Unit II – Problem 1 – Microbiology: Orthomyxoviruses and Paramyxoviruses

- **What are the commonly associated viruses with the following syndromes?**
  - **Influenza**: influenza viruses.
  - **Croup**: parainfluenza viruses.
  - **Bronchiolitis**: Respiratory Syncytial Virus (RSV).
- **Orthomyxoviruses vs. paramyxoviruses:**

Property	Orthomyxoviruses	Paramyxoviruses
Viruses	Influenza A, B and C	Measles, mumps. RSV and parainfluenza viruses
Genome	Segmented (8 pieces); single-stranded RNA of negative polarity	Non-segmented; single-stranded RNA of negative polarity
Virion RNA polymerase	Yes	Yes
Capsid	Helical	Helical
Envelope	Yes	Yes
Size	Smaller (110 nm)	Larger (150 nm)
Surface spikes	Hemagglutinin and neuraminidase on different spikes	Hemagglutinin and neuraminidase on same spikes
Giant cell formation	No	Yes

- **Virulence (ability of the virus to cause disease) is mediated through the following:**
  - **Hemagglutinin (HA):** it is a receptor-binding protein which helps the virion to get into host cells.
  - **Neuraminidase (NA):** it is an enzyme which helps the offspring virions to get out of host cells.
- **Influenza viruses:**
  - **Types of influenza viruses:**

Type-A	VERY IMPORTANT because it causes worldwide pandemics أوبئة عالمية
Type-B	Causes local outbreaks of influenza especially among young population.
Type-C	Infects most people when they are young and RARELY causes a serious disease

  - **Structure of influenza virus:**
    - ✓ There are around 500 spikes emerging out from its lipid envelope:
      - ❖ 80% is hemagglutinin.
      - ❖ 20% is neuraminidase.

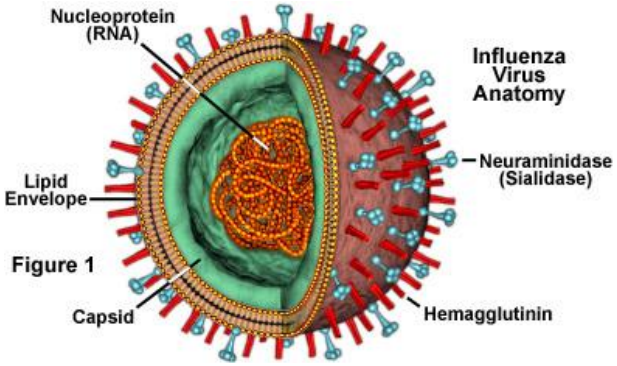
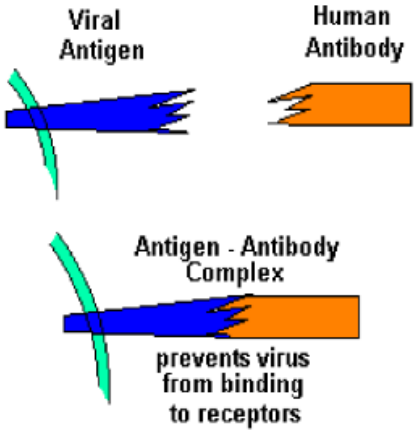


Figure 1

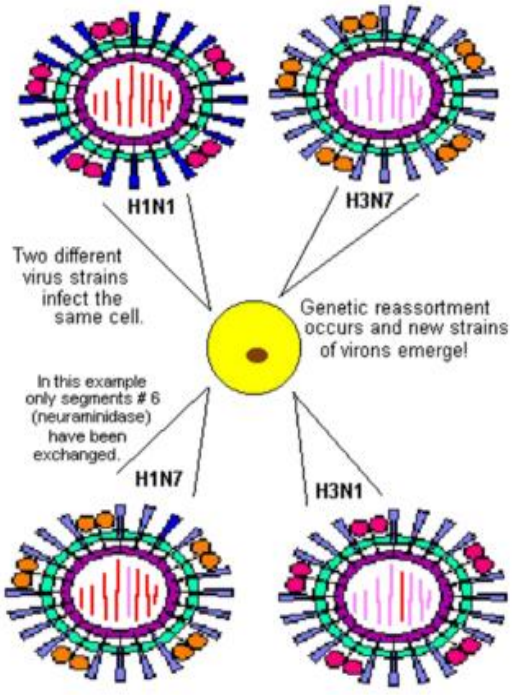
  - **Site of infection**: commonly upper respiratory tract (why?) → because its mucosa has a lot of receptors for influenza virus.
  - **Transmission:**
    - ✓ Inhalation of respiratory droplets.
    - ✓ Rubbing your eyes, nose or mouth after shaking hands with a patient who is shedding the virus.

- **Clinical course**: 2-3 days after exposure to the virus patients will suffer from fever, headache, fatigue/malaise, runny nose and cough.
- **Body response against influenza virus:**
  - ✓ Release of interferons.
  - ✓ Formation of specific antibodies:
    - ❖ Some will bind to hemagglutinin thus preventing the virus from binding to receptors of host cells.
    - ❖ Others will bind to neuraminidase thus preventing further spread of the infection.

      Notice that each group of antibodies is SPECIFIC TO ONE STAIN OF INFLUENZA VIRUS and provide no immunity against other strains (if you don't have antibodies against them ☹).



