



ORTHOMYXOVIRUSES PARAMYXOVIRUSES

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ORTHOMYXOVIRUSES





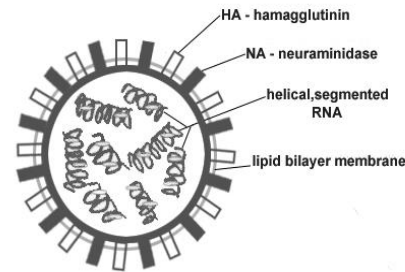
Orthomyxoviruses

- **Myxo** is a Greek word meaning mucous.
- Influenza viruses replicate in mucous membranes of the upper and lower respiratory tract.
- They are exceptions to the rule that RNA viruses replicate in the cytoplasm as they replicate in the nucleus.





Orthomyxoviridae (INFLUENZA VIRUSES)

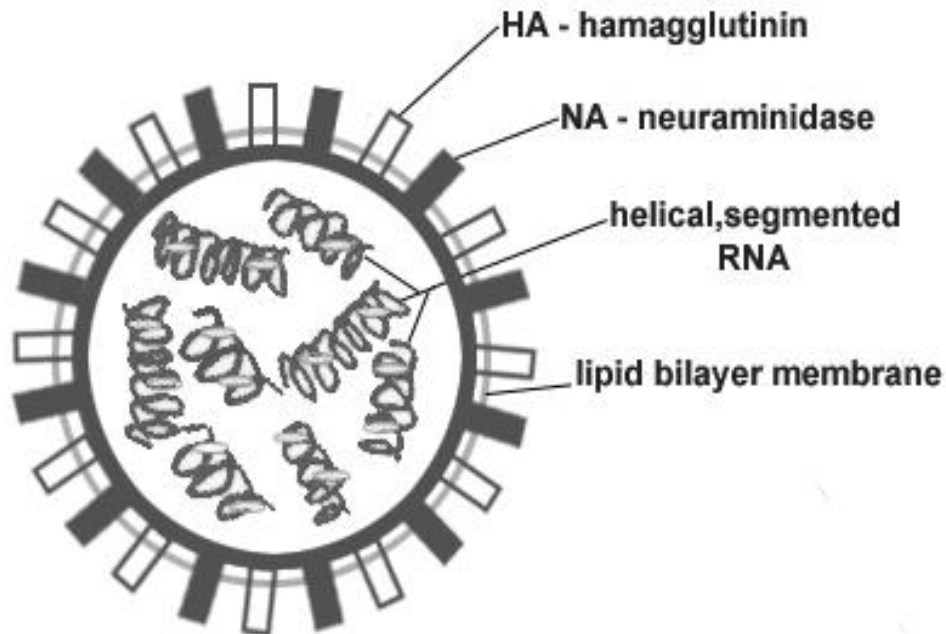


- **Segmented single-stranded RNA genome (eight pieces of ssRNA)**
- They are enclosed in a **lipid envelope** and a layer of glycoprotein spikes known as **haemagglutinin (HA) & neuraminidase (NA)** which are the major antigenic determinants.





Structure of Influenza virus





Structure of Influenza virus

- **Haemagglutinin (HA)** mediates binding to cell surface receptors to initiate infection. Ab against HA neutralizes viral infectivity.
- **Neuroaminidase (NA):** cleaves neuraminic acid on the host cell surface to release the progeny virus from the infected cell. Ab against NA does not neutralize viral infectivity but reduces disease severity by decreasing the amount of virus released from the infected cell.





Classification & Antigenic Types

- Influenza viruses are divided into types A, B and C
on the basis of the ribonucleoprotein antigen:
 - **Type A:** causes influenza in humans & animals (birds & pigs)
 - **Type B:** causes influenza in humans ONLY
 - **Type C:** causes mild respiratory disease





Subtypes of Influenza A Virus

- ONLY **influenza A** virus is further classified into subtypes based upon HA & NA antigens (**16 HA subtypes & 9 NA subtypes**), circulating in birds, humans, swine & horses.





