Respiratory System Module
2023-2024

Viral Respiratory Tract Infections
(A)

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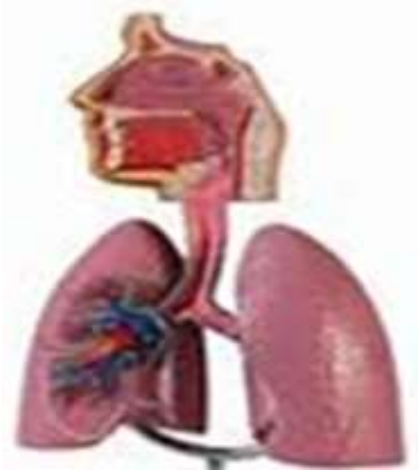


Orthomyxoviruses

Orthomyxoviruses (under E.M)

Includes the following main genera:

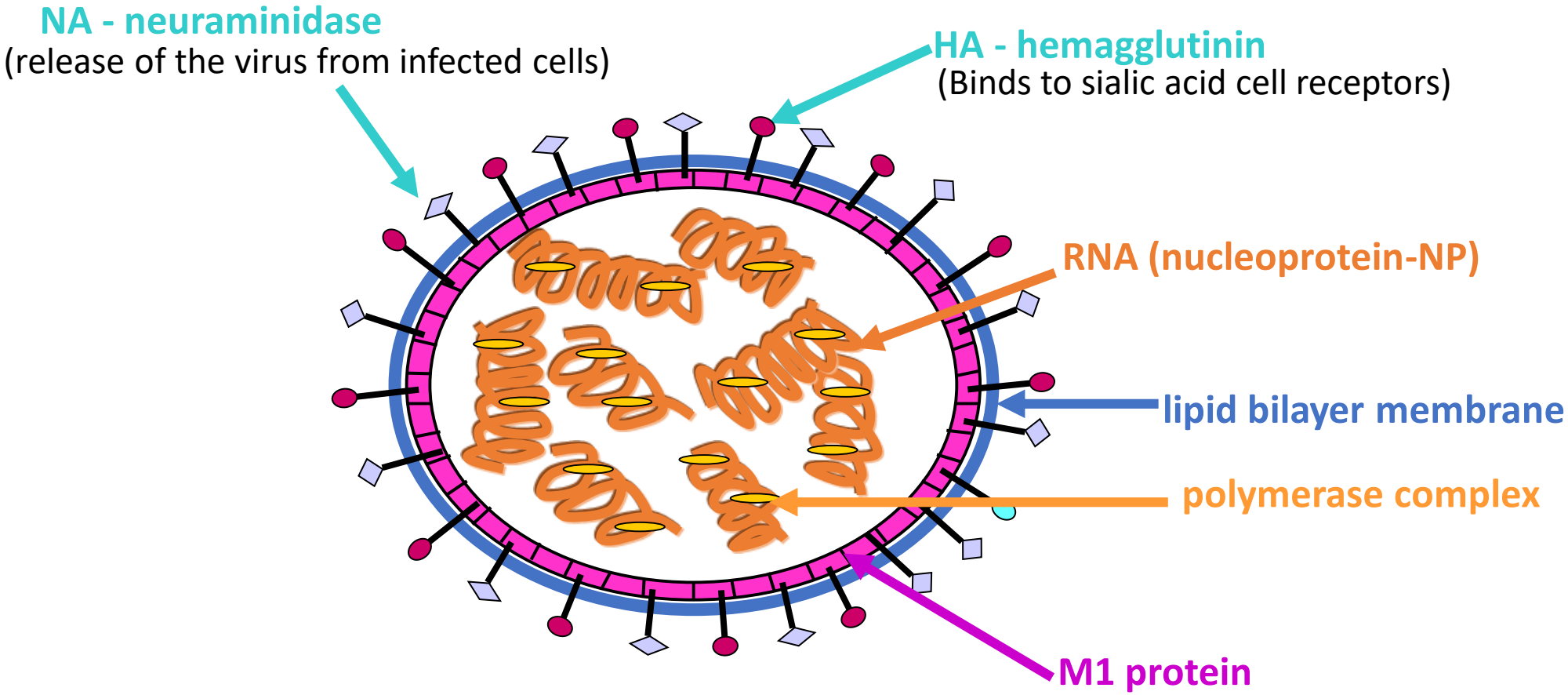
1. Influenza A
2. Influenza B
3. Influenza C

Structure:

1. RNA enveloped viruses, ~ 80-120 nm in diameter.
2. Has RNA dependent RNA polymerase (important for infectivity/has transcription errors ~ 1: 10kb of the genome).
3. RNA:

Single stranded, negative sense, approximately 8 segments (types A and B), 7 segments in type C.

Orthomyxoviruses



type A, B, C : NP, M1 protein

sub-types: HA or NA protein

Nomenclature

- Influenza A has 16 distinct H subtypes and 9 distinct N subtypes, of which only H1, H2, H3, N1, and N2 have been associated with epidemics of disease in humans.
- Influenza B and C viruses have also H and N antigens but they do not receive subtype designations, since intratypic variations are less extensive than those in influenza A viruses.

Orthomyxoviruses / Antigenicity

There are two types of antigens in influenza viruses:

1. Group specific antigens:

A. Determined by Ribonucleoproteins.

B. Distinguish types A, B and C.

2. Type specific antigens:

A. The HA and NA.

B. For serotyping.

- HA antibodies are neutralising (protect) while NA antibodies are not.

Orthomyxoviruses

3. Haemagglutinin (16 subtypes):
   - H or HA.
   - allows the virus to adhere to endothelial cells in the respiratory tract (binding to sialic acid-containing receptors).
   - main determinant of immunity (stimulates the production of neutralizing antibodies).
   - Agglutinates certain species of erythrocytes.

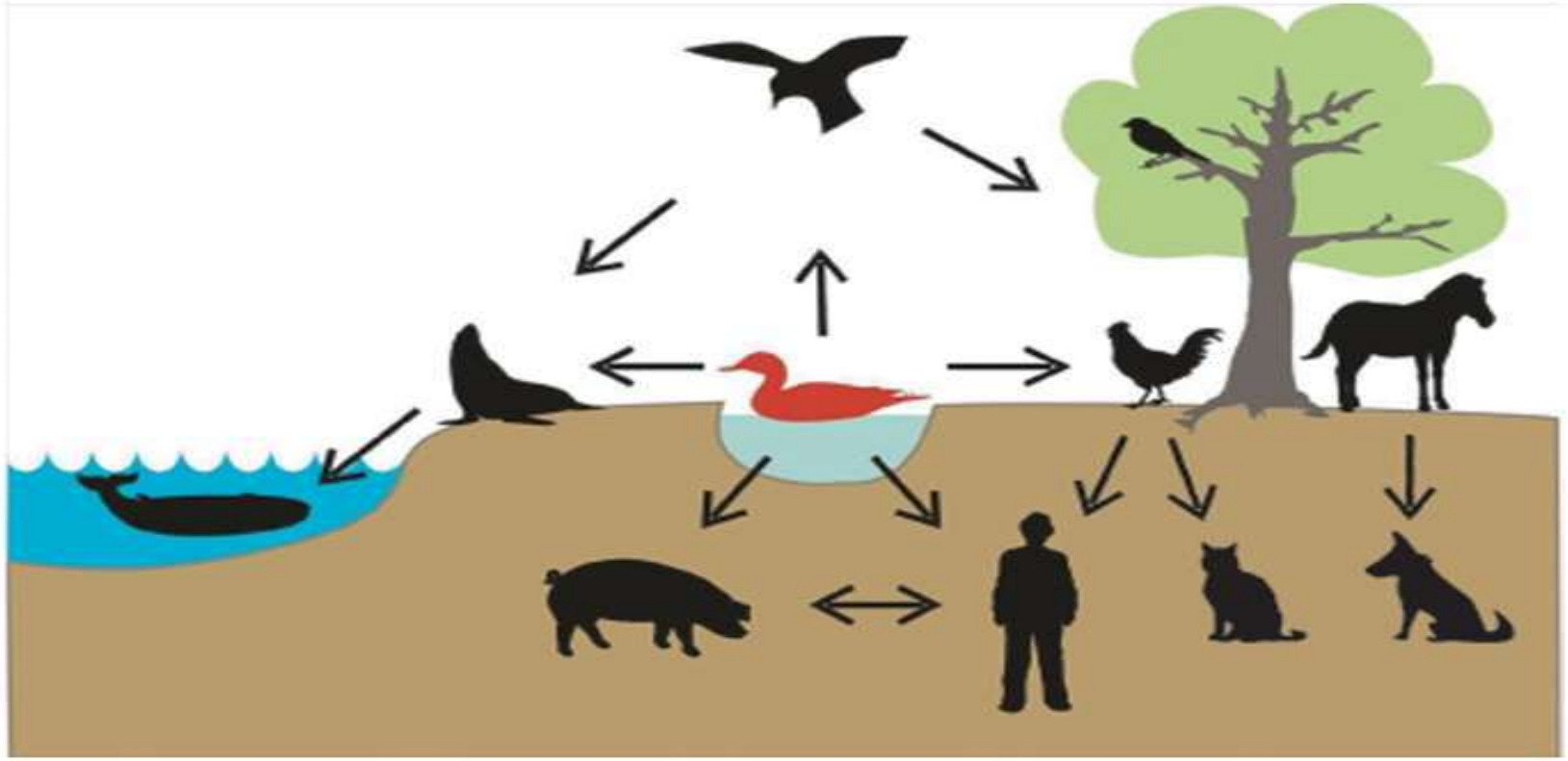
4. Neuraminidase (9 serotypes):
   - N or NA.
   - allows the release of newly formed viruses within the host.
   - determinant of disease severity.
   - ➢ E.g. H1N1, H3N2, H5N1….

