Orthomyxoviridae ortho = real

Consist of three genera according to

NP
Matrix protein

Influenza type "A"

Influenza type "B"

Influenza type "C"

Infect

Human only

Responsible for occasional epidemic influenza

Because

It may exhibit minor antigenic changes

Minor causes of influenza in human and swine

Antigenic stable

So

Only cause subclinical or minor illness

1 page
Periodic pandemic of influenza disease

Which means a disease that affects a wide world population

Because is highly variable "A"Influenza type in antigenicity

Lead to appearance

(or new subtype (New strains)

Most cases of epidemic influenza disease

And also responsible for

Which means a disease that affects significant no population but generally less than the pandemic disease
Structure of influenza virus

1. Shape and size
   - Spherical
   - Filamentous
   - Spherical when first isolated from human

2. Enveloped virus
   - Also has two surface glycoprotein projected as a spike from the lipid bilayer of the virus
   - Surrounding by bilayer or two layer of lipid derived from the host cell by budding during release of the virus
   - Matrix layer

(HA (Hemagglutinin)

- 500 projecting spike
  - HA %80
  - NA %20

- It’s trimer molecules or triangular in cross section
- It’s most important antigen against which neutralizing antibodies are directed
- So these antibodies will stop infection by stopping attachment of the virus

Neuraminidase (NA) glycoprotein or sialadase

- Derived its name from its ability to agglutinate with erythrocyte under certain condition
- Every monomer of HA consist of

Page 4
Neuraminidase (NA) glycoprotein or (sialadase)

Its mushroom-like composed of 4 identical monomer (tetramer) is

Tender stalk in base

function

This enzyme produces its function at the end of life cycle of remove silica acid from glycoconjugate on cell receptor

So

With pox shape in head

There is a catalytic site on the top of each head

So

Each NA has 4 active site

So

It facilitate release of v. particles from infected cell during budding process

So

Ab against NA

Prevent spread of the virus from one cell to another

Lead to reduce severity of infection
Every monomer of HA consist of

HA 1

(out) HA1

HA 2

Incorporate with the lipid bilayer of the virus

CooH Terminal of HA1

N Terminal of HA 2

NH 3

HA 1

S – S

HA 2

CooH (carboxy) terminal end (hydro phobic)

HA = 566 amino acid

HA 2 = responsible for fusion of viral envelope to the cell membrane

Pinocytosis
Structure of influenza virus

1. Matrix layer
   - Located underneath the lipid bilayer and give rigidity to the lipid bilayer and connected it to nucleic acid.

2. Core
   - Segmented (8 segments)
   - Single negative strand RNA (SS⁻ RNA)
   - Each segment carry code for a single protein.

3. Proteins
   - Influenza virus particle contains different proteins (8 segments = 8 proteins)

4. Influenza type
   - A, B = 8 segments
   - Lack neuraminidase so minor cause of influenza because not spread from one cell to another and also influenza "C" Agic stable.

5. Influenza type "C" 7 segment
   - Agic stable
Influenza virus particle contain different proteins
(8 segment = 8 protein)

Neucloprotein (NP) associated with viral RNA to Form aribonucleoprotein RNP

Polymerase

three Large protein

PB1

PB2

PA

Associated to viral RNA and responsible For RNA transcription and replication

M1 M2 represent of matrix protein

NS1

NS2

Non structural protein

unknown Function

Each segment

P2

P1

NP

RNA

P3

Lon channel

Haemagghitin

Lipid envelope

Illustration of an influenza virus

RNP

Capsid

Neuraminidas e (Sialidase)

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Clinical manifestation of influenza virus incubation period 1-4 day depending on Does of inoculum Immune state of patient

(1) uncomplicated infection

In adult

Fever

headache

Chills

dry cough which may be persist For 1-3 day

followed by

generalized muscle itches

high Fever Last For 3 day

Respiratory symptom Last for 3-4day

In children

High in children of gastrointestinal manifestation such as

Febrile convulsion

Vomiting

High Fever

Disease is self limited

Reye's syndrome

Fatty degeneration of the liver is associated with this syndrome

Immune state of patient

complicated pneumonia

Reye's syndrome

Fever

Chills

Headache

Dry cough which may be persist for 1-3 day

High fever lasts for 3 day

Generalized muscle itches

Respiratory symptom lasts for 3-4 day

High fever

Vomiting

Disease is self limited

Reye's syndrome

Immune state of patient

complicated pneumonia

Causes unknown but

High mortality rate 10-40%

Disease is self limited

Causes unknown but

High mortality rate 10-40%

there is a possible relationship between salicylate use and subsequent development of Reye's syndrome

Causes unknown but

High mortality rate 10-40%

so

its advisable that children with Flu like syndrome not be given aspirin containing compound For Fever.
Complicated pneumonia

- Combination viral bacterial pneumonia is approximately three times common than primary influenza pneumonia
- Staph aureus are most common causes (42%)
- Some strains of staph secret protease which able to cleave HA of influenza
- Lead to production of much higher titers of infection in Lung
- So such viral activation Lead to extensive spread of viral infection

