Avian Influenza: Armageddon or Hype?

Presented by MedicEd.com, Inc.
Edited by Louis Durkin, MD FACEP

1 Credit Hour Course Approved for the Following Levels:
» First Responder
» EMT Basic
» EMT Intermediate
» EMT Paramedic

Objectives

1. Understand the mechanism of transmission of viral illnesses from the animal population to humans
2. Understand why Avian influenza may be the source of the next human pandemic
3. List the approach to personal protection when dealing with viral illnesses such as Influenza

Definitions:

- Epidemic—The occurrence of cases of an illness in a community or region which is in excess of the number of cases normally expected for that disease in that area at that time.
- Pandemic—An epidemic that strikes a very wide area, usually hemisphere-wide or world-wide.

Overview

- Three influenza pandemics during the last century:
  o 1968 (H3N2)
  o 1957 (H2N2)
  o 1918 (strain uncertain)
- Each case by emergence of a new virus that contained components of previous human influenza viruses and avian influenza viruses.
- Avian influenza is caused by the H5N1 influenza virus.
- Influenza A virus.
Avian influenza H5N1:

- Sporadic transmission to humans in 2004-2005 killed 114 people and raises concern that next pandemic is imminent.
- Two striking features:
  - Predominance of children and young adults.
  - High mortality rate.

Highly-pathogenic N5H1 influenza virus now endemic among bird and poultry populations in Asia.

Concerns

Sporadic transmission from birds to humans of H5N1 raises concerns:

- H5N1 may mutate.
- H5N1 may combine with genetic material from human influenza virus creating a new strain capable of human-to-human transmission and potential pandemic.

WHO describes the H5N1 as a “public health crisis” and declared that the world is as close as ever to the next pandemic.

Evolution of 1968 H3N2 Influenza Pandemic

Avian H3   Human H2

Human H3

Virus:

- Ultramicroscopic infectious agent that replicates itself only within cells of living hosts.
- Many are pathogenic.
- A piece of nucleic acid (DNA or RNA) wrapped in a thin coat of protein.

Influenza viruses are RNA viruses.
Segmented genome thus great antigenic diversity.

Influenza virus classifications:

- Core protein:
  - A
  - B
  - C
- Species of origin (swine, avian, etc.)
- Geographic site of isolation.
- Serial Number
- Glycoprotein subtypes (Influenza A only)
Two major antigenic glycoproteins embedded in membrane:

- Hemagglutinin (HA)
- Neuramidase (NA)

Induce antibody response in humans.

**Avian influenza:**

- 16 HA subtypes
- 9 NA subtypes
- Many subtypes possible.
- All subtypes found in birds.

**Influenza A:**

- Responsible for frequent (usually annually) outbreaks or epidemics of varying intensity
- Occasional pandemics.
- Subtypes circulating:
  - H1N1
  - N1N2
  - H3N2

**Influenza B:**

- Outbreaks every 2-4 years.
- Human influenza viruses (H1 & H3) circulate continuously and undergo antigenic drift.
- Inefficient proofreading during viral RNA replication causes transcription errors and amino acid substitutions in HA and NA.
- Allows new variants to evade pre-existing immunity thus causing outbreaks.

**Why are pigs involved?**

- Pigs have receptors for both avian and human influenza viruses in their tracheas.
- Domestic pig supports the growth of both human and avian viruses.

**Why does influenza always seem to come from Southeast Asia?**

- Agricultural practices.
- Humans, birds and swine are in close proximity.

Avian viruses replicate inefficiently in humans. However, some subtypes can replicate in the human respiratory tract and cause disease.

**Avian influenza virus types:**

- H5N1
- H9N2
- H7
- 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.

**H5N1**

• 2003: Reemerged in a family group returning from Hong Kong to China.
• 2003-2006: Highly pathogenic variant caused extensive outbreaks in Asia.
  - Cambodia
  - China
  - Indonesia
  - Laos
  - Malaysia
  - Thailand
  - Vietnam
  - Russia
  - Kazakhstan
  - Mongolia

**N1:**

- Human cases = 130 (>50% mortality)
- Locations:
  - Thailand
  - Cambodia
  - Vietnam
  - Indonesia
  - China
- Spread to domestic cats.

