AVIAN INFLUENZA (AI)

Influenza avium
Fowl Plague

Summer term 2010
Influenza A

- Multiple species
  - Humans
  - Avian Influenza

- Most virulent group

- Classification by surface antigens into subtypes
  - Hemagglutinin (H or HA)
  - Neuraminidase (N or NA)
Surface Antigens and Subtypes

- 16 HA and 9 NA for influenza A
  - All in aquatic birds

- Hemagglutinin (HA)
  - Function: Sites for attachment to infect host cells

- Neuraminidase (NA)
  - Function: Remove neuraminic acid from mucin and release from cell
Schema of influenza virion
Name of influenza isolates

A/turkey/England/199/79 (H7N7)

1. antigenic type
2. host of origin
3. geographical location
4. strain reference number
5. year of isolation
6. for typ A the H and N subtype
Avian influenza (AI)

Great variability of clinical sings

• from symptomless infection

• across mild diseases of upper respiratory tracts

• to acute generalize disease with high mortality, describe previously as “fowl plague”
Avian Influenza

- Pathogenicity based on genetic features and/or severity of disease in poultry
  - Low pathogenic AI (LPAI)
    - H1 to H16 subtypes
  - **Highly pathogenic AI (HPAI)**
    - Some H5 or H7 subtypes
    - LPAI H5 or H7 subtypes can mutate into HPAI
Avian Influenza Viruses

Low Pathogenicity
(L P A I)
H 1 ~ H 1 5

Highly Pathogenic
(H P A I)
H 5, H 7

Localized
Respiratory, GI tract

Systemic

Lance Jennings, Canterbury Health Labs
Influenza A Viruses

- Mutate frequently
  - Antigenic drift
    - Point mutations accumulated during virus replication
  - Antigenic shift
    - Hybrid virus emerges when cell infected with two different influenza viruses
      - Human, avian, swine, equine
    - Transfer of influenza virus to a different species

Transfer of influenza virus to a different species
Avian influenza (AI)

Antigenic variation

Antigenic ‘drift’

- accumulation of amino acid substitutions
- changes in the HA molecules are clustered in specific surface areas, the are antigenically significant regions of the HA
- these point mutations are responsible for the annual influenza epidemics
1 Each year’s flu vaccine contains three flu strains—two A strains and one B strain—that can change from year to year.

2 After vaccination, your body produces infection-fighting antibodies against the three flu strains in the vaccine.

3 If you are exposed to any of the three flu strains during the flu season, the antibodies will latch onto the virus's HA antigens, preventing the flu virus from attaching to healthy cells and infecting them.

4 Influenza virus genes, made of RNA, are more prone to mutations than genes made of DNA.

5 If the HA gene changes, so can the antigen that it encodes, causing it to change shape.

6 If the HA antigen changes shape, antibodies that normally would match up to it no longer can, allowing the newly mutated virus to infect the body’s cells.

This type of genetic mutation is called “ANTIGENIC DRIFT.”
Avian influenza (AI)

Antigenic ‘shift’

• more radical change in the HA and/or NA proteins

• is generally associated with the appearance of new influenza pandemics

• genetic reassortment between human and animal viruses is one of the molecular mechanisms causing influenza pandemics
The genetic change that enables a flu strain to jump from one animal species to another, including humans, is called "ANTIGENIC SHIFT."

Antigenic shift can happen in three ways:

B. Without undergoing genetic change, a bird strain of influenza A can jump directly from a duck or other aquatic bird to humans.

A. Without undergoing genetic change, a bird strain of influenza A can jump directly from a duck or other aquatic bird to an intermediate host such as a chicken or pig.

1. A duck or other aquatic bird passes a bird strain of influenza A to an intermediate host such as a chicken or pig.

2. A person passes a human strain of influenza A to the same chicken or pig. (Note that reassortment can occur in a person who is infected with two flu strains.)

3. When the viruses infect the same cell, the genes from the bird strain mix with genes from the human strain to yield a new strain.

4. The new strain can spread from the intermediate host to humans.
History

- 1878: First identified case in Italy
- 1924-25: First U.S. cases
- Low pathogenic avian influenza first identified mid-twentieth century
- 1970’s: Migratory waterfowl carriers
- Outbreaks in mink, seals and whales
Economic Impact

- **1983: U.S. outbreak (H5N2)**
  - $65 million in losses
  - Destruction of 17 million birds
  - 30% increase in egg prices

- **1999-2000: Italy outbreak (H7N1)**
  - $100 million in compensation to farmers
  - 18 million birds destroyed
  - Indirect losses of $500 million
Economic Impact

- **1997: Hong Kong outbreak (H5N1)**
  - $13 million for depopulation and indemnities
  - 1.4 million birds

- **2001: Hong Kong outbreak (H5N1)**
  - 1.2 million birds
  - $3.8 million
Economic Impact

- 2003: European outbreak (H7N7)
  - Over 33 million birds destroyed
  - ¼ of Netherlands’ poultry stock
  - Cost?

- 2003-2004: SE Asia (H5N1)
  - 8 countries
  - >100 million birds destroyed
  - Cost?

- 2004-2005: SE Asia and Eurasia
  - Spread to Eurasia by migratory birds
Morbidity/Mortality

- Approaches 100% in commercial poultry flocks
- Deaths within 2 to 12 days after first signs of illness
- Survivors in poor condition
Animal Transmission

- Initial source of infection
  - Other poultry, migratory waterfowl, pet birds
- Spread by aerosol, shared drinking water, fomites
- Virus in respiratory secretions and feces
- Virus present in eggs but eggs unlikely to survive and hatch
Main risks of transmission by contamination with manure and secretions containing virus

**Figure 1.** Possible direct and indirect contacts between infected and non-infected poultry that can bring Avian Flu into a Farm with healthy poultry
Human Transmission

- Previously considered non-pathogenic for humans
- 1997, Hong Kong
  - 18 humans infected, 6 died
  - H5N1 virus linked to outbreak in live bird market and area farms
- 2003, the Netherlands
  - 83 confirmed cases in humans, 1 death
  - H7N7 strain
Clinical Signs

- Incubation period: 3-14 days
- Birds found dead
- Drop in egg production
- Neurological signs
- Depression, anorexia, ruffled feathers
- Combs swollen, cyanotic
- Conjunctivitis and respiratory signs
Post Mortem Lesions

- Lesions may be absent with sudden death
- Severe congestion of the musculature
- Dehydration
- Subcutaneous edema of head and neck area
Post Mortem Lesions

- Nasal and oral cavity discharge
- Petechiae on serosal surfaces
- Kidneys severely congested
- Severe congestion of the conjunctivae
Sampling

- Before collecting or sending any samples, the **proper authorities should be contacted**
- Samples should only be sent **under secure conditions and to authorized laboratories** to prevent the spread of the disease
- HPAI samples may be zoonotic
Diagnosis

- Clinically indistinguishable from virulent Newcastle Disease
- Suspect with:
  - Sudden death
  - Drop in egg production
  - Facial edema, cyanotic combs and wattles
  - Petechial hemorrhages
- Virology and serology necessary for definitive diagnoses
Differential Diagnosis

- Virulent Newcastle disease
- Avian pneumovirus
- Infectious laryngotracheitis
- Infectious bronchitis
- Chlamydia
- Mycoplasma
- Acute bacterial diseases
  - Fowl cholera, *E. coli* infection
Diagnosis

- **Laboratory Tests**
  - HP AI is usually diagnosed by virus isolation

- **Presence of virus confirmed by**
  - AGID
  - ELISA
  - RT-PCR

- **Serology may be helpful**
Treatment

- No specific treatment
- Supportive care and antibiotics for secondary infections
- Antivirals (amantadine) effective in reducing mortality
  - Not approved in food animals
  - Results in resistant viruses
Clinical Signs in Humans

- **1997: Hong Kong (H5N1)**
  - Fever, respiratory, vomiting, diarrhea, pain
  - Fatal cases: severe bilateral pneumonia, liver dysfunction, renal failure, septic shock

- **1979: MP AI in harbor seals (H7N7)**
  - Conjunctivitis in humans in contact
Clinical Signs in Humans

- 2003: Netherlands (H7N7)
  - Conjunctivitis
  - Mild influenza or respiratory symptoms
  - Fatal case: acute respiratory distress syndrome
- 2004-2005: S.E. Asia, EurAsia
Recommended Actions

- Confirmatory diagnosis
- Depopulation may occur
  - Infected premises
  - Contact-exposed premises
  - Contiguous premises
Control and Eradication

- Eliminate insects and mice
- Depopulate flock and destroy carcasses
- Remove manure to bare concrete
- High pressure spray to clean equipment and surfaces
- Spray with residual disinfectant
Prevention

- Import restrictions
- Surveillance
- Appropriate biosecurity
  - Control human traffic
  - Introduction of new birds into flock
  - Avoid open range rearing in waterfowl prevalent areas
- Education of the poultry industry
- Prompt response to MP AI outbreaks
Figure 2. Levels of biosecurity according to some husbandry practices.
Badly organised poultry farm.

Well organised poultry farm.

Figure 5
Quarantine: if the farmer needs to buy some animals, he must put them in a closed and separate place with no contact with your other animals for at least 2 weeks. Because even if the new animals look healthy, no one can know if they carry the virus or not. If they do, not only they will die but all your poultry may also die.

For poultry, you can put these new animals in a large basket, and make sure that your other poultry cannot come near the basket.

1. New animals have been bought and are brought into the farm
2. The new animals are kept in a close and separate place for at least 3 weeks, and observed everyday
3. If after at least 3 weeks, they are still healthy, they are put with the rest of the animals

Figure 7. Principles of Quarantine
Vaccination

- only killed vaccine
- DIVA strategy
Avian Flu in Czech Republic

- wild birds
- 12 swan in spring 2006
<table>
<thead>
<tr>
<th>Year</th>
<th>Subtype</th>
<th>High pathogenicity?</th>
<th>Location</th>
<th>Birds killed</th>
</tr>
</thead>
<tbody>
<tr>
<td>1983</td>
<td>H5N2</td>
<td>yes</td>
<td>Pennsylvania</td>
<td>17 million</td>
</tr>
<tr>
<td>1995</td>
<td>H5N2</td>
<td>yes</td>
<td>Mexico</td>
<td>?</td>
</tr>
<tr>
<td>1997</td>
<td>H5N1</td>
<td>yes</td>
<td>Hong Kong</td>
<td>1.6 million</td>
</tr>
<tr>
<td>1999-2000</td>
<td>H7N1</td>
<td>no</td>
<td>Italy</td>
<td>13 million</td>
</tr>
<tr>
<td>2002</td>
<td>H7N2</td>
<td>no</td>
<td>Virginia</td>
<td>4.7 million</td>
</tr>
<tr>
<td>2003</td>
<td>H7N7</td>
<td>yes</td>
<td>Netherlands</td>
<td>&gt;30 million</td>
</tr>
<tr>
<td>2004</td>
<td>H5N1</td>
<td>yes</td>
<td>Asia</td>
<td>&gt;100 million</td>
</tr>
<tr>
<td>2004</td>
<td>H7N2</td>
<td>no</td>
<td>Delaware</td>
<td>?</td>
</tr>
<tr>
<td>2004</td>
<td>H5N2</td>
<td>yes</td>
<td>Texas</td>
<td>?</td>
</tr>
<tr>
<td>2004</td>
<td>H7N3</td>
<td>yes</td>
<td>BC/Canada</td>
<td>?</td>
</tr>
</tbody>
</table>
Avian Influenza

1918 Army Photo of Victims of the Spanish Flu

( 1957: Asian flu – 1968: Hong Kong flu)
Výskyt jednotlivých subtypů chřipky A v lidské populaci (zdroj: CDC)
Genesis of strain A(H5N1) a A(H9N2) – Hong Kong 1997-1999

- A/Goose/Guangdong/1/96-like
- A/Teal/HK/W312/97-like
- A/Quail/HK/G1/97(H9N2)-like
- A/human/HK/1073/99(H9N2)
- A/chicken/HK/Z58/97(H5N1)-like
- A/HK/156/97(H5N1)
This map represents the provinces that experienced outbreaks of H5N1 type of Avian Influenza in the past 2 weeks (map updated to 30 December 2005). The original data have been collected and aggregated at the most detailed administrative level and for the units available for each country.

Source: AI outbreaks: FAO, OIE and Official government sources
This map represents the provinces that experienced outbreaks of H5N1 type of Avian Influenza in Europe from October through 13 January 2006. The original data have been collected and aggregated at the most detailed administrative level and for the units available for each country. Source: AI outbreaks: FAO, OIE and Official government sources.
**A(H5N1) evoluce of strain**

- Increasing circulation over several years
- Many variants - reassorted with other avian viruses
- Epidemic, highly virulent current strains are genotype Z

*Figure 2* Seasonality of the isolation of avian H5N1 viruses from domestic poultry in mainland China during July 2000 to January 2004 (see Table 1). The mean monthly temperature in southern China (approximated from the monthly average temperatures of the cities Changsha, Kunming and Xiamen) is shown for reference.
Lék Tamiflu představuje první linii obrany proti potenciální pandemii nemoci. Lék zabraňuje viru, aby se rozšířil mimo hostitelskou buňku.

**Životní cyklus viru**

1. virus se vdechnutím dostává do těla
2. napadá obal buňky
3. dýchací ústrojí
4. vniká do buňky
5. protein viru (neuraminidase) je schopen prolomit stěnu buňky
6. inhibitory (zpomáhavče) buňky se "přilepí" na proteiny viru

**Jak lék zpomaluje životní cyklus viru**

1. hostitelská buňka zaniká
2. opouští hostitelskou buňku a napadá další
3. vzniká do buňky
4. rozmnožuje se uvnitř buňky
5. výrobce: Roche Švýcarsko
6. společnost zvýšila v roce 2005 prodej léku o 16%
7. lék neslouží jako prevence před infekcí, pouze mírní následky
8. kyselina obsažená v čínském bádání, běžně používaného při vaření, je součástí léku TAMIFLU

**Inhibitory přilepené na proteinech viru zabraňují jeho proniknutí stěnou buňky ven a jeho šíření k dalším buňkám**
Výskyt HPAI v chovu

Ohniska nákazy
A1 Tisová (utraceno)
A2 Nořín (utraceno)
H Chocenín (54.200 ks)
B České Hradiště (17.000 ks)

Chovy v ochranném pásmu
C Peka (0)
L Dvařík (0)
E Zářecká Lhota (3.000 ks)
M Loučky (10.000 ks + 55.000 ks)

Chovy v pásmu dozoru
D Díbákov
G Brteč
I Skořenice
K Nedošín
P Nová Sídla
R Zhoř
S Litomyšl
T Úsík
U Dolní Újezd u Litomyšle

5 km
Průniky zón ptačí chřipky - všechny dosavadní případy

Legend
- červené čtverečky = města
- modré šipky = města
- žluté čtverečky = města
- černé kruhy = čtvrť kulatý

Legenda
- Červená - město
- Modrá - město
- Zelená - město
- Žlutá - město
- Černá - město

Města
- Liberec
- Mladá Boleslav
- Teplice
- Ústí nad Labem
- Praha
HPAI outbreaks: Outbreaks reported in poultry and cases in wild birds

Six months period (9 July 2007 - 9 January 2008)

This map represents occurrences of HPAI observed from 9 July 2007 to 9 January 2008. H5 cases are represented in this map only for countries in which H5N1 is known to be endemic and where N-subtype characterization is not being performed for secondary cases. Countries with HPAI occurrence only in wild birds are not considered as infected according to OIE status. The original data have been collected and aggregated at the most detailed administrative level and for the units available for each country.

NOTE: FAO compiles information from numerous sources (FAO representatives or country missions, FAO reports, OIE, official government sources, EC, Reference laboratories and others) and produces these composite maps in a representative effort to provide full and accurate information. Omissions and errors are regretted, but FAO welcomes messages to that effect with supporting documentation to make the required changes based on FAO validation and verification procedures. Send messages to EMPRES-livestock@fao.org
HPAI outbreaks: Outbreaks reported in poultry and cases in wild birds

Six months period (9 July 2007 - 9 January 2008)

This map represents occurrences of HPAI observed from 9 July 2007 to 9 January 2008. H5 cases are represented in this map only for countries in which H5N1 is known to be endemic and where N-subtype characterization is not being performed for secondary cases. Countries with HPAI occurrence only in wild birds are not considered as infected according to OIE status. The original data have been collected and aggregated at the most detailed administrative level and for the units available for each country.

NOTE: FAO compiles information from numerous sources (FAO representatives or country missions, FAO reports, OIE, official government sources, EC, Reference laboratories and others) and produces these composite maps in a representative effort to provide full and accurate information. Omissions and errors are regretted, but FAO welcomes messages to that effect with supporting documentation to make the required changes based on FAO validation and verification procedures. Send messages to EMPRES-livestock@fao.org
Cumulative Number of Confirmed Human Cases of Avian Influenza A/(H5N1) Reported to WHO

- From year 2003 totally 404 cases and 254 deaths
- 1st. Indonesia - totally 141 cases and 115 deaths
- 2nd. Viet Nam – totally 107 cases and 52 deaths
- 3rd. Egypt – totally 53 cases and 23 deaths
27 January, 2010

An outbreak of avian influenza was discovered yesterday at a broiler breeder pullet farm in Kibbutz Ein Shemer (about halfway between Tel Aviv and Haifa), Israel. The disease was found in a broiler breeder house, 15 weeks of age, than contain 43,000 birds. The Israeli Veterinary Services ordered all birds in the farm to be culled. and a quarantine in all poultry enclosures within a 10-kilometer radius.

According to Haaretz.com mortality started 10 days before diagnosis has been made.