS especially in the brain) as screening can't show it and isolation of the virus from the brain isn't possible .

So we can clearly see the importance of the vaccine in avoiding all of the fatal possible complications of measles