- **How are new strains of viruses formed?**
  - ✓ Antigenic drift (mutations): as mentioned previously, influenza viruses have RNA genome (composed of 8 segments: segment 4 contains a gene for HA and segment 6 contains a gene for NA). When RNA replicates, there are higher chances for it to require errors which act as mutations that will accumulate on the genome and changing it with subsequent replications thus resulting in formation of a new strain.
  - ✓ Antigenic shift (new combinations):
    - ❖ This occurs ONLY WITH INFLUENZA A but not B or C.
    - ❖ If the host cell is infected with two different strains of influenza A, the offspring virions may contain a mixture of each parents' genes.



- A strain of influenza A may infect one species for decades and then suddenly jump to infect a new species (due to antigenic shift) resulting epidemics. Therefore, influenza virus is a virus which normally causes only a SLIGHT ILLNESS but can undergo genetic recombination with other species and comes back as a KILLER VIRUS!
- **Avian Flu (H5N1):**
  - ✓ H5N1 was discovered in 1961 in some birds from South Africa. It was found that is devastating مدمر for chickens BUT HARMLESS TO HUMANS at that time.
- **Swine flue (H1N1):**
  - ✓ It is a quadruple reassortant virus: which means that it has two genes from pigs (in Europe/Asia), avian gene جين إنفلونزا الطيور and a human gene.

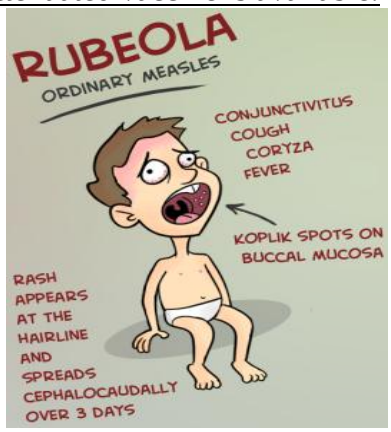
- **Paramyxoviruses:**

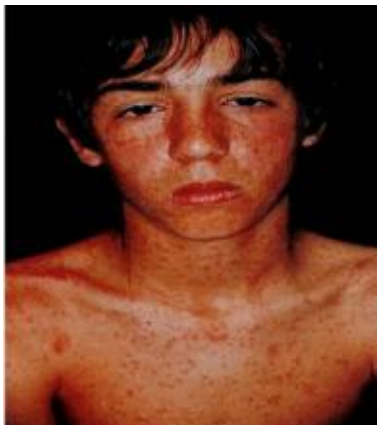
- **Envelope spikes of paramyxoviruses:**

Virus	Hemagglutinin	Neuraminidase	Fusion protein
Measles	+	-	+
Mumps	+	+	+
RSV	-	-	+
Parainfluenza virus	+	+	+

Notice that measles and mumps fusion proteins are hemolysins also.

- **Parainfluenza virus:**
  - ✓ Types: 1-4
  - ✓ Characteristics: enveloped; non-segmented single-stranded RNA with negative polarity; the infected cells will fuse together originating a syncytium (this is considered as a cytopathic effect).
- **Measles:**
  - ✓ Epidemiology: commonly affects malnourished children of developing countries.
  - ✓ Transmission: respiratory droplets.
  - ✓ Pathogenesis: the rash is caused by
    - ❖ Cytotoxic T-cells attacking the virus infected vascular endothelial cells in the skin.
    - ❖ Antibody-mediated vasculitis.
  - ✓ A live attenuated vaccine is available.

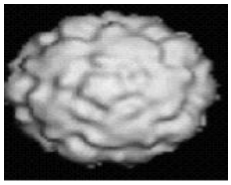




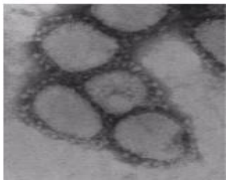
- **Mumps:**
  - ✓ Transmission: respiratory droplets.
  - ✓ Characteristics: a single serotype exists and single-stranded RNA with negative polarity.
  - ✓ Diagnosis: clinical.
  - ✓ Complications: monolateral orchitis (inflammation of the testicle) and meningitis (RARE!).
  - ✓ A live attenuated vaccine is available.

- **Respiratory Syncytial Virus (RSV):**
  - ✓ Epidemiology: it affects infants (up to 1 year of age) especially at WINTER.
  - ✓ It results in bronchiolitis: inflammation and obstruction of bronchioles due to swelling of their walls.

- **Common cold viruses:**
  - **They account for 1/3 to 1/2 of all acute respiratory infections in humans.**
  - **Rhinoviruses are responsible for 30-50% of common colds while coronaviruses are responsible for 10-30%:**



    - ✓ Rhinovirus:
      - ❖ Single-stranded RNA virus.
      - ❖ It belongs to picornavirus family.
      - ❖ It is acid-labile غير مستقر في الظروف الحمضية
      - ❖ At least 100 serotypes are identified.



    - ✓ Coronavirus:
      - ❖ Single-stranded RNA virus.
      - ❖ Enveloped with pleomorphic morphology.
      - ❖ There are two serogroups: OC43 and 229E.

- **Laboratory diagnosis of respiratory viral infections:**
  - **Rapid diagnosis:**
    - ✓ Sample: nasopharyngeal aspirate.
    - ✓ Antigen detection:
      - ❖ Immunofluorescence.
      - ❖ Rapid method.
    - ✓ Molecular detection:
      - ❖ Real time PCR.
  - **Virus isolation**: culture (a sample for viral culture is obtained via nasopharyngeal aspirate and cultured inside viable cells –because viruses are intracellular organisms- to produce a monolayer. This can be visualized under the inverted microscope in which objective lenses are in the bottom).
  - **Serology**: detection of specific antibodies in the serum (IgM or IgG) by Enzyme-Linked Immunosorbent Assay (ELISA) method. Steps of ELISA: