

Preparing for the next flu pandemic



Influenza viruses

- Types A, B & C
- Only types A & B cause significant disease
- Influenza A has many subtypes, classified according to 16 “H” and 9 “N” proteins.
- 3 subtypes has caused human epidemics :
H1N1 (1918 Spanish flu), H2N2 (1957 Asian flu),
H3N2 (1968 Hong Kong flu)
- Influenza A viruses also infect birds, pigs and horses (H5N1 :tigers, cats, monkeys, ferrets)



Human infections caused by avian influenza

- Avian flu viruses rarely infect humans
- 1997 – HK – H5N1 – 18 cases (6 deaths)
- 1999 – HK – H9N2 – 2 cases (no deaths)
- 2003 – HK – H5N1 – 2 cases (1 death)
- 2003 – Netherlands – H7N7 – 83 cases (1 death)
- 2003 – HK – H9N2 – 1 case (no deaths)
- 2004/5 – H5N1- 126 cases (64 deaths)



Incubation period & transmission

Incubation period –

Typically 2 days, range 1-4 days

Mode of transmission –

Mainly large droplet spread - 1 metre;
Environmental contact (H5N1 viruses can survive for up to 6 days)



H5N1 transmission

- **Animal to human** – preparing diseased birds, handling fighting cocks, playing with poultry, consumption of duck's blood, eating undercooked poultry.
- **Environment to human** – contamination of hands from infected fomites & self-inoculation.



H5N1 transmission

- **Human to human** – one probable case of child-to-mother transmission in Thailand in Oct 2004.
- Nosocomial infection to HCWs rare – 1 case reported in Vietnam.



H5N1 clinical features

- Symptoms – fever >38 C, cough +/- sputum.
- Other common symptoms - sore throat, rhinitis, muscle aches, diarrhea, vomiting.
- Progression to pneumonia occurs early, breathlessness.
- Asymptomatic infections seen in HK.



Infectious period

- 1 day before onset of symptoms to 5 days in adults and 3 weeks in young children.
- Infectiousness related to amount of viral shedding.
- Viral shedding correlated with severity of illness.
- Minimal symptoms, asymptomatic can still be infectious.



Comparison with SARS

Similarities :

- Some similar symptoms – fever and cough, muscle aches, +/- breathlessness.
- Mode of transmission – droplet spread.
- Fever screening, use of PPE



Comparison with SARS

Differences :

- More infectious than SARS.
- Persons can be infectious even when asymptomatic.
- Shorter incubation period (median 3-4 days) compared to SARS (up to 10 days).
- Contact tracing difficult. Issues for isolation and quarantine. Community-wide measures to reduce contact may be most important.



Vaccines

- Human vaccine against H5N1 avian flu under development to establish immunogenicity, optimal dosages, dosing schedules, use of adjuvant, shorten regulatory approvals.
- To be effective, need close match with pandemic strain. First doses 4-6 months into pandemic (egg-based).
- Clinical trials underway; commercial availability 2008.
- Issues – risk with egg-based production? Other technologies – cell culture, DNA vaccines.



Antiviral drugs

- Four antiviral drugs available against influenza.
- M2 inhibitors (amantadine, rimantadine) not effective against H5N1
- Neuraminidase inhibitors (oseltamivir, zanamivir) probably effective (in-vitro and animal studies)
- Zanamivir (Relenza) – oral inhalation.
- Oseltamivir (Tamiflu) – oral capsules.



Antiviral drugs


- Can be used for treatment and prophylaxis.
- Must be given early (within 2 days) to be effective. Reduces duration of symptoms by 1-2 days. About 40-50% effectiveness in reducing likelihood of developing pneumonia.
- For prophylaxis, about 80-90% effective in preventing disease.
- Tamiflu resistance? Alternative – Relenza.



Influenza Pandemic – Risk Assessment

- New sub-type of the influenza A virus, A/ H5N1 virus, humans have no immunity.
- Human cases experienced severe illness with a very high mortality rate.
- Avian flu outbreaks continue to spread in region. Likelihood of eradicating avian flu in this region is bleak. Backyard farms. High risk practices. Poverty. Lack of compensation.
- Geographical extension to Turkey, Romania.
- When and how severe cannot be predicted.
- Reassortment, Adaptive mutation

Situation Update (14 Nov 2005)

- THAILAND
 - 21 confirmed cases of avian flu (13 deaths)
 - VIETNAM
 - 92 confirmed cases (42 deaths)
 - CAMBODIA
 - 4 confirmed cases (4 deaths)
 - INDONESIA
 - 9 confirmed cases (5 deaths)
- 

Pandemic Planning Assumptions

- Two or more waves in same year or in successive flu seasons
- Second wave may occur 3-9 mths later; may be more serious than first (seen in 1918)
- Each wave lasts about 6 weeks



Singapore's Pandemic Plan

- Surveillance.
- Response & Impact Mitigation.
- National immunity.



Surveillance

- Detect importation, occurrence as early as possible.
- External surveillance.
- Internal surveillance
 - Community ARIs, viral isolation
 - Atypical pneumonias
 - Unexplained deaths + resp illness
 - Lab diagnosis - PCR



Response & Impact Mitigation

- Desired Outcomes
 - Minimise disruption to economy and society
 - Maintain essential services
 - Reduce morbidity and mortality through treatment of all influenza-like cases
 - Slow down and limit the spread of influenza to reduce the surge on healthcare system
 - How effectively can we do this?



National immunity

- Obtain vaccines as soon as possible.
- Vaccinate entire population.
- Vaccination centres.
- High resistance to Tamiflu in subsequent waves.



Pandemic Response Plan

- Concept
 - Colour-coded Risk Management approach
 - **Green** - animal
 - **Yellow** - inefficient human-to-human
 - **Orange** – pandemic: efficient H to H, but limited transmission
 - **Red** – widespread infection
 - **Black**- out of control, high mortality, morbidity



Pandemic Response Plan

- Concept

- **Green/yellow** -- Effective surveillance to detect the importation of a novel influenza virus; ring fence cases through isolation and quarantine.
- How early can we detect cases?
- Can we ring-fence effectively?



Pandemic Response Plan

- **Yellow->Orange** – Govt to act early
 - border control (more for public confidence?)
 - infection control
 - info mgt for all healthcare personnel across public, private, VWO sectors
- Ring-fencing of cases as long as feasible.



Pandemic Response Plan

- Concept

- **Orange & above:** Mitigate impact of 1st wave


- MOH

- tight infection control in healthcare institutions
 - Treatment of all cases with ILI – designated flu clinics.
 - chemoprophylaxis of essential services

- Whole of Govt

- social distancing e.g. when to close schools? When to scale down normal work? Limit travel.
 - very strong public comms

Organisations & BCP

- **GREEN :**
 - Maintain situation awareness, develop BCP, preparedness training
 - **YELLOW :**
 - Provide updates & educate staff on good personal hygiene, implement infection control measures, temperature checks, increase cleaning of work areas
- 

Organisations & BCP

- **ORANGE/RED/BLACK**
 - Implement BCP
 - Update staff about MOH directives, don't report to work if sick but go to Flu clinics instead
 - Contacts – self-quarantine, monitor for fever
 - Limit social gatherings, increase social space, consider telecommuting, limit travel to affected countries



International efforts

- WHO updated Pandemic Preparedness Plan
- Pandemic planning around the world
- Stockpiling of antivirals
- Vaccine development, manufacturing capacity
- Country efforts e.g. US, Canada, Australia
- FAO/ OIE/ WHO/ WB Meeting on Avian and Pandemic Flu Preparedness, Geneva
- Pledging Conference, Beijing, Jan 2006



Thank You