**Cats....**

The other white meat.

**H9N2:**

- 1999: Hong Kong
- 2003: Hong Kong
  - Caused mild, self-limited respiratory infection in children.

**H7:**

- 2003: H7N7 outbreak in the Netherlands
  - Influenza-like illness
  - Mild respiratory illness
- H7N3 caused conjunctivitis in Canadian poultry workers.
Transmission:

- Inhalation of infectious droplets
- Direct contact
- Indirect (fomite) contact [possibly]

Transmission:

- H5N1:
  - Bird-to-human
  - Environment to human [possible]
  - Limited non-sustained human-to-human

Vaccination

- Fast track process underway
- Initial studies (Phase 1) of 450 patients:
  - Rochester, NY
  - Baltimore, MD
  - Los Angeles, CA

Treatment

Effective drugs:

- M2 channel blockers
  - Amantadine (Symmetrel)
  - Rimantadine (Flumadine)
- Neuraminidase inhibitors
  - Oseltamivir (Tamiflu)
  - Zanamivir (Relenza)

Treatment

- H5N1 in Thailand has developed mutations in the M2 protein which makes it resistant to amantadine and rimantadine (neuraminidase inhibitors remain effective).
- Oseltamivir (Tamiflu) effective when given early in the course of the infection.
- Oseltamivir (Tamiflu) ineffective when given late in the course of the infection.
- Treat for 5-8 days.

Drug resistance:

- Mutation of the hemagglutinin or neuraminidase genes.
- Drug resistance has been documented in human strains—specifically in children.
- Prophylactic treatment of a Vietnamese girl caused drug resistance for oseltamivir.
Prevention

- Poultry outbreak:
  - Quarantine
  - Depopulation
  - Area surveillance
- Workers:
  - PPE (gowns, gloves, frequent hand washing)
  - N95 mask
  - Prophylaxis
  - Vaccination with current influenza vaccine

Prevention
- Avian influenza should be treated in the same manner as SARS.

Post-Exposure Prophylaxis

- Household contacts of H5N1 patients should receive oseltamivir daily for 7-10 days.
- Monitor temperature.
- Quarantine.

Summary

- Epidemiology
  - Highly pathogenic H5N1 influenza viruses are now endemic in bird populations in Asia and spreading west.
  - Sporadic human-to-human transmission has occurred raising likelihood of reassorting with coinfecting human influenza virus producing novel strain capable of human-to-human transmission.
  - Predominance of children
  - High mortality rate

Summary

- Clinical symptoms and diagnosis:
  - Fever
  - Pneumonia
  - Diarrhea
  - Encephalopathy
- Diagnosis made by laboratory tests

Treatment

- No outcome trials to date
  - Oseltamivir (Tamiflu) may be of benefit (75 mg BID x 7 days)
- Optimal dose and duration unknown.
Prevention

- No licensed vaccines
- Appropriate biosafety precautions
- Isolation precautions similar to that for SARS

“Experts at the WHO and elsewhere believe that world is now closer to another influenza pandemic than at any time since 1968, when the last of the previous century's three pandemics occurred. WHO uses a series of six phases of pandemic alert as a system for informing the world of the seriousness of the threat and of the need to launch progressively more intense preparedness activities.”

Summary

- North America has avoided H5N1 because current infected migratory birds have not entered North American flyways.
- With increasing human-to-human transmission, foreign air travel places North America at increased risk.
- If the virus mutates or reassorts with human influenza virus—then we are definitely facing a pandemic.

Resources:

- WHO: [http://www.who.int/csr/disease/avian_influenza/en/]
- CDC: [http://www.cdc.gov/flu/avian/]
- NIAID: [http://www3.niaid.nih.gov]