INFLUENZA-2
Avian Influenza

VL – 7
Dec. 9th 2013

Mohammed El-Khateeb
Overview

1. Background Information
2. Origin/History
3. Brief overview of genome structure
4. Geographical Distribution
5. Pandemic Nature
6. Diseases Caused
7. Treatment & Vaccines
Avian Influenza

- A contagious viral infection and/or disease of many avian species including poultry, wild and exotic birds, ratites, shore birds and migratory waterfowl.

- The highly pathogenic form of the disease is characterized by severe depression, decrease in egg production, high mortality, edema, hemorrhage, and frank necrosis.

- All H5 and H7 infections are reportable to the World Organization for Animal Health (OIE).
Avian Influenza

History

- 412 BC - first mentioned by Hippocrates
- 1580 - first pandemic described
- 1878 Fowl plaque was described (Italy)
- 1901 Fowl plaque is caused by a virus
- 1955 It is type A influenza virus
- 1970 AGP test introduced
- 1972 Waterfowl is a reservoir
- 1979 Virulence and hemagglutinin cleavability was established
- 1997 Direct transmission of H5 AIV from birds to humans
What is Avian Influenza (AI)?

- Avian influenza (AI) is an infectious, viral disease of birds caused by several subtypes of the type A strain of the influenza virus.

- Avian influenza viruses usually do not infect humans but several cases of human infection have been reported since 1997.
Where does AI virus come from?

- All known subtypes of influenza A viruses circulate among wild birds, especially migratory waterfowl (e.g. ducks and geese) which are considered natural reservoirs for influenza A viruses.

- Domestic poultry like chickens and turkeys are not natural reservoirs for AI virus and usually develop clinical disease when infected with AI virus.
Where does influenza A virus come from?

Human influenza A viruses start as avian (bird) influenza viruses.
Classification

- Influenza viruses are subtyped according to surface glycoproteins: hemagglutinin (HA) and neuraminidase (NA)
  - Currently, there are 16 hemagglutinins (H1 to H16) and 9 neuraminidases (N1 to N9)
    - 144 possible sub-types
  - **Hemagglutinin** attaches the virus to the surface of the host cell so the virus can replicate
  - **Neuraminidase** lets the newly replicated viruses out of the cell to infect more cells
Influenza A HA and NA Subtypes

H1, H2, H3, H4, H5, H6, H7, H8, H9, H10, H11, H12, H13, H14, H15, H16, N1, N2, N3, N4, N5, N6, N7, N8, N9
How do AI viruses change or mutate?

- **Antigenic Drift**
  - Occurs through small changes in the virus that happen continually over time
  - Produces new virus strains that may not be recognized by antibodies to earlier influenza strains

- **Antigenic Shift**
  - An abrupt, major change in influenza A viruses, resulting in a new influenza virus that can infect humans (one that has not been seen in humans for many years)
Mutation and Reassortment 1

1. Mutation

AVIAN virus

2. Reassortment

HUMAN virus

Reassortant HUMAN- AVIAN virus
Mutation and Reassortment

1. Mutation
   - AVIAN virus
   - HUMAN virus

2. Reassortment
   - Reassortant HUMAN- AVIAN virus
By 2004, expanded to other mammalians. Now found in:

- Tigers,
- Leopards,
- Pigs,
- Domestic cats,
- Palm civets,
- Humans
Geographical Spread

Migratory Bird Patterns
How does AI virus spread?

- Exposure of poultry to migratory waterfowl
- Exposure of commercial poultry to AI-infected backyard, game bird, or hobby flocks
- Contact with AI-infected live bird markets
- Bird to bird contact (through feces)
- Aerosol droplets
- Manure, equipment, vehicles, egg flats, crates, contaminated shoes and clothing
- Wildlife vectors/scavengers
What is the incubation period?

- Usually 3 to 7 days
- Depends on:
  - strain of virus
  - dose of inoculum
  - age and immune status of bird
  - management and environmental factors
How long can AI virus survive?

- AI virus is shed in feces for 7 to 14 days after infection
- AI virus can survive in manure for up to 105 days especially with high moisture and low temperature
  - 1 gram of contaminated manure can infect 1 million birds
Avian Influenza

- **Pathogenesis:**
  - H5 and H7 strains capable of evolving into highly pathogenic strains,
  - Recent H5 virus strains increasingly pathogenic.
  - Virulence related to HA molecules
What are the types of Avian Influenza in domestic poultry?

- **Low pathogenic avian influenza (LPAI)**
  - Mild or no clinical signs
  - Low to moderate mortality
  - However, the low pathogenic H5 and H7 strains are capable of mutating under field conditions into highly pathogenic strains

- **Highly pathogenic avian influenza (HPAI)**
  - Sudden onset
  - Severe clinical signs
  - High mortality
Clinical Signs

- Incubation period 3-5 days
- Severe depression
- Decreased food and water consumption
- Drastic decline in egg production
- Many birds affected
Avian Influenza

**Diagnosis**

- Viral culture
- Polymerase Chair Reaction (PCR) assay for avian influenza A (H5N1) RNA
- Immunofluorescence for antigen with use of H5 monoclonal antibody
- Four-fold rise in H5-specific antibody
IF stainings: viral antigen-positive cells in the entire respiratory tract, but most in the trachea and lungs.
Treatment & Vaccines

- Currently available Tamiflu® (oseltamavir) and Relenza® (zanamavir), developed resistance to Symmetrel® (amantadine) and Flumadine® (rimantadine).