- Usually occur in:
  - Elderly patients
  - Chronic pulmonary disease patient
  - Patient with chronic disease
  - Pregnant women

- Death occur due to:
  - Cardiovascular disease
  - Pneumonia disease patient
  - Renal disease
  - Chronic pulmonary disease patient
  - Elderly patients
  - Chronic pulmonary disease patient
  - Patient with chronic disease
  - Pregnant women
Some of mechanisms Responsible for genetic variability of human influenza (A) viruses

- **Antigenic shift**
  - Major Agic changes in Haemagglutinin (H A) or Neuraminidase (NA) or both of them
  - Lead to appearance of different subtype (new strain)
  - Lead to Immune system with not longer able to recognize of these strain or Ags
  - Lead to Periodic pandemic influenza disease
  - Appear Every 10 ….. 40 years

- **Antigenic drift**
  - Minor changes in Agic determinant only of HA or NA or both resulting from point mutation in these genes coding for surface glycoprotein
  - Lead to Changes in few or single a.a of HA or NA glycoprotein
  - Variation within subtype it self
  - Epidemic infl. Disease
  - Appear every 2 ….. 3 year

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Reassortment of the surface glycoprotein gene between Human and animal strain of influenza viruses

Reassortment of the surface glycoprotein gene between Human and animal strain of influenza viruses

Lung cells of Human

Infl. A (H₁N₁) Agic shift

That mean for example (H₁N₁) disappear for long time and reappear again

1890 H₂N₈
1900 H₃N₈
1918 H₁N₁ Spanish flu.
1957 H₂N₂ Asian flu.
1968 H₃N₂ Hogkong flu.
1977 H₁N₁ Russian flu.
1997 H₅N₁ Avian flu.

Re emergence or recycle of influenza A virus strain

Different pandemic influenza due to Agic shift
Mutation: Recent data associated with origin of the Lethal 1918 influenza A (H1N1) pandemic infection which killed between 20-40 million peoples suggested that appearance of these strains (H1N1) not from reassortment but from mutation of the genes of what was originally a purely swine virus because swine strains of influenza A(H1N1) without these mutation less pathogenic to human.

That mean

A wholly species – specific virus from swine can infect another species (e.g. human) directly without undergoing genetic Reassortment as described previously.

Influenza virus can passed from one species (bird) through intermediacy host (pigs) to a third species (e.g. human)

Also
**Nomenclature**

- **Type**: A, B
- **Area of First Isolated**: duch, horses, avian
- **Host of Origin**: avian
- **No. of Isolates**: Like 1988
- **Year of Isolation**: 1988
- **Antigenic Description**: HA and NA

*Example*: Influenza type A / avian / Hong kong / 1 / 1988 / H3 N2

**Immunity**

- Long Live immunity and subspecies specific
- **Humoral Immunity**: Abs against HA and NA are important immunity to influenza virus
- **CMI**: Also play very important roles

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The Following strain are isolated

From human
H1, H2, H3, H5 (HA) only
From human and Animals
H1, H2, H - - - - - - - - - - H16

From human
N1 Only
From human and animals
N1, N2, N - - - - - - - - - - - - N9

**Lab dx**

**Specimen**

- Throat swab
- Mouth washing
- Nasopharyngeal aspirate

**Cell culture**

- Inoculate 10 – 11 day in old egg
  - Incubated For 3 day at 33c
  - harvest amniotic or allantoic Fluid
  - identification
  - Haemagglutination with chicken RBCS

**Identification by Hemagglutination inhibition test (HAI)**

- Inoculate primary monkey Kidney
  - Incubate For 7-10 day at 33c
  - Cyto pathological effect (CPE)
  - Haemadsorption with quinea pig RBcs

**Serology**

- CFT
  - is type specific test
  - to know whether is type A, B, C

- HAI
  - is strain specific test
  - to know whether is A, H1, or H2
Prevention by using influenza vaccine to most liable group child and immune suppressed persons

- Inactivated vaccine (killed)
  - Subunit vaccine
    - Whole virus vaccine
      - surface glycoprotein from prevalent strain (virulent)
      - not cause disease but produce immunity
    - Recombination hybrid mean having
      - and core for other strain
  - Recombinant vaccinia virus vaccine

- Live attenuated vaccine
  - Temperature sensitive mutant multiply with Low temperature e.g. 32°C
    - so grow in upper Rasp-tract
    - while in Lung 37°C can not grow
      - so
      - not cause of pneumonia
  - cold adapted mutant
  - New approach to vaccine designs
  - Gene cloning
    - Recombinant vaccinia virus vaccine
    - E-coli
  - Synthetic peptide
Chemotherapy

Amantidin or Rimantidin

Inhibit uncoating process only against A strain while the second For Both A and B

Attach to ion channel M-protein

in 1999

Neuraminidase inhibitor effecting against A+B influenza viruses e.g.

Zanamivare (Relenza) R
Oseltamivare (tamiflu) R