Update on Avian Influenza

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Overview

• Introduction: Differences between seasonal flu, pandemic flu and avian flu
• Influenza A viruses
• Avian influenza – Epidemiology and pathobiology (LPAI and HPAI)
• Avian influenza in commercial poultry – Current situation
• Asian lineage H5N1 HPAI
• H7N9 influenza in China
• Prevention and Control
Seasonal Influenza

Influenza virus type A and B

http://www.cdc.gov/flu/index.htm
Pandemic influenza

Emergency hospital, Camp Funston, Kansas 1918
Courtesy of National Museum of Health and Medicine

1918 “Spanish Flu” (H1N1) 20-40 million deaths
1957 “Asian Flu” (H2N2) 1 million deaths
1968 “Hong Kong Flu” (H3N2) 1 million deaths

Nancy Cox, 2009, Science
China's deadly new H7N9 bird flu virus may be harder to track than predecessors, scientists say.

**H5N1 HPAI**
668 total cases/393 deaths

**H7N9 LPAI**
464 total cases/174 deaths

**H10N8 LPAI**
3 total cases/2 deaths
Influenza in animals

**H7N3 HPAI**

*Mexico Kills 8 Million Chickens to Contain H7N3 Virus*

By C. Hsu | Aug 8, 2012 EDT

**H5N8 HPAI**

*Bird flu worries spread in Europe*

By S. Capelouto, CNN. November 24, 2014

**H3N2v**

*Health officials warn fair attendees not to pet pigs due to swine flu fears*

Published August 31, 2012. FoxNews.com

**H5N2 HPAI**

*Canada bird flu virus identified as 'highly pathogenic' strain.*

Published Dec. 5 2014 FoxNews.co
Influenza A viruses
Influenza A viruses

- Influenza A viruses infect humans, birds and other animals including horses, pigs, dogs

- The natural reservoir of influenza A viruses is wild aquatic birds

- Classified based on the viral surface proteins hemagglutinin (HA or H) and neuraminidase (NA or N)
  - 16 H subtypes (or serotypes) and 9 N subtypes

© Paul Digard, Dept Pathology, University of Cambridge.
Influenza A viruses

• Orthomyxoviridae family, genus Influenzavirus type A

• Single-stranded (-) sense segmented RNA genome

New influenza A viruses are constantly emerging
Influenza A viruses
Wide host range, strain dependent
## Influenza A viruses

### Table

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Human</th>
<th>Swine</th>
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<th>Wild Ducks</th>
<th>Shorebirds</th>
<th>Poultry</th>
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<td>++</td>
<td>+</td>
<td>+</td>
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<td>H16</td>
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<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

*H17 – type A influenza from bats*

Interspecies Transmission of Influenza A Viruses

Avian Influenza
Avian influenza virus: Pathogenicity

- Pathogenicity: Ability to produce lesions, disease and/or death in a host
- Determined by several factors: virus, host, and environmental
- Host differences – *Galliformes* vs. *Anseriformes*

- Pathotypes:
  - High pathogenicity (*HPAI*): some H5 and H7 viruses
  - Low pathogenicity (*LPAI*): most H1-13 virus

*LPAI* H5 or H7 subtypes can mutate into *HPAI* viruses
AI viruses are routinely isolated from wild bird species.

The vast majority of HPAI viruses never re-enter the wild bird system.
What do we mean by highly pathogenic?

Only applies to **gallinaceous poultry** (chickens, turkeys, quail)

– Regulatory definitions from OIE

1. Highly pathogenic avian influenza (HPAI) virus lethal for 75% or more of intravenously inoculated susceptible chickens (IVPI > 1.2) within 10 days.
2. H5 or H7 subtype that has an amino acid sequence at the hemagglutinin cleavage site ‘compatible’ with HPAI due to multiple basic amino acids

• Notifiable avian influenza
  – H5/H7 HPAI
  – H5/H7 low pathogenicity notifiable AI (LPNAI)
• Other low pathogenicity avian influenza viruses are not notifiable (H1-4, H6, H8-16)

World Organization for Animal Health
Low Pathogenicity Avian Influenza

*Chickens and turkeys*

Infections - variable clinically
- Respiratory signs
- Rhinitis and tracheitis