Current Subtypes of Influenza A Virus

- **Influenza A/H1N1:** the causative agent of swine flu (2009 influenza pandemic & the 1918 Spanish flu pandemic).
N.B., In the 1918 flu pandemic, 500 million people were infected with the influenza / H1N1 & at least 50 million people died worldwide)
- **Influenza A/H5N1:** causing avian (bird) flu (infecting humans who closely handle infected birds).
- **Influenza A/H3N2:** one of the human strains of influenza virus





Antigenic Variation

- In types A & B, the haemagglutinin & neuraminidase antigens undergo genetic variation (leading to the emergence of new strains)
- Type C is antigenically stable





Antigenic Change of the Influenza Viruses

Influenza epidemics are of two types:

(1) Yearly **epidemics** are caused by both type A & type B viruses

&

(2) The less frequent (every 10 years app.) severe influenza **pandemics** are always caused by type A virus.





Mechanisms of Antigenic Changes 1

1. Antigenic Drift

- Minor antigenic changes
 - Due to mutations in viral RNA
 - Yearly **epidemics**
 - **Occurs in all types (A, B & less commonly C)**
 - Generates strains that retain a degree of serologic relationship with the currently prevailing strain (Abs against old strain cross-react with new strain).
- **relatively mild**





Mechanisms of Antigenic Changes 2

2. Antigenic Shift

- Major antigenic change in HA and/or NA
- **GENE REASSORTMENT** → completely new antigens
- **Epidemics or pandemics (every 10 years)**
- Occurs in type A only
- Yields an antigen showing no serologic relationship with the prevailing strains resulting in severe infection (due to lack of pre-existing protective immunity to the new virus).





Gene Reassortment 1

- If a single host cell is co-infected with two different influenza viruses, the genome segments of each virus replicate.
- When new progeny viruses are assembled, they can package RNA segments from either parental virus.
- This accounts for the periodic appearance of novel type A strains that cause influenza pandemics.





Gene Reassortment 2

- Pigs play an important role in genetic reassortment because their cells have receptors for both avian and human influenza strains.
- Genetic reassortment does not occur in type B influenza viruses as they have no animal host (i.e., no source for new RNA segments).





Pathogenesis

- **Transmission:** droplets & contact (direct by shaking hands or indirect with contaminated surfaces.
- NA liquefy mucus & help spread through the respiratory tract.
- HA helps attachment to target cells.
- **Incubation period:** 1-2 days.
- Infection of mucosal cells results in cellular destruction. Viraemia is rare.





Clinical Picture

- **C.P.:** fever, chills, malaise, muscle pain (myalgia) & respiratory symptoms such as rhinitis and/or pharyngitis.
- Pure viral pneumonia may occur rarely but more commonly bacterial pneumonia associated with influenza (caused by secondary bacterial infection by *S. pneumoniae*, *S. aureus* & *H. influenzae*).





Diagnosis

- During influenza pandemics, diagnosis is mainly clinically.
- Lab. diagnosis is done using nasal or throat washings by:
 - Antigen detection (by ELISA or IF)
 - Detection of viral RNA (by RT-PCR)
 - Isolation of the virus on tissue culture





Treatment 1

- **Amantadine & rimantadine:**
 - They inhibit uncoating
 - They are no longer recommended because:
 - They are effective only against type A.
 - Rapid emergence of drug resistance
 - They have adverse side effects





Treatment 2

- **Neuraminidase inhibitors** (e.g., zanamivir & oseltamivir):
 - They are active against types A & B.
 - They can reduce the severity of influenza, **ONLY** if given within 1-2 days of disease onset.





Prevention 1

Influenza vaccines

- **Inactivated (Killed) vaccine:**
 - It is given IM
 - It is not a good immunizing vaccine as it yields little secretory IgA
 - Two doses administered at least one month apart are required for previously unvaccinated infants and children <9 years of age. In adults, only one dose is administered. A booster is not recommended.
- **Live attenuated vaccine:** given intra-nasally are good alternatives to inactivated vaccine as they elicit good immune response by sIgA.





