

# Orthomyxoviruses

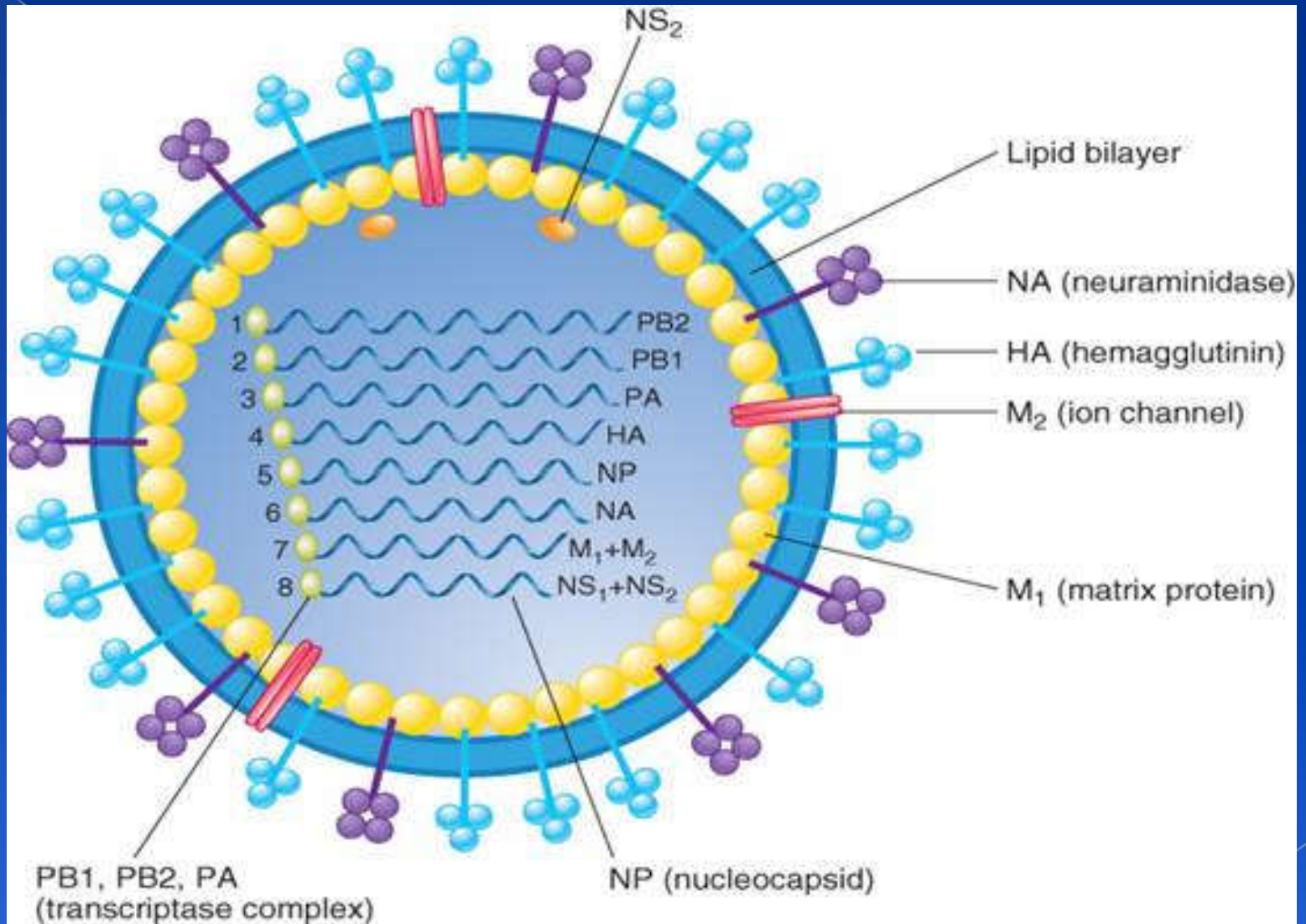
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**3<sup>rd</sup> year medicine**

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## ○ Structure:

- Genome: single stranded RNA segmented (8).
- Helical Nucleocapsid.
- Envelope: lipoprotein with glycoprotein spikes:
  - 1) Haemagglutinin “HA” : bind to cell surface receptor sialic acid to initiate infection.
  - 2) Neuraminidase “NA”: facilitate virus release from infected cells.
  - 3) Changes in of HA , NA determine antigenicity of the subtype circulating in birds, human, swine.
- The most famous subtypes:
  - ✓ H1N1: in humans, pandemic 2009 “swine flu”
  - ✓ H5N1: circulating in birds “avian flu”, infect humans
    - Virus jumped directly from birds to humans.
    - Contain gene segments from avian viruses only.
    - If reassortment occur with human strains it will spread from person to person