- Vaccines available for poultry however no vaccine for human use

- Countries working on developing a vaccine for H5N1 and H9N2
A flu virus contains eight gene segments. The goal is to combine the desired HA and NA genes from flu strain 1 with the six other genes from flu strain 2, which grows well in eggs and is harmless in humans.

1. After removing the dangerous part of the HA gene, scientists splice the HA and NA genes from flu strain 1 into circular pieces of DNA called plasmids.

2. Additional plasmids are created using the remaining six genes found in flu strain 2.

3. Scientists insert the HA and NA plasmids from flu strain 1 and the six plasmids carrying genes from flu strain 2 into animal cells growing in the laboratory.

4. The genes in the plasmids instruct the animal cells to make the desired new flu strain.
Can H7N9 spread from person to person?

- The spread of infection in birds increases the opportunities for direct infection of humans
  - Humans concurrently infected with human and avian influenza strains could serve as a "mixing vessel" for the emergence of a novel subtype with sufficient humans genes that can be transmitted from person to person
- However, the virus has not yet developed the ability to pass easily from human to human
Timeline of Emergence
*Influenza A Viruses in Humans*

- **1918**: Spanish Influenza (H1N1)
- **1957**: Asian Influenza (H2N2)
- **1968**: Hong Kong Influenza (H3N2)
- **1977**: Russian Influenza
- **1976**: Swine Flu Outbreak, Ft. Dix
- **1997**: Avian Influenza
- **2003**: Reassorted Influenza virus (Swine Flu) (H1)
- **2009**: H1N1 Pandemic

Note: The timeline shows the emergence of influenza viruses and the reassortment events that led to new strains.
Avian Influenza Infections in Humans

- 1997: Hong Kong (HPAI H5N1)
  - Infected chickens and humans
  - 18 sick (6 died)
  - Spread primarily from birds to humans
  - Person-to-person infection noted but rare
  - 1.5 million chickens destroyed
Avian Influenza

- **H5N1**
  - 1997: 18 human cases (Hong Kong)
    - 33% mortality
    - 61% pneumonia
    - 51% needed ICU care
    - All genes of avian origin showing virus had “jumped species.”
    - Little evidence of human-to-human transmission.
Avian Influenza Infections in Humans

- **2003: China and Hong Kong (HPAI H5N1)**
  - Occurred among members of a Hong Kong family that had traveled to China
  - 1 person recovered, another died
  - Another family member in China died
  - Origin unknown
Avian Influenza

- **H5N1**
  - 2003: Reemerged in a family group returning from Hong Kong to China.

- Cambodia
- China
- Indonesia
- Laos
- Malaysia
- Thailand
- Vietnam
- Russia
- Kazakhstan
- Mongolia
H1N1/H5N1

H1N1: Easily spread, Rarely fatal
H5N1: Spreads slowly, Often fatal
Avian Influenza Infections in Humans

- **2003: Netherlands (HPAI H7N7)**
  - Occurred among poultry workers and their families during an AI outbreak in poultry
  - 89 cases reported (mostly conjunctivitis and some respiratory signs)
  - 1 veterinarian died from acute respiratory infection
  - Most cases occurred due to direct contact with infected poultry
World wide Human Mortality Rate=63% June 2008
Avian Influenza Infections in Humans

- **2013: China (H7N9)**
  - 126 cases (24 deaths) as of 29 April 2013
How do humans get infected with H7N9?

- Mainly through direct contact with infected poultry
  - When people sell or slaughter and consume infected birds
  - Exposure during slaughter, defeathering, butchering, and preparation of poultry for cooking

- So far, evidence suggests that the source of H7N9 virus is poultry and live bird markets and the most likely route of transmission from poultry to humans
Why should we be concerned about H7N9?

- H7N9 has not been previously reported in humans
  - No background or pre-existing immunity
- H7N9 is more easily transmissible from poultry to humans than H5N1
  - However, unlike H5N1 infections, poultry infected with H7N9 appear healthy
Pandemics are rare but deadly

- **1918-19 Spanish Flu (H1N1)**
  - 20-50 million infected worldwide
  - >500,000 deaths U.S.

- **1957-58 Asian Flu (H2N2)**
  - 70,000 deaths U.S.

- **1968-69 Hong Kong Flu (H3N2)**
  - 50,000 deaths U.S.

- **2009-2010 Swine Flu (H1N1)**
  - 60 million infected worldwide
  - 18,000 deaths
1918 “Spanish influenza”  ➔  1957 “Asian influenza”  ➔  1968 “Hong Kong influenza” ➔  Next pandemic influenza

**H1N1 influenza virus**
- Bird-to-human transmission of H1N1 virus
- Hemagglutinin
- Neuraminidase
- All 8 genetic segments thought to have originated from avian influenza virus

**H2N2 influenza virus**
- H2N2 avian virus
- H1N1 human virus
- Reassortment
- 3 new genetic segments from avian influenza virus introduced (HA, NA, PB1); contained 5 RNA segments from 1918

**H3N2 influenza virus**
- H3 avian virus
- H2N2 human virus
- Reassortment
- 2 new genetic segments from avian influenza virus introduced (HA, PB1); contained 5 RNA segments from 1918

**Next pandemic influenza**
- Avian virus
- H3N2 human virus
- All 8 genes new or further derivative of 1918 virus
- ?

(Click to zoom in)
Can another pandemic happen again?

- Only when three conditions have been met:
  1. A new influenza virus subtype emerges
  2. It infects humans, causing serious illness
  3. It spreads easily and sustainably among humans*

*has not yet occurred with H7N9 or H5N1
What can we do to prevent AI in humans?

- Practice normal hygienic precautions
  - Wash hands with soap and water for 15-20 seconds
  - Cover your mouth when you cough or sneeze
- Get vaccinated for seasonal flu
- Stay home and rest if you have the flu
- Practice "social distancing" if there is a flu outbreak
- Avoid live bird markets
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.”
SWINE INFLUENZA
Swine Influenza (swine flu) is a respiratory disease of pigs caused by type A influenza viruses (H1N1 subtype) that causes regular outbreaks in pigs. People do not normally get swine flu, but human infections can and do happen.

Swine flu viruses have been reported to spread from person-to-person, but in the past, this transmission was limited and not sustained beyond three people.
SWINE FLU

- Pigs can be infected with both human and avian influenza viruses in addition to swine influenza viruses.
- Infected pigs get symptoms similar to humans, such as cough, fever, and runny nose.
- Because pigs are susceptible to avian, human and swine influenza viruses, they potentially may be infected with influenza viruses from different species (e.g., ducks and humans) at the same time. If this happens, it is possible for the genes of these viruses to mix and create a new virus.
Swine Influenza A(H1N1)

- Swine Influenza (swine flu) is a respiratory disease of pigs caused by type A influenza that regularly cause outbreaks of influenza among pigs.

- Most commonly, human cases of swine flu happen in people who are around pigs.

- Swine flu viruses do not normally infect humans, however, human infections with swine flu do occur, and cases of human-to-human spread of swine flu viruses have been documented.
Swine Influenza A(H1N1) *Transmission to Humans*

- Through contact with infected pigs or environments contaminated with swine flu viruses
- Through contact with a person with swine flu
- Human-to-human spread of swine flu has been documented also and is thought to occur in the same way as seasonal flu, through coughing or sneezing of infected people
Swine Influenza A(H1N1)
Transmission Through Species

Reassortment in Pigs
Swine Influenza A(H1N1) Facts

- Virus described as a new subtype of A/H1N1 not previously detected in swine or humans
- Outbreak in Fort Dix, New Jersey, USA occurred in 1976
- CDC determines that this virus is contagious and is spreading from human to human
- The virus contains gene segments from 4 different influenza types:
  - North American swine
  - North American avian
  - North American human and
  - Eurasian swine
Swine Influenza A(H1N1) Global Response

- The WHO raises the alert level to Phase 6
  - WHO’s alert system was revised after Avian influenza began to spread in 2004 – Alert Level raised to Phase 3
  - In Late April 2009 WHO announced the emergence of a novel influenza A virus
  - April 27, 2009: Alert Level raised to Phase 4
  - April 29, 2009: Alert Level raised to Phase 5
  - June 11, 2008: Alert Level raised to Phase 6

Source: WHO
New Influenza A (H1N1),
Number of laboratory confirmed cases as reported to WHO

Status as of 24 June 2009
06:00 GMT

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

Map produced: 24 June 2009 10:00 GMT

Data Source: World Health Organization
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

© WHO 2009. All rights reserved

Source: WHO
% seropositive sows (HI), 2002-03
*SIV subtype isolated

Ireland
H1N1: 17.8*
H3N2: 4.2*
H1N2: 0.6

Germany
H1N1: 70.8*
H3N2: 58.6*
H1N2: 32.1*

Poland
H1N1: 8.0*
H3N2: 0
H1N2: 0

Czech Republic
H1N1: 11.7*
H3N2: 0.1
H1N2: 3.0

Belgium
H1N1: 80.8*
H3N2: 53.8*
H1N2: 57.8*

Spain
H1N1: 38.5*
H3N2: 38.0*
H1N2: 52.8*
HOW DOES SWINE FLU SPREAD?

- Spread of this swine influenza A (H1N1) virus is thought to be happening in the same way that seasonal flu spreads.
- Flu viruses are spread mainly from person to person through coughing or sneezing of people with influenza.
- Sometimes people may become infected by touching something with flu viruses on it and then touching their mouth or nose.