Prevention 2

Influenza vaccines:

- They are recommended for people at risk of developing complications from influenza infection, e.g., elderly patients & HCWs.
- They contain the circulating strains of types A & B viruses & should be reformulated annually.





Prevention 3

Chemoprophylaxis

- **Amantadine & rimantadine**
- **Neuraminidase inhibitors** (oseltamivir & zanamivir)





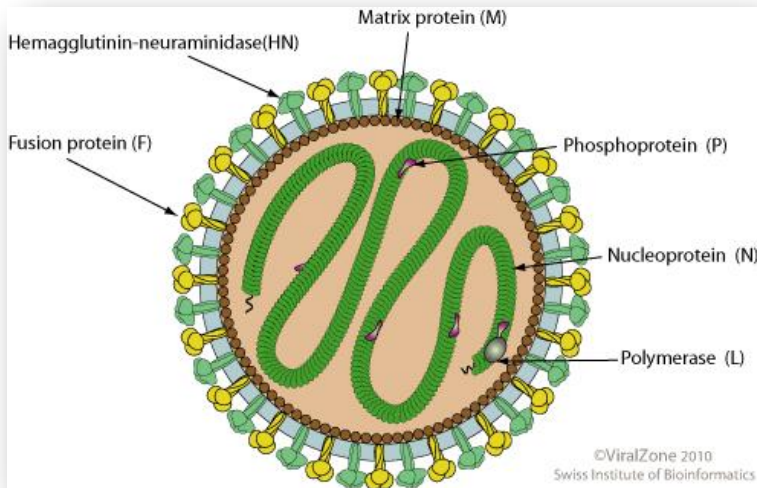
Paramyxoviruses



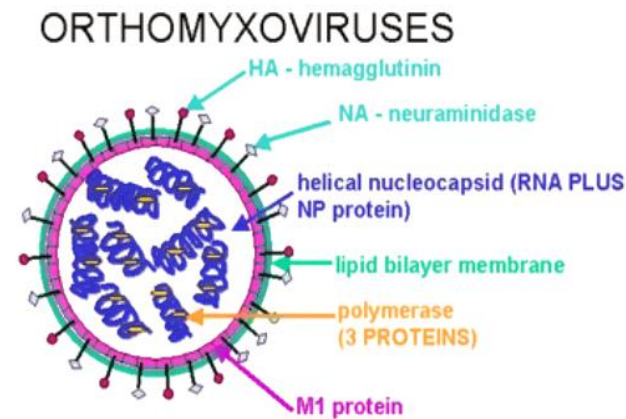


Paramyxoviruses

- Enveloped ssRNA viruses
 - Unlike orthomyxoviruses, their genome is **non-segmented**



