Influenza

general consideration

* acute viral respiratory illnesses
* one of the most important emerging and reemerging infectious diseases
* affect mainly upper and\or lower respiratory tract
* result in outbreaks occur nearly every year

affinity to mucin (mucous secreting cells + glands)

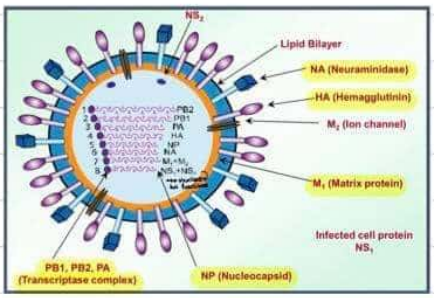
myxoviruses

- orthomyxoviruses
  - octo = 8 segments of RNA
  - Smaller
  - Segmented RNA genome
  - liable to Agic vairation
  - Influenza viruses
- Paramyxoviruses
  - larger
  - single piece of RNA
  - not liable to Agic vairation
  - Parainfluenza, Mumps virus, Measles virus, respiratory Syncytial virus

Characteristics of influenza virus

→ Spherical, single-stranded RNA, segmented genome [8 segments in A and B, 7 segments in C (neur amidase segment is absent)]

→ on surface ⇝ glycoprotiens\spikes hemaglutinin (HA), neuraminidase (NA)



Antigenic Structure & Classification

★ type specific Ag (core Ag)

classified into types A, B, C, D → doesn't infect humans

depending on nucleocapsid (ribonucleoprotien) + matrix protien

no cross between types

type A

wide host range

- most common, most severe, infects human as well as animals → antigenic shifts + drifts
- pigs & birds are the reservoirs playing a role in occurence of influenza epidemics
- results in epidemics, outbreaks, pandemics

type B

- milder disease, infects human only → antigenic drifts, [not known to undergo antigenic shift]
- results in epidemics and minor outbreaks

type C

- antigenically stable, minor respiratory disease
- not involved in epidemics (sporadic)
- antigenic drifts

★ Strain (subtype) specific Ag

depending on two surface glycoprotiens

18 ← HA & NA → 11

example:- H1N1, H5N1, H3N2

Neuraminidase (N)

cleaves neuraminic acid

Spreading of infection

Haemagglutinin (H)

binds to host cell surface receptor (epithelial cells, mucous secreting cells)

diffusion, initiation of infection

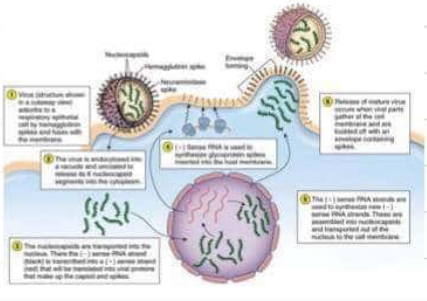
Severity

A > B > C

antigenic stability

A < B < C

Influenza virus replication Cycle



+Sialic acid receptor

receptor mediated endocytosis

↳ endosome → RNA segments → nucleus (replication)

ER (HA, NA)

through PM (final assembly)

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→ the target of neutralizing Abs\ hemagglutinates RBCs

Hemagglutinin

Structure	Function
trimer of identical dimers (HA1, HA2) of "lolipops"	Sialic acid receptor sites bind to host cell's glycoproteins allowing for infection to occur

→ plays a minimal role in immunity to influenza

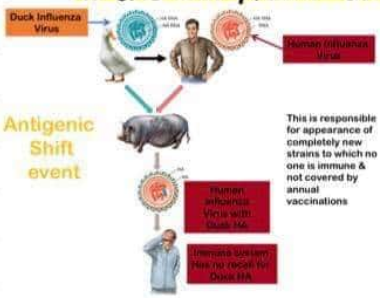
Neuraminidase

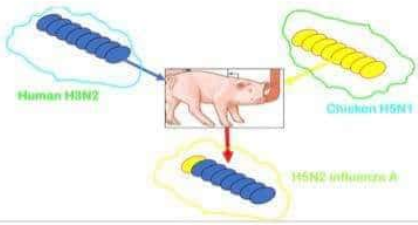
Structure	Function
tetramer of identical monomers	cleaves off sialic acid ⇝ Spreading of infection cleaves off neuraminic acid (present in mucin) ⇝ ↓ viscosity, ↑ spreading

Antigenic variation

1- antigenic shift

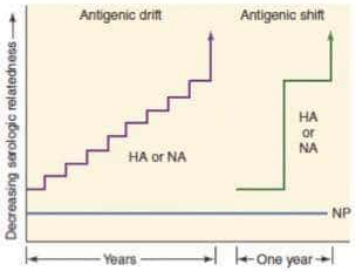
type A ⇒ wide host range (humans, animals)
genetic reassortment (segments)
major change, new subtype, pandemic
no one can predict antigenic shifts





2- antigenic drift

minor changes, same subtype, point mutations, amino acid substiution, over time result in new subtype
may result in epidemic, flu vaccines are produced against them



Classification and nomeclature

- type, host of origin, geographic origin, strain number and year of isolation. Subtype (HA, NA)
- the host of origin is not indicated for human isolates

Pathogenesis

→ destruction of infected cells
→ no viremia
→ Sudden onset
→ Systemic symptoms [cytokines productio

common cold ⇝ gradual, no systemic symptoms

Mode of transmission

highly contagious diseases
1- contact (direct, indirect)
2- air-borne
3- droplet
short incubation peroid 1-3 days

→ peak first 48 hours after symptoms appear (1 day before symptoms → 7 days after symptoms)

Clinical findings

- high fever, myalgia, arthrlgia
- non-productive cough
- shortness of breath, runny nose

Pulmonary complications

primary influenza pneumonia (persist + increase)

Secondary bacterial pneumonia (most commonly Staph aureus, resolve)

Mixed viral and bacterial pneumonia

encephalopathy (Reye Syndrome)

groups at ↑ risk for influenza complication

children < 2 years
adults ⩾ 65 years
pregnant women

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labrotary diagnosis

* isolation of virus [culture] 3-10 days egg-based culture → monkey kidney cells
PCR rapid (< 1 day), sensitive, specific
Serology 4 folds increase in antibodies, needs time

treatment and prevention

- whole virus vaccine
- Subunit vaccine (HA and NA subunits)
  Split-virus vaccine

- Inactivated subunit (TIV)
  IM ; ~~trivalent~~ \ quadrivalent
- live attenuated vaccine (LAIV)
  intranasal, ~~trivalent~~ \ quadrivalent
  contraindecated in pregnant women, egg protien allergy

→ given to high risk groups (pregnant women, health care workers, children 6 months → 5 years)

treatment:
① M inhibitors (amantidine): aren't used, resistance
② NA inhibitors (~mivir): oseltamivir (tamiflu), zanamivir

Avian influenza (AI)

Wild → Silent domestic (ducks, chicken) → Clinical disease
highly pathogenic, low pathogenic both can infect humans (contact)
brid to bird (through feces)
H5N1, H7N9
↳ lower respiratory tract
more severe and fatal
ineffective transmission cycle between humans

Swine influenza

H1N1
↳ rarely fatal
effecient transmission cycle between humans

Pandemic

1- new subtype (antigenic shif)
2- effecient human-to-human transmission
3- produces severe disease in humans

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