5. M proteins (1 & 2): between the capsid and the envelope (only in type A):

   Act as an ion channel to mainly change the endosomal pH.

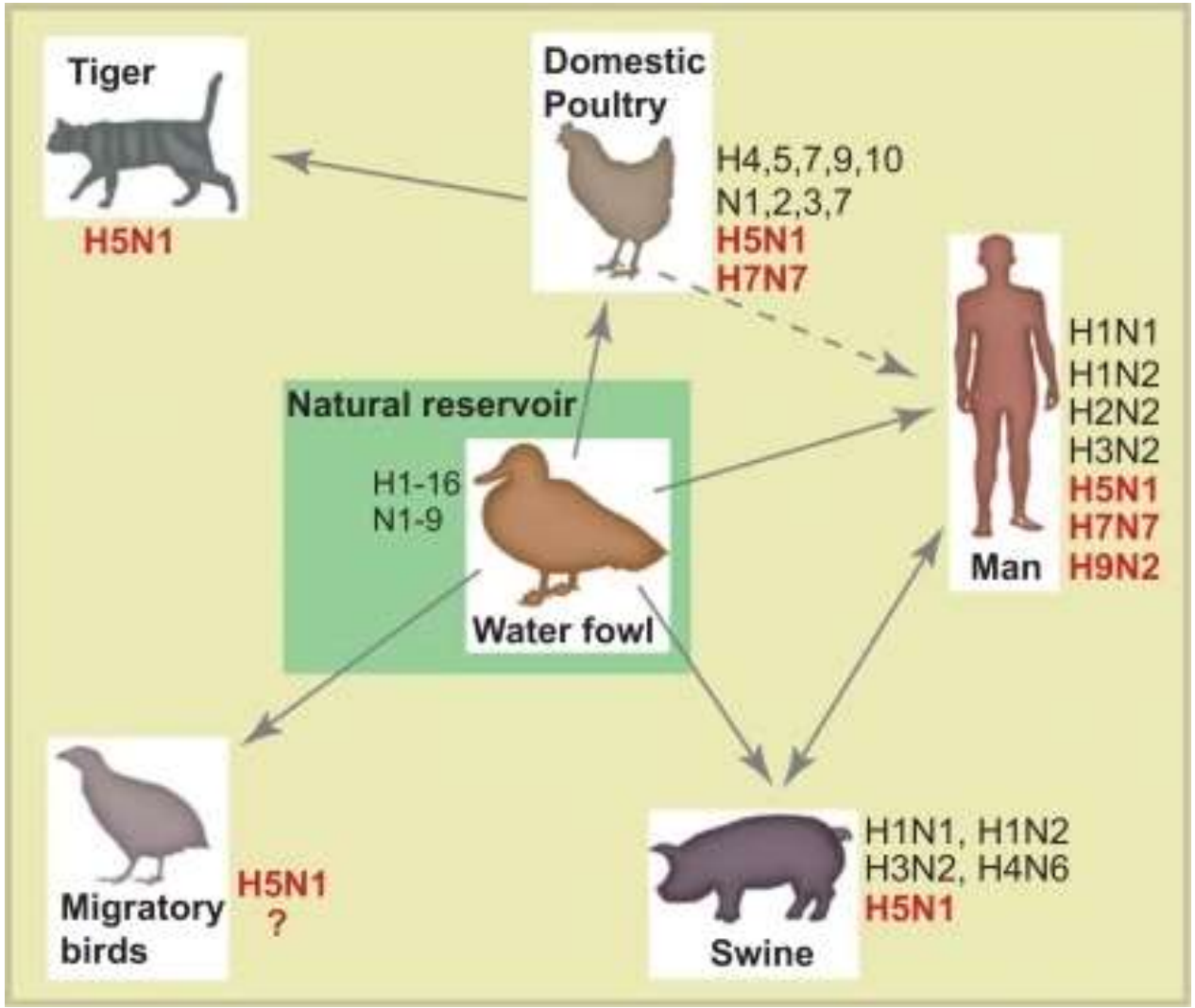
6. Ribonucleoproteins.