Non-segmented genome



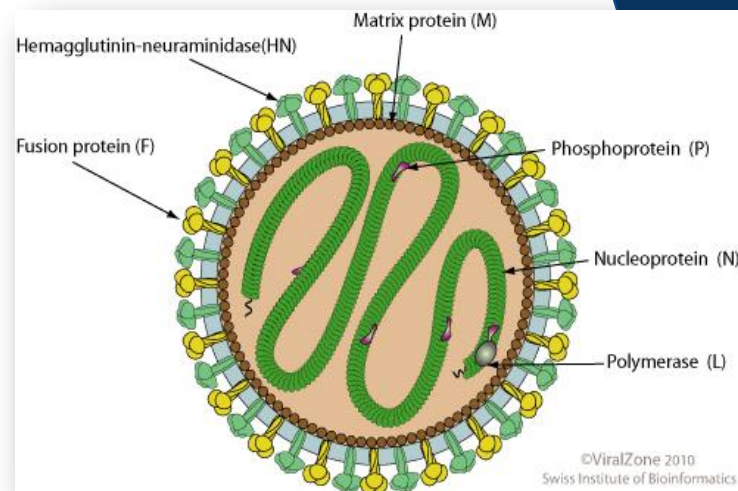
Segmented genome





Paramyxoviruses

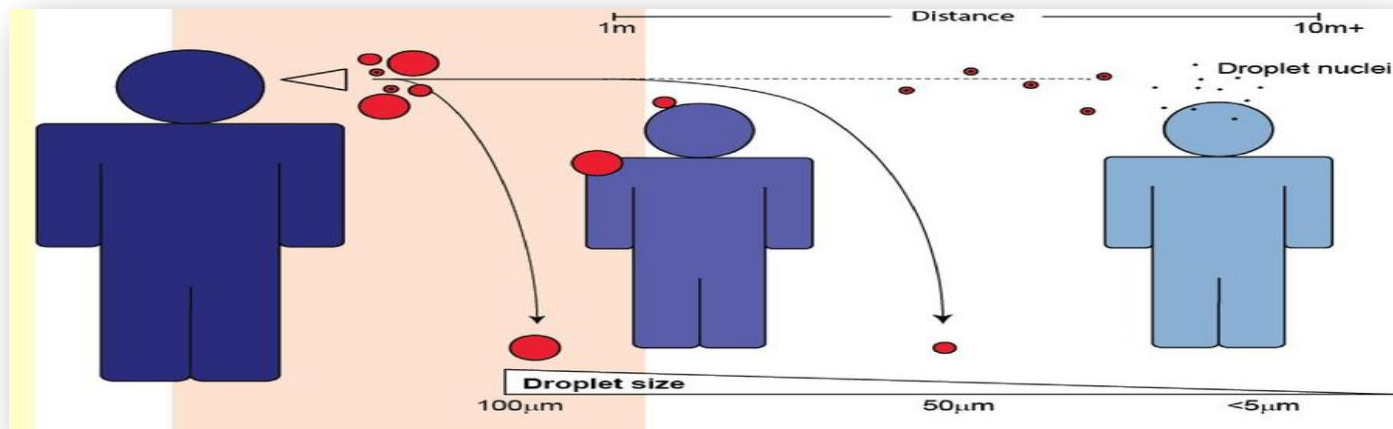
- They include
 1. Parainfluenza viruses,
 2. Measles virus,
 3. Mumps virus,
 4. Respiratory syncytial virus,
 5. Human metapneumovirus





Parainfluenza Viruses

- Parainfluenza viruses are transmitted *via* **respiratory droplets**.





Parainfluenza Viruses

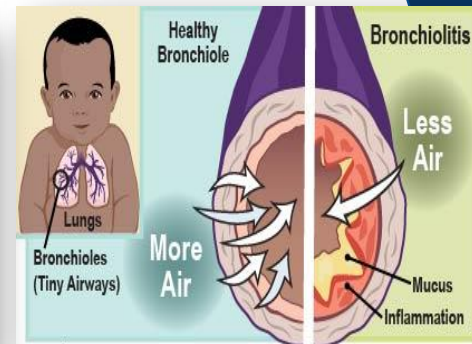
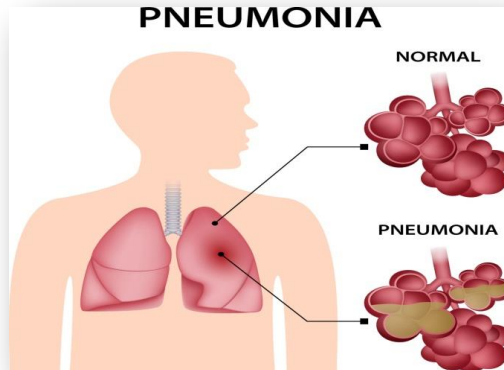
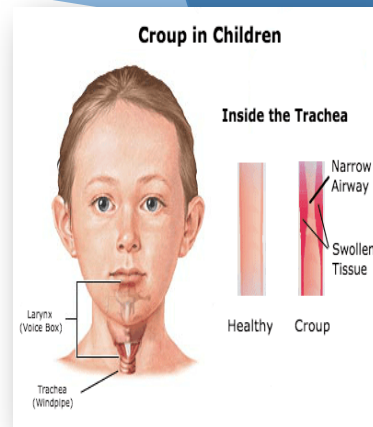
- Incubation period is **2-6 days**
 - They cause **upper and lower respiratory tract disease without viraemia**, particularly in **infants and young children**.





