# Inf – ER Combined Meeting

Reporter R2蘇錡鋒
Supervisor VS洪世文
2011/01/22

# Discussion

1.Influenza
2.Complications of influenza

## Influenza

- Influenza viruses are members of Orthomyxoviridae family of viruses, and are negative strand RNA viruses.
- Influenza viruses can be classified as A, B, or C.
  - Influenza C 主要感染六歲以下兒童，成人大都具有protective antibody

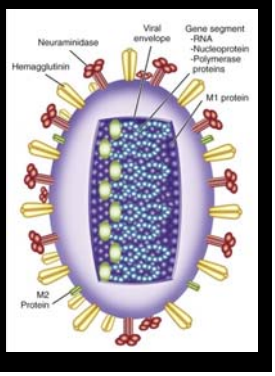
TABLE 165-1 – Differences among Influenza A, B, and C Viruses

| | Influenza A | Influenza B | Influenza C |
|---|---|---|---|
| Genetics | 8 gene segments | 8 gene segments | 7 gene segments |
| Structure | 10 viral proteins | 11 viral proteins | 9 viral proteins |
| | M2 unique | NB unique | HEF unique |
| Host range | Humans, swine, equine, avian, marine mammals* | Humans only | Humans and swine |
| Epidemiology | Antigenic shift and drift | Antigenic drift only; two main lineages cocirculate | Antigenic drift only; multiple variants |
| Clinical features | May cause large pandemics with significant mortality in young persons | Severe disease generally confined to older adults or persons at high risk; pandemics not seen | Mild disease without seasonality |

HEF, hemagglutination, esterase, and fusion activity; NB, membrane protein.

## Classification of Influenza A

- 根據以下二種surface protein分類：
  - Hemagglutinin (H1 ~ 16)
  - Neuraminidase (N1 ~ 9)
- 曾經大流行：H1N1, H2N2, H3N2
  - H1N1 and H3N2 are currently circulating as seasonal influenza




## Genes and protein products of influenza A virus

| RNA Segment Number | Gene Product Description | Name of Protein | Proposed Functions |
|---|---|---|---|
| 1 | PB1<br>PB1-F2 | Basic polymerase 1 | RNA transcriptase<br>Proapoptotic |
| 2 | PB2 | Basic polymerase 2 | Cap binding, endonucleolytic cleavage |
| 3 | PA | Acidic polymerase | Unknown |
| 4 | HA | Hemagglutinin | Viral attachment to cell membranes; membrane fusion |
| 5 | NA | Neuraminidase | Cleaves sialic acid from cell surface; released from membranes; prevents aggregation |
| 6 | NP | Nucleoprotein | Encapsidates RNA; regulation of transcription/replication |
| 7 | M | Matrix | Surrounds viral core; controls nuclear export of RNA |
| | M2 | Matrix 2 | Ion channel; necessary for uncoating |
| 8 | NS1 | Nonstructural | Antagonizes type I interferons; may be involved in regulation of mRNA transport from nucleus |
| | NEP (NS2) | Nuclear export protein | Transport of newly assembled RNP from nucleus to cytoplasm |

zanamivir and oseltamivir → sialic scid analogs

## Transmission

- Influenza is thought primarily transmitted from person to person by large droplets (> 5 um) that are generated when infected persons cough or sneeze.
- Contact transmission

## Clinical features

- incubation period for influenza:1–2 days
- The triad of fever, respiratory symptoms and constitutional symptoms had a sensitivity of 60%
  - respiratory symptoms: cough, sore throat, or nasal symptoms
  - constitutional symptoms: headache, mailase, myalgia, sweats/chills or fatigue

## Diagnosis

| | Time to Result | Advantages | Disadvantages |
|---|---|---|---|
| Rapid antigen<br>Sensitivitiy 50 ~70%<br>Specific 95 ~ 100% | <30 mins | Fast, not technically difficult, point of care testing | Marginal sensitivity especially in adults, does not distinguish subtypes of influenza |
| Immunofluorescence | 1–4 hrs | Fast and versatile | Not widely available, requires technical expertise |
| Nucleic acid testing | 4–24 hrs | Very sensitive, subtypes virus, detects other respiratory pathogens | Requires technical expertise |
| Culture<br>Gold standard | 24 hrs–5 days | Very sensitive, detects other respiratory viruses | Slow results |
| Antibody testing | Several weeks | Highly specific and sensitive | Labor intensive, slow results |

## Complications of influenza

- Pulmonary complication
  - Primary viral pneumonia
  - Secondary bacterial pneumonia
  - Mixed viral and bacterial penumonia
  - Localized viral pneumonia
  - Other pulmonary complication: croup, exacerbation of chronic pulmonary disease
- Extrapulmonary complication
  - Myositis and rhabdomyolysis
  - Cardiac complication: myocarditis
  - CNS complication: encephalitis
  - Reye's syndrome

## 回到1918年…

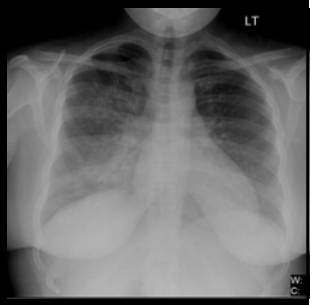
**Two clinical syndromes**

- Acute bronchopneumonia, characterized by necrosis, hemorrhage, edema, and vasculitis, associated with heavy growth of bacteria on sputum samples and autopsied lung tissue
- ARDS associated with the rapid onset of cyanosis, delirium, incontinence, and lungs filled with frothy blood-tinged sputum

Primary viral pneumonia

## Primary viral pneumonia

- Confirmation of primary viral pneumonia came in 1958 to 1959
- Findings included necrotizing bronchitis, hyaline membranes, intra-alveolar hemorrhage and edema, and interstitial inflammation



## Secondary bacterial pneumonia

- Patients typically have a history of influenza infection with near resolution of symptoms, followed-up 4 to 14 days later by a recurrence of fever, dyspnea, productive cough, and consolidation on chest radiographs.
- Pathogen: *Streptococcus pneumoniae, S. aureus, Haemophilus influenzae,* and other Gram-negative rods

| | Primary Viral Pneumonia | Secondary Bacterial Pneumonia | Mixed Viral and Bacterial Pneumonia | Localized Viral Pneumonia |
|---|---|---|---|---|
| Setting | Cardiovascular disease; pregnancy; young adult | Age, >65 y; pulmonary disease | Any associated with A or B | Normal |
| Clinical history | Relentless progression from classic 3-day influenza | Improvement, then worsening after 3-day influenza | Features of both primary and secondary pneumonia | Continuation of classic 3-day syndrome |
| Physical examination | Bilateral findings, no consolidation | Consolidation | Consolidation | Area of rales |
| Sputum bacteriology | Normal flora | *Pneumococcus, Staphylococcus, H. influenzae* | *Pneumococcus, Staphylococcus, H. influenzae* | Normal flora |
| Chest radiography | Bilateral findings | Consolidation | Consolidation | Segmental infiltrate |
| White blood cell count | Leukocytosis with shift to left | Leukocytosis with shift to left | Leukocytosis with shift to left | Usually normal |
| Isolation of influenza virus | Yes | No | Yes | Yes |
| Response to antibiotics | No | Yes | Often | No |
| Mortality | High | Low | Variable | Very low |

## Myositis and rhabdomyolysis

- > 50% of patients hospitalized with influenza A → CPK 上升
- Clinical severity varies but can include renal failure and problems with ambulation involving proximal leg muscles.
- Symptoms generally resolve in 4 to 6 wks.

## CNS complication - I

- encephalopathy (Reye's syndrome), encephalomyelitis, transverse myelitis, aseptic meningitis, focal neurologic disorders, and Guillain–Barre' syndrome.
- pathogenesis is unclear
  - direct viral invasion
  - development of antigen/antibody complexes
  - overproduction of systemic cytokines

## CNS complication - II

- In 1999, an outbreak of encephalopathy/ encephalitis was associated with influenza A in Japan.
  - 82% < younger than 5 yrs
  - 85% had no underlying disease
  - All had altered levels of consciousness and 80% had seizures.
  - Thrombocytopenia (50,000) and elevated aspartate aminotransferase (1000 U/L) were associated with mortality rates of 83% and 74%, respectively.

## Reye's syndrome

- The classic manifestation is a change in mental status that occurs several dyas after a typical respiratory illness.
- Reye's syndrome is an acute, noninflammatory encephalopathy
  - Lumbar puncture: normal protein and cell counts
  - Elevation of blood ammonia level
- 與aspirin使用有關

## Viral myocarditis - I

- Myocarditis may be predominantly elicited without viral pneumonia.
- The onset of acute carditis starts on day 4 to 7 of the onset of viral symptoms.
  - Patients may have worsening shortness of breath or recurrence after initial improvement.
  - chest pain or palpitations.

## Viral myocarditis - II

- ECG finding: sinus tachycardia, atrial or ventricular arrhythmias, conduction abnormalities, and non-specific S and T wave abnormality
- Troponin I has high specificity (89%) and low sensitivity (34%) in adults presenting with acute myocarditis.

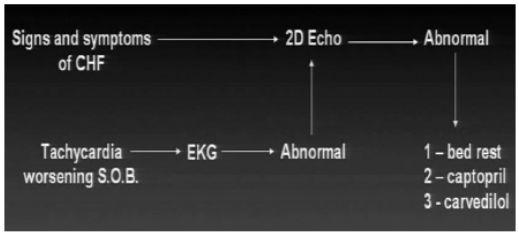



**Figure 2.** Diagram for diagnosis and treatment of acute viral myocarditis.

## Thanks for your attention!