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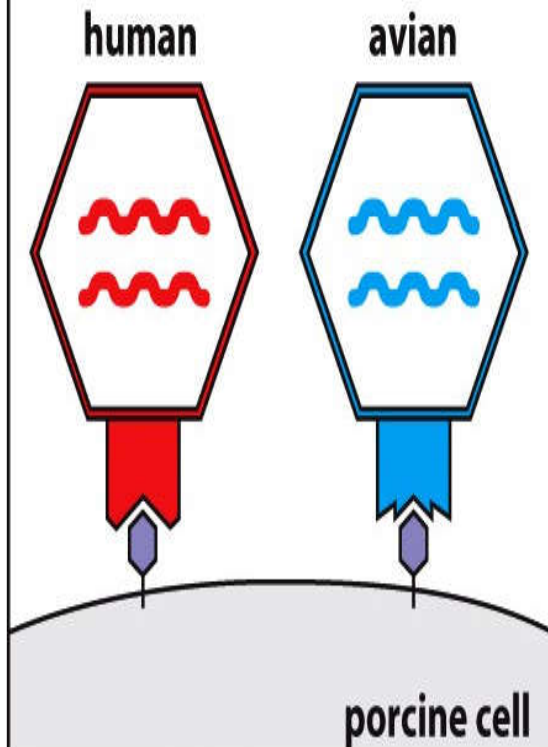
## Influenza virus

- Three types A,B,C.
- Influenza A:
  - Pandemic every 10 years.
  - Outbreaks every year
- Influenza B: outbreaks
- Influenza C: mild respiratory disease

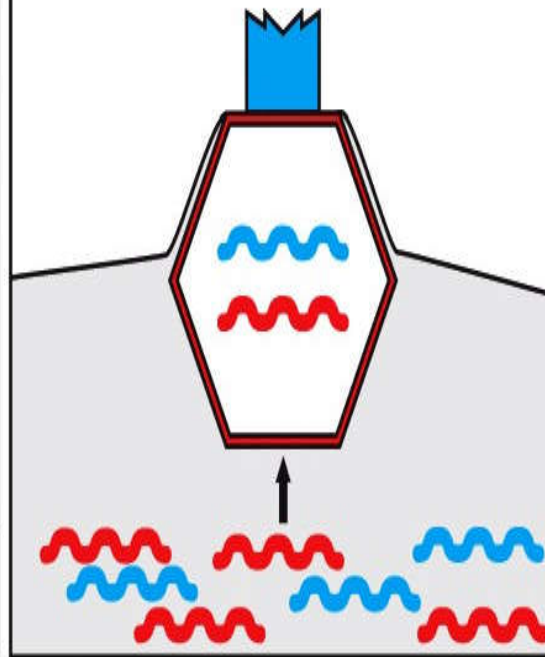
# Antigenic variations:

- Common phenomenon in influenza virus due to changes in HA and NA.
- Occur in type A, less in type B, type C antigenically stable.
- Two types:
  - > Antigenic drift: minor changes due to mutation occur in both A and B viruses, resulting in strains that cause yearly outbreaks.
  - > Antigenic shift:  
major changes due to reassortment of gene segments, occur when one cell is infected simultaneously with two different influenza A viruses (avian and human influenza A viruses) mixture of parental gene segments assembled into progeny virions resulting in a new variant of human influenza A virus bearing the avian virus HA.  
Pig cells have receptors for both avian and human influenza strains and can be coinfecting by more than one strain acting as a mixing pot in which reassortment between two or more viruses (avian, human, pig influenza A viruses) occur.  
2009 pandemic due to A/H1N1 represent a quadruple reassortment of two swine strains, one human, one avian strain of influenza.

**A secondary host is infected with a human and an avian strain of virus**



**Recombination of viral RNA in the secondary host produces virus with a different hemagglutinin**



**No cross-protective immunity in humans to virus expressing a novel hemagglutinin**

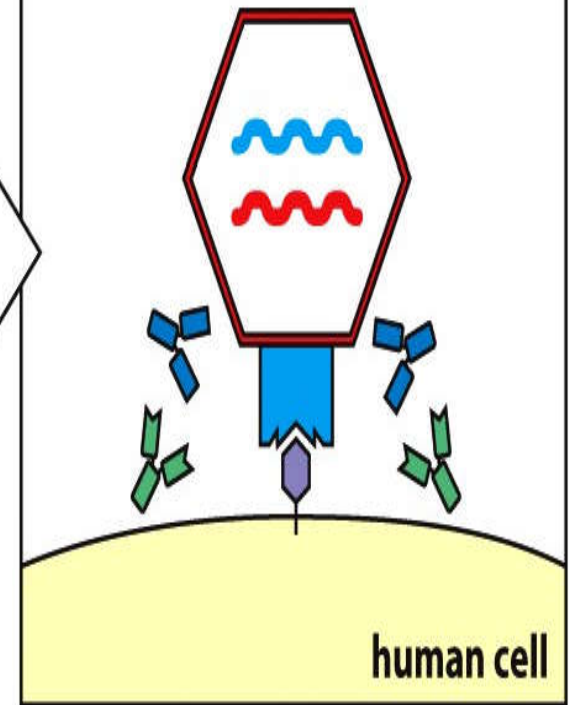
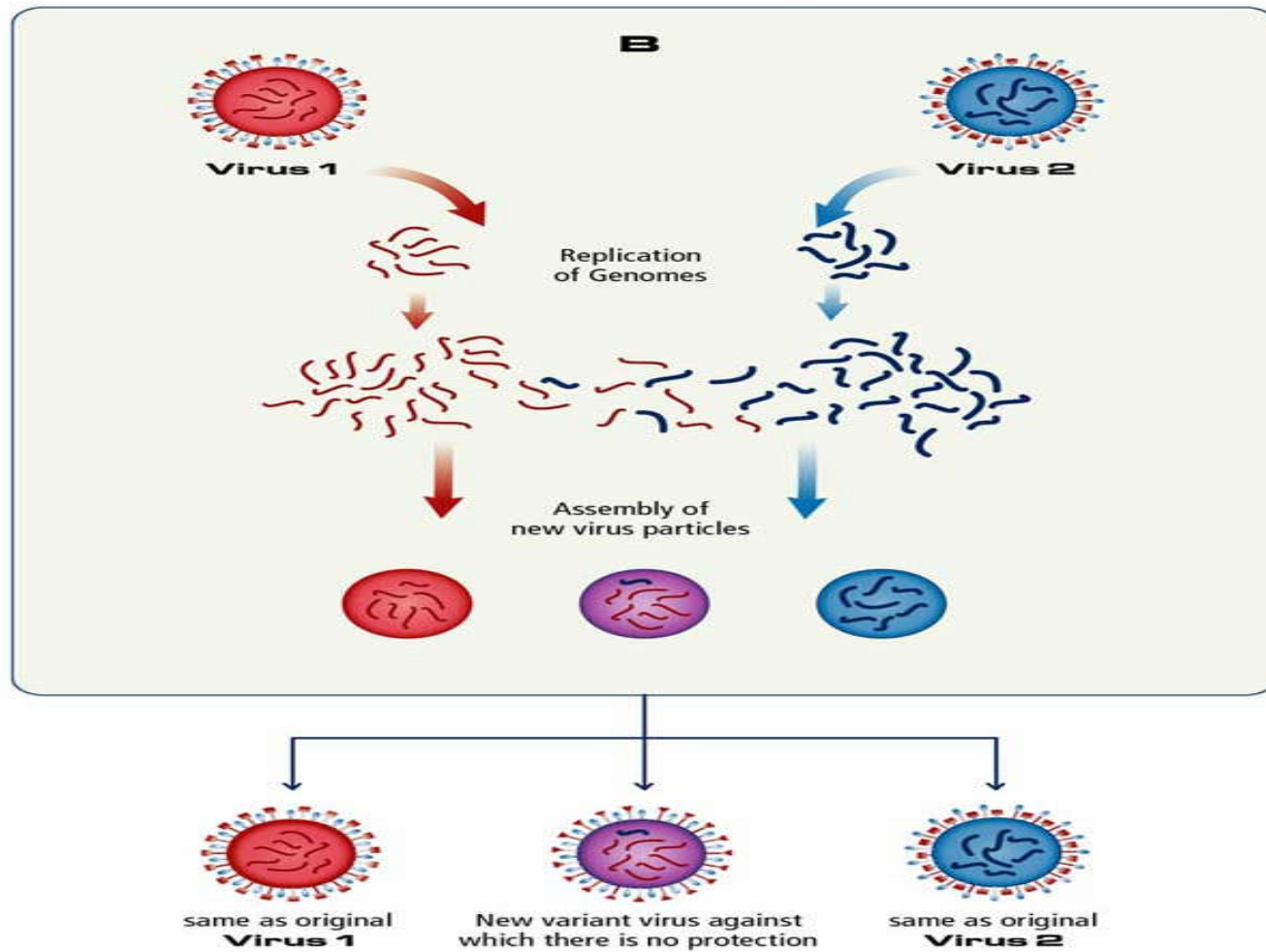
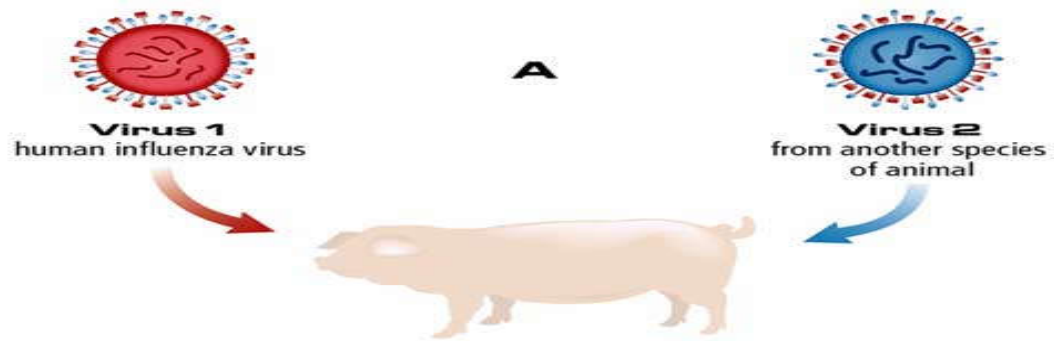


Figure 11.3 The Immune System, 3ed. (© Garland Science 2009)



- ⦿ Influenza B virus is only a human virus there is no animal source of new RNA segments and does not undergo antigenic shifts.
- ⦿ Antigenic shifts appear less frequently every 10 years causing epidemics , drift appear every year and are the cause for changing the strains used for vaccine production on yearly basis.



# Pathogenesis

- Infection occur by inhalation of airborne droplets.
- Neuraminidase of the inhaled virus degrade the protective mucous layer allowing the virus to reach the mucous membranes of the respiratory tract where it multiply locally causing rhinitis, pharyngitis, bronchitis.
- Incubation period 1-4 days.
- Fever, myalgia, headache, dry cough, malaise, anorexia.
- Systemic manifestations duo to circulaing cytokines.
- Complications: in elderly and deblitated=viral ao bacterial pneumonia,
- Avian flu caused by A/H5N1 cause sever disease with pneumonia and multiorgan failure, mortality rate 50% duo to progressive pneumonia.

# Diagnosis:

- Sample: nasal aspirate, throat swab, sputum.
- ELISA for detection of viral antigens,
- RT-PCR for detection of viral nucleic acid
- Isolation of virus in cell culture ,  
embryonasted egg.

# Vaccination

1. Inactivated influenza vaccine (IIV):
  - Inactive whole virus or
  - subvirion containing purified virus disrupted with detergents or
  - purified surface antigen glycoprotein HA, NA.
  - Contain the annually recommended strains that represent the seasonal influenza virus that are predicted to be circulating during influenza season
  - For persons above 6 months including those that are healthy or with chronic conditions and pregnant women

○ Living attenuated influenza vaccine “LAIV”:

- Cold adapted vaccine containing temperature sensitive mutants of influenza A and B .
- It replicates in cooler nasal mucosa induce local IgA
- For non pregnant healthy persons 2–49 years.

Both IIV and LAIV contain strains of influenza virus antigenically equivalent to annually recommended strains of influenza

Vaccine contain Influenza A (H3N2), Influenza A (H1N1), Influenza B.

The vaccine reformulated every year to contain the current antigenic strains that are the result of the antigenic drift or shift.

- 2007, FDA approved the first vaccine for humans against H5N1, the vaccine is prepared yearly from the circulating strain of the virus, inactivated whole virus vaccine given I.M in two doses separated by one month, it could be used if current H5N1 avian virus spread from human to human.

# Treatment

- Neuraminidase inhibitors : zanamivir, oseltamivir for treatment, prevention of influenza A, B.
- Amantadine, rimantadine .