Parainfluenza Viruses

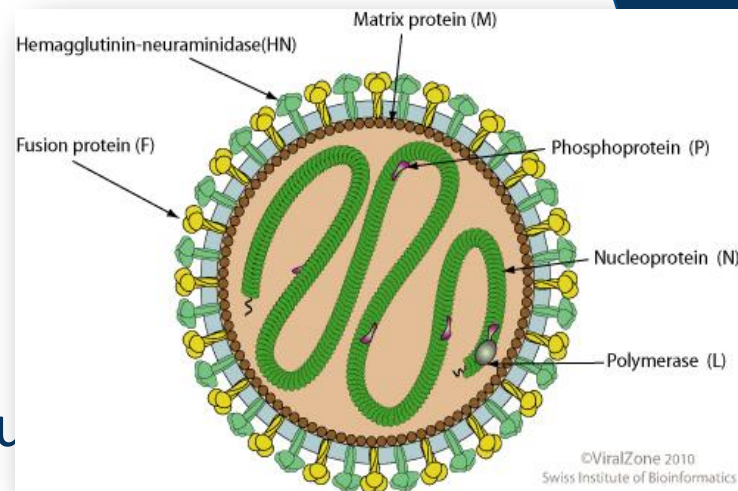
- Infections may include
 - Pharyngitis,
 - Croup (laryngotracheobronchitis),
 - Bronchiolitis,
 - Pneumonia





Paramyxoviruses

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Measles (Rubeola) Virus

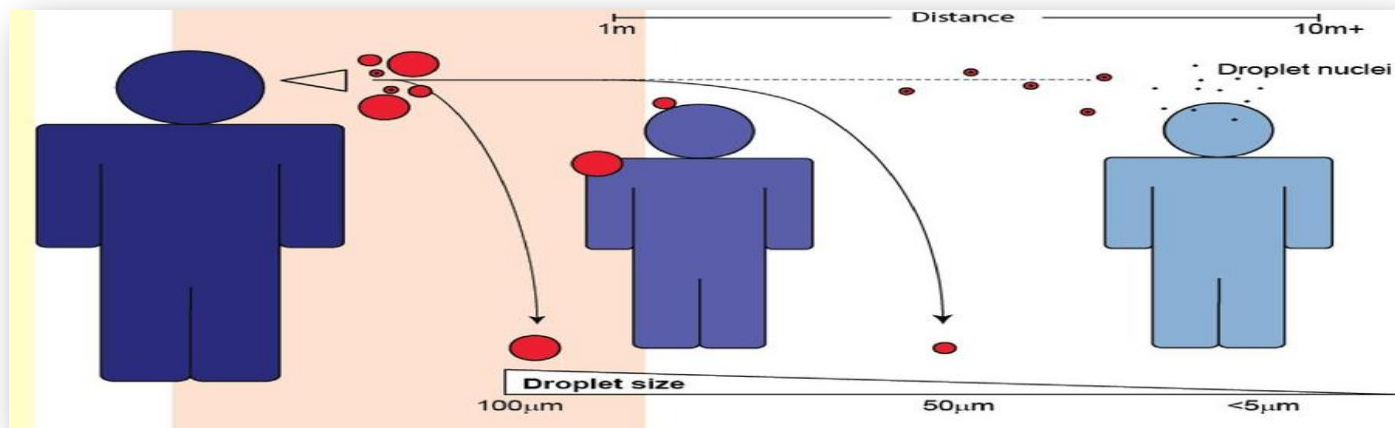
- Measles an acute **highly infectious** disease of children
- Only **one stable antigenic** type
- **Man** is the only natural host for the virus





Measles (Rubeola) Virus Pathogenesis

- Transmission: **aerosol (airborne)**





Measles (Rubeola) Virus

Pathogenesis (1) & Clinical findings (1)

- Measles virus **replicates locally** in the mucosa and regional lymph nodes of the **upper respiratory tract**
- Incubation period = **8 – 12 days**





Measles (Rubeola) Virus

Pathogenesis (2)

&

Clinical findings (2)

- **Blood** (viraemia)

- **Prodromal phase**

- fever,
- Cough,
- Coryza (runny nose)
- Conjunctivitis

- often referred to as the “3 Cs”





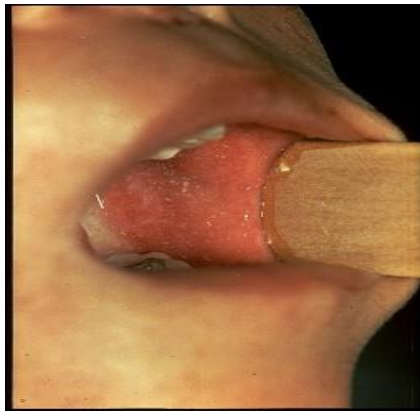
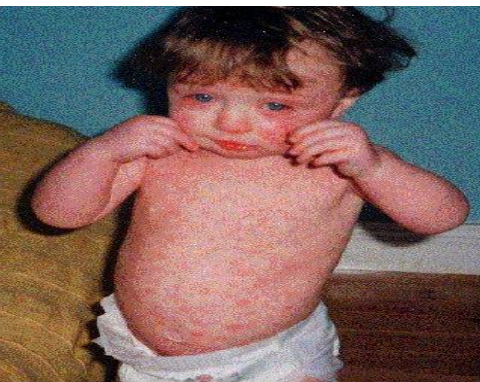
Measles (Rubeola) Virus

Pathogenesis (3)

&

Clinical findings (3)

- Measles virus **localizes in skin and mucous**



- 2-3 days later, **specific diagnostic signs** develop:
 - **Koplik's spots** (small white spots on bright red buccal mucosa)
 - Characteristic **maculopapular skin rash** beginning at the head and proceeding gradually down the body.





Measles (Rubeola) Virus

- Malnourished children develop **more severe disease**.
- **Complications of measles include:**
 1. Secondary bacterial infections, e.g. otitis media, pneumonia
 2. Primary measles virus pneumonia (giant cell pneumonia)
 3. Encephalitis (1 in 1000) (mortality rate 10%) (**autoimmune disease**)
 4. Subacute sclerosing panencephalitis (SSPE): a rare fatal disease of CNS may develop years after apparent recovery.
- The virus **persists in brain and acts as a slow virus**.
- 5. Abortion, premature labour or stillbirth in pregnant women.





Measles (Rubeola) Virus Prevention

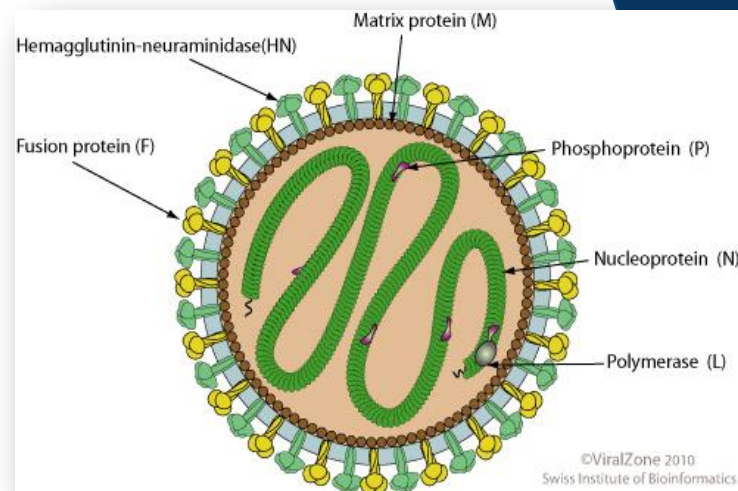
- **Measles vaccine:**
 - **Living attenuated**
 - Combined with 2 other living attenuated virus vaccines, mumps and rubella (**MMR vaccine**)
 - Subcutaneously in **two doses**,
 - The first at 15 months and the second at school age (4-6 years)
- Immunity is **life-long** because:
 - **One stable antigenic type**
 - A stage of **viraemia**, allowing circulating antibodies (IgM and IgG) to neutralize the virus.