Influenza A reservoir



Wild aquatic birds are the main reservoir of influenza A viruses. Virus transmission has been reported from wild waterfowl to poultry, sea mammals, pigs, horses, and humans. Viruses are also transmitted between pigs and humans, and from poultry to humans. Equine influenza viruses have recently been transmitted to dogs.

influenza A subtypes



Burden of influenza virus

- Acute febrile illness with variable degrees of systemic symptoms, ranging from mild fatigue to respiratory failure and death.

- WHO estimated that 3-5 million cases of severe illness and about 250,000 to 500,000 deaths occur annually.

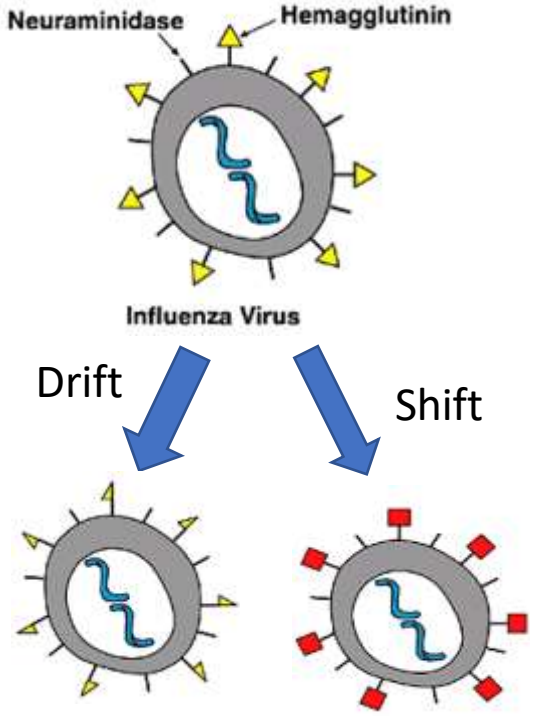
Antigenic changes (common in type A)

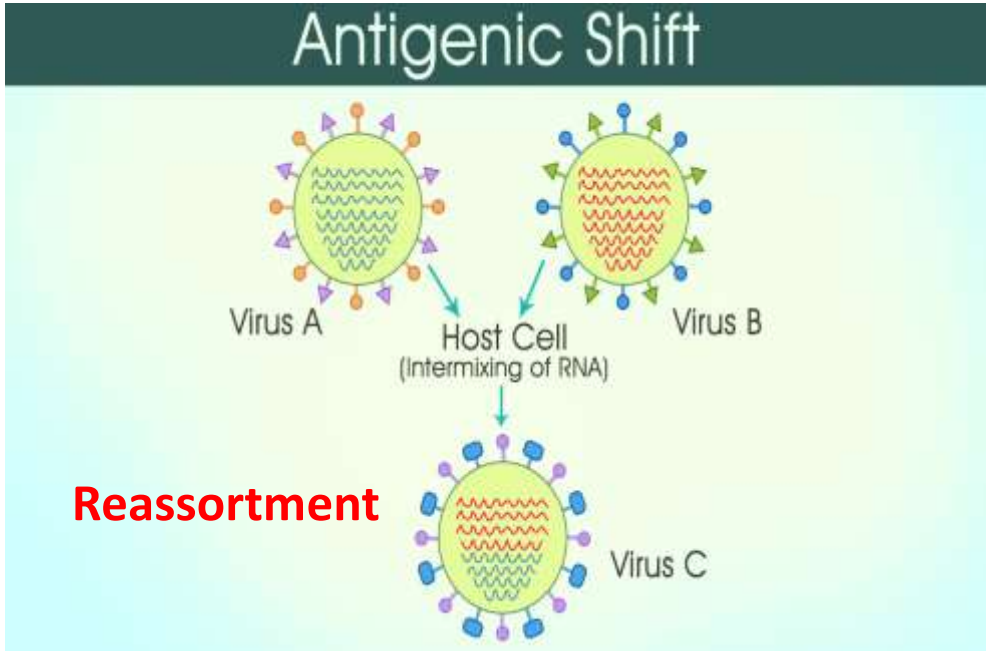
1. Antigenic ***shift*** (type A) > pandemics:

- ***Re-assortment/swapping*** in the genomic RNA i.e a major change that may lead to the appearance of new HA and NA.
- pre-existing antibodies *do not* protect.
- Occurs when more than one variety of Influenza virus infect the same cell.

2. Antigenic ***drift*** (all types) > outbreaks/epidemics:

- HA and NA accumulate ***mutations***.
- immune response *no longer FULLY protects.*





Orthomyxoviruses

Physical & biological characteristics:

1. Can survive in cold sea water for several weeks.
2. Can stay in dust for more than 2 weeks/~1 week on human body.
3. Inactivated by:

A. 30 minutes heat at 56°C.

B. 20% Ether, Phenol, 70% Ethanol, Formaldehyde, soaps and many others.

4. Type A has many hosts, B infects human, C infects human and pigs.

Nomenclature / WHO

1. If isolated from human:

- Type > place where strain isolated> strain number> year of first isolation > subtype:
- For example: **A / Beijing / 32 / 92 (H3N2)**

2. If not isolated from a human, we mention the source:

e.g: A/swine/Iowa/3/70 (H1N1)

Orthomyxoviruses / pathogenesis

- Usually no viremia.
- Multifactorial:

1. Host factors e.g. immunity, congenital abnormalities
2. Viral factors:

- Infectious dose/droplet size
- Viral-respiratory cells tropism.

3. environmental:

crowdedness, season...

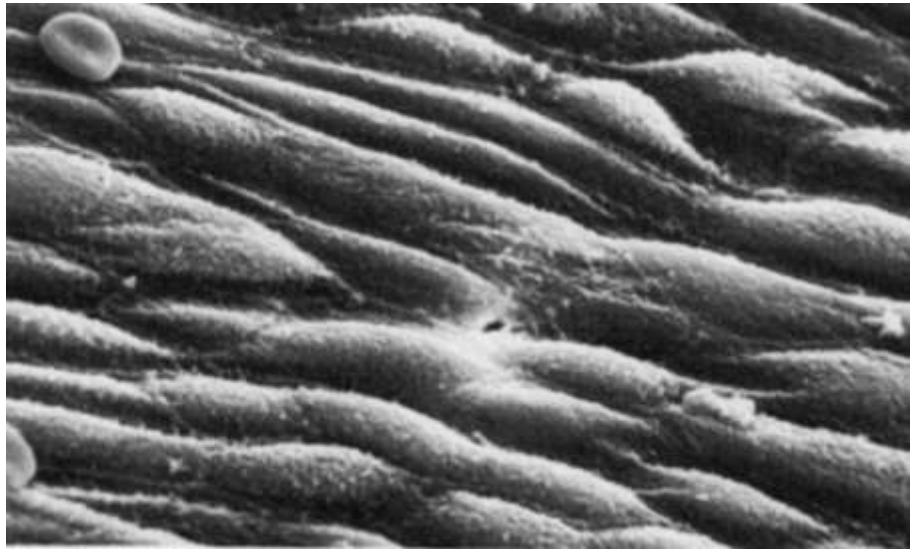
Mechanism:

1. Structural and functional damage of resp. cells > desquamation > affects resp. clearance mechanism and stimulates an inflammatory response.
2. Direct tissue toxicity.
3. increased susceptibility to bacterial infections (superinfection).

Orthomyxoviruses / clinically

- Mode of transmission: Respiratory droplets/airborne (Aerosol generating procedures) - More in winter, crowded areas.
- Incubation period: 1-4 days.
- Symptoms may last 3-7 days on average.

NORMAL TRACHEAL MUCOSA



3 DAYS POST-INFECTION

Clinically / cont'd

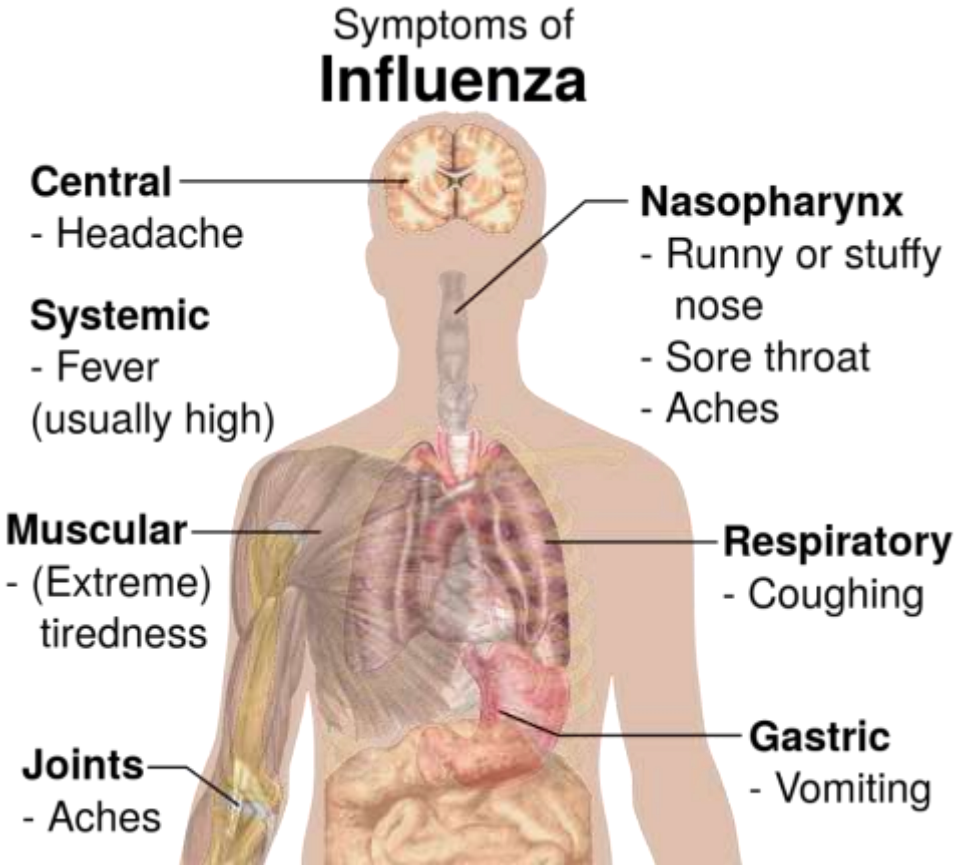
1. Main symptoms (mainly type A):

Sudden onset:

- Fever, Chills (1-5 Days) (Febrile Convulsions In Children).
- Headache, Myalgia, Cough, Anorexia.
- Rhinitis, ocular symptoms.
- type B is somewhat milder, type C is usually afebrile.

Severity more in;

1. Extreme ages and immunocompromised.
2. Chronic lung and heart diseases.



The Stages of the Flu

Days 1–3

Incubation

- The virus enters your body and multiplies.
- You feel fine.

Days 4–5

First Symptoms

- You develop a sore throat and fever.
- You are contagious.

Days 6–10

Severe Symptoms

- You have a headache, fever, and sore muscles.
- You are sneezing and coughing.
- You are contagious.

Days 11–15

Recovery

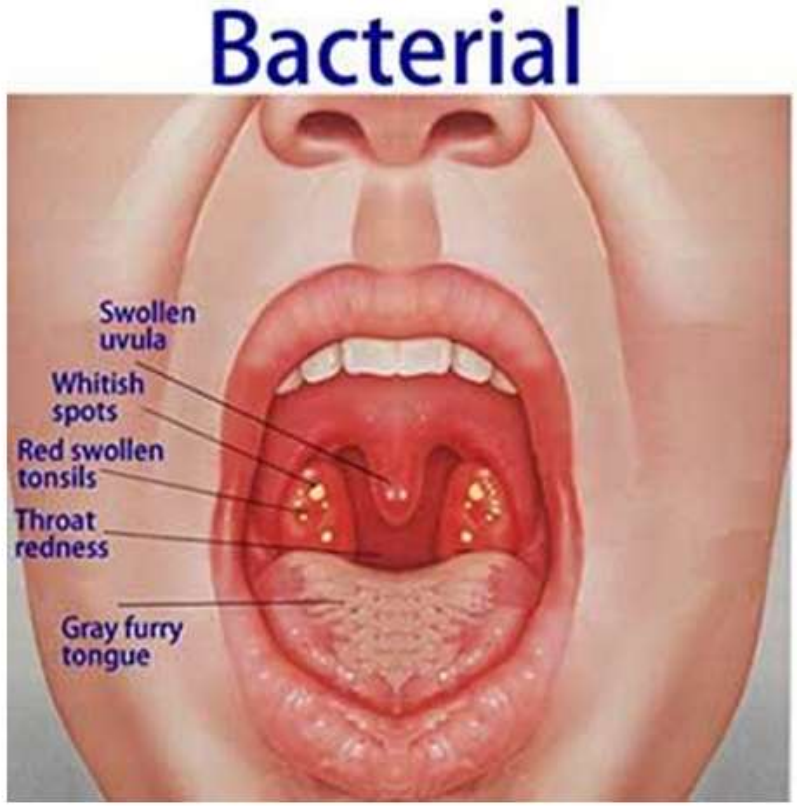
- You feel a little better and your fever is down.
- Your immune system is winning.
- You may still be contagious.