Paramyxoviruses

- They include
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Mumps Virus

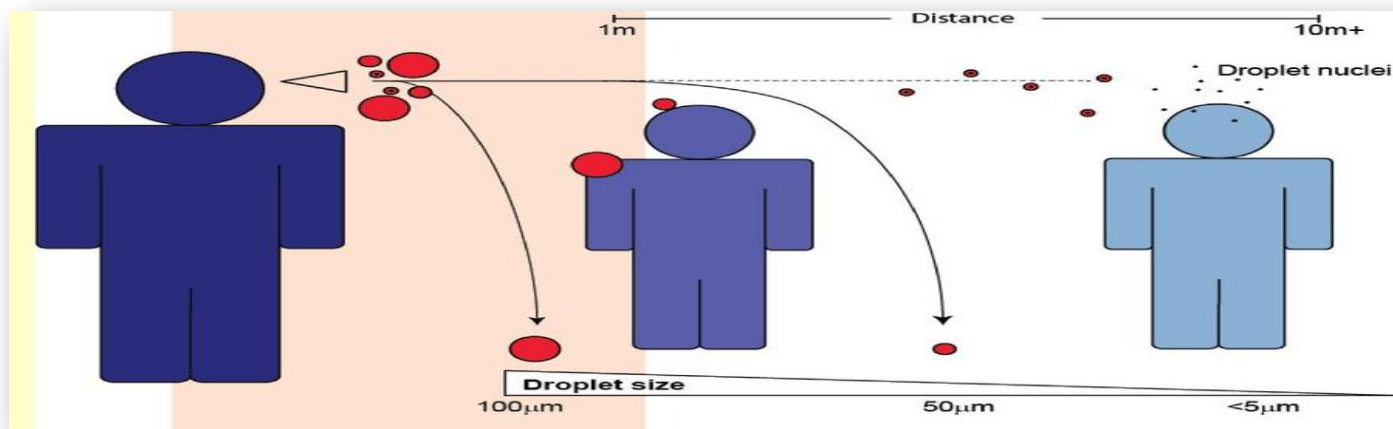
- Mumps an **acute contagious** disease of **children**
- **One stable antigenic type**
- **Man** is the only host





Mumps Virus Pathogenesis

- Transmission: **droplets**





Mumps Virus

Pathogenesis (1) & Clinical findings (1)

- Measles virus **replicates locally** in the respiratory mucosa and regional lymph nodes
- Incubation period = **2 – 3 weeks**





Mumps Virus

Pathogenesis (2)

&

Clinical findings (2)

- **Blood** (viraemia)

- Fever





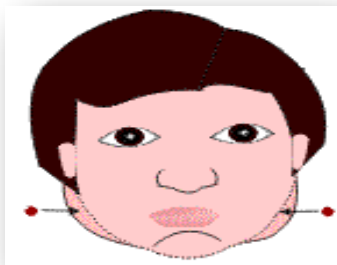
Mumps Virus

Pathogenesis (3)

&

Clinical findings (3)

- Mumps virus **localizes in salivary glands especially the parotid glands**



- Painful **non-suppurative swelling** of one or both parotid glands (parotitis)





Mumps Virus

Pathogenesis (4)



Clinical findings (4)

- The virus may disseminate into **testes, pancreas and brain**.
- Complications of mumps include:
 - **Orchitis in post-pubertal males** which, if bilateral, can result in sterility.
 - **Pancreatitis**
 - **Meningitis**





Mumps Virus

- At least 1/3 of infections are **asymptomatic**.





Mumps Virus Prevention

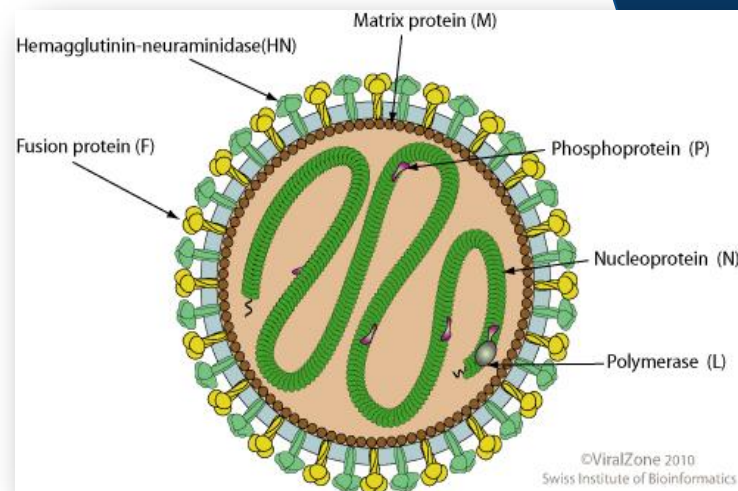
- **Mumps vaccine:**
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Paramyxoviruses

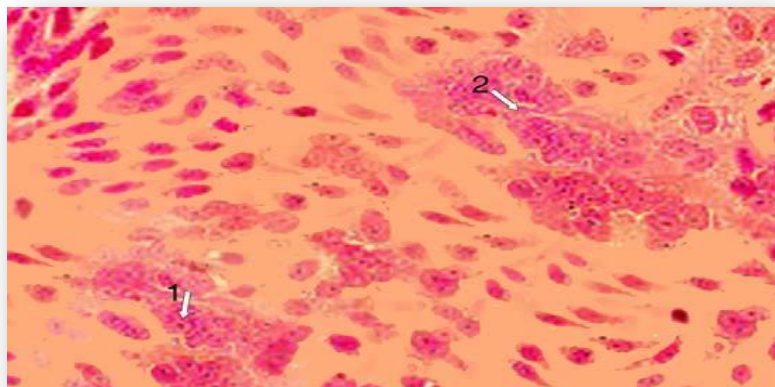
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Respiratory Syncytial Virus (RSV)

- It is so called due to its ability to cause fusion of host cells forming multinucleated giant cells (syncytium).
 - This can be seen as a **characteristic CPE in cell culture**.





Respiratory Syncytial Virus (RSV)

- **Humans** are the natural host of RSV.
- Transmission by **respiratory droplets or contaminated hands.**





Respiratory Syncytial Virus (RSV)

- The most important cause of **lower respiratory tract disease** in infants **and young children**
→ febrile bronchitis, bronchiolitis and pneumonia
- Adults → common cold-like illness
- **No viraemia**





Respiratory Syncytial Virus (RSV)

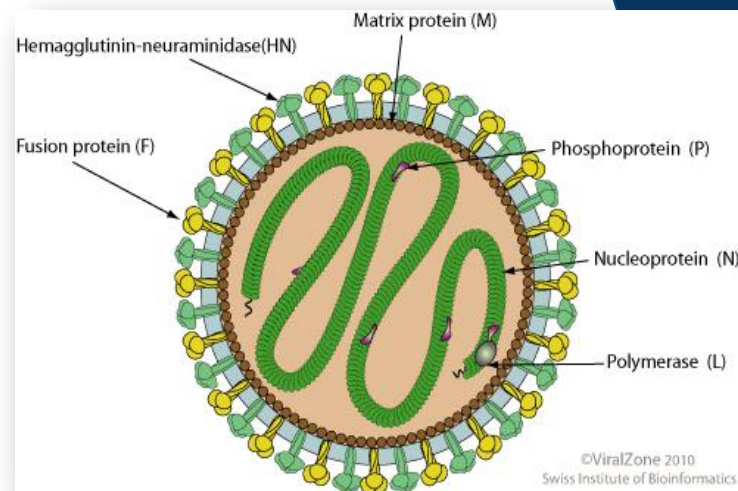
- **Treatment:**
 - **Ribavirin** administered by **aerosol**
- **Prevention:**
 - No vaccine is available
 - **Hand washing** is the major preventive measure





Paramyxoviruses

- They include
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 3. Mumps virus,
 4. Respiratory syncytial virus,
 5. Human metapneumovirus





Human Metapneumovirus (hMPV)

- hMPV is the second major cause of **lower respiratory tract infection** in infants and young children.
- It is similar to RSV regarding mode of transmission, diseases and prevention.





Thank you