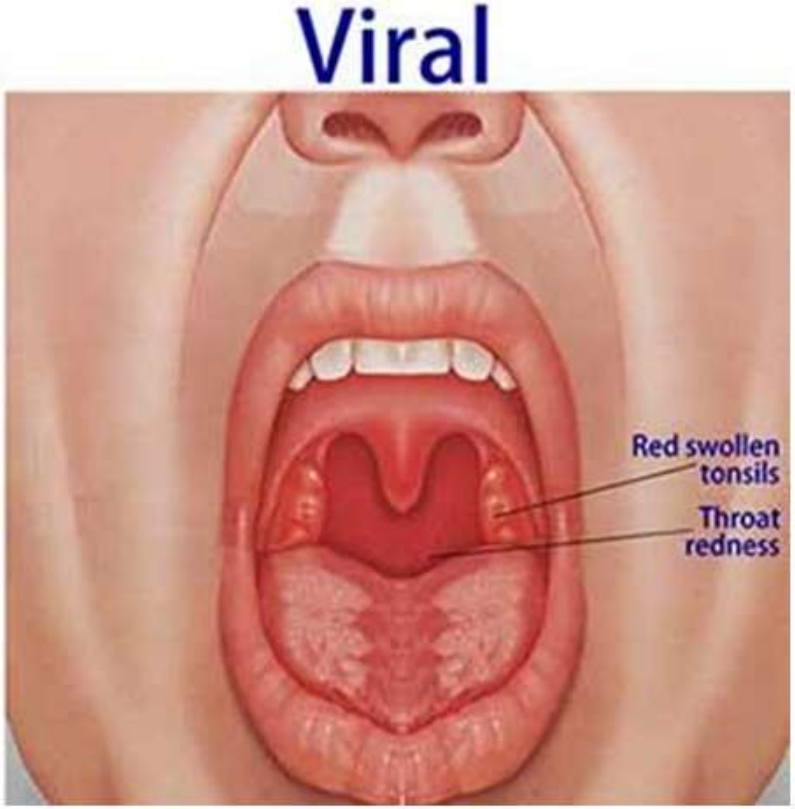
Days 16–18

End of Infection

- Your aches and pains have disappeared.
- Your temperature is normal.
- You still do not feel as energetic as usual. You must continue to take care of yourself.

Bacterial vs. Viral Pharyngitis





Sore throat

- Painful swallowing is common to both bacterial and viral sore throats, but bacterial sore throats often come with red and swollen tonsils at the back of the throat.
- Cough with a viral sore throat.
- You may very well also see white patches or streaks of pus there.
- Fever is also common to both, but the fever associated with bacteria tends to be higher and more severe than with a viral infection.

Cold or Flu

COLD SYMPTOMS


loss of appelite


sneezing


cough


runny nose


lacrimation


sore throat

COLD or FLU?

FLU SYMPTOMS


heat


weakness


headache


drowsiness


increased sweating


muscle pain

Clinically / cont'd

2. pulmonary complications:

- CROUP (YOUNG CHILDREN)
- PRIMARY INFLUENZA VIRUS PNEUMONIA
- SECONDARY BACTERIAL INFECTION
  - *Streptococcus pneumoniae*
  - *Staphlyococcus aureus*
  - *Hemophilus influenzae*

3. Non-pulmonary complications:

- Cardiac: myositis (rare, > in children, > with type B).
- liver and CNS.
  - Reye's syndrome

1. (encephalopathy+liver degeneration).
2. Precipitated by Aspirin.
3. Reye's also caused by parainfluenza and chickenpox.

Pandemics

- 1918 Spanish Flu H1N1: 20-40million deaths
- 1957 Asian Flu H2N2: 1-4 million deaths
- 1968 H3N2 Hong Kong Flu 1-4 million deaths
- 1977 H1N1 again
- In 2009, H1N1 (Swine) thousands of deaths

(The 2009 H1N1 virus was a hybrid of swine, avian and human strains, Influenza A (H1N1)

Orthomyxoviruses / diagnosis

1. Culturing the virus (in cells or eggs) from nasopharyngeal samples: takes long time (~ 7 days)
2. serology to detect at least a 4 fold increase in antibody titer
   A. Needs 2 serum samples (paired) during the acute illness and 10-14 days later.
   B. Good for epidemiology.
3. Immunofluorescent detection of viral antigens in respiratory samples, fast.
4. PCR to detect viral RNA: very sensitive but not widely available.

Treatment and prevention

1. Symptomatic:

Fluids, analgesia BUT no ASPIRIN in children (<18).

2. Drugs (should be given early):

A. Amantadine and rimantadine:

- For type A
- High resistance – not used anymore
- Mechanism of Action: inhibit viral uncoating (M2 protein)

Treatment / cont'd

B. Neuroaminidase inhibitors

Zanamavir (Relenza/inhalation) and Oseltamivir (Tamiflu/orally), Permivir (Rapivab I.V).

. Treatment of type A and B.

. Mode of action: neuroaminidase inhibitors > inhibit viral release.

C. Cap-dependent endonuclease inhibitor

- Baloxavir marboxil
- Active against both influenza A and B viruses
- Acts by interfering with viral RNA transcription and blocks virus replication

Orthomyxoviruses / general prevention measures

1. Hand washing with soap, Alcohol-based hand wipes, or gel sanitizers are also effective.
2. Cover your nose and mouth with a tissue when you cough or sneeze. Throw the tissue in the trash after you use it.
3. Avoid touching your eyes, nose, or mouth.
4. Avoid contact with sick people.
5. Masks, social distancing

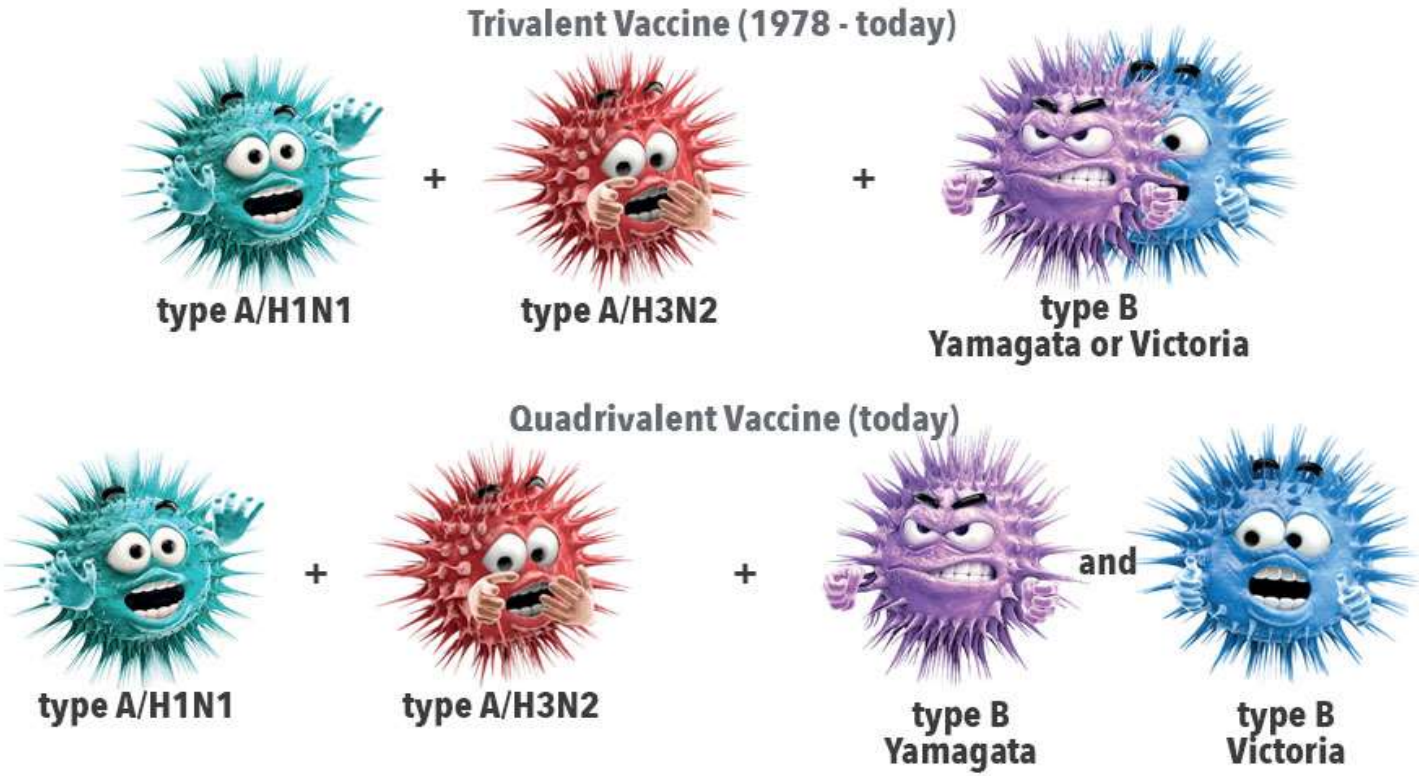
Prevention / vaccine

- The aim is to produce HA antibody in the vaccines 2 weeks post vaccine.
- Should have the most 2 recent influenza A and 1-2 influenza B strains (determined by the WHO).
- Major vaccine types:

1. Inactivated (formaldehyde), egg grown – I.M
2. Life attenuated - Nasally

2. sub-unit vaccine for children.

- CURRENTLY
- type A - H1N1, type A - H3N2 and 1-2 types of B



Vaccine

In general, avoid in:

- Severe egg allergy or previous vaccine allergy
- Acute fever
- In pregnant and people with immunosuppressant conditions; avoid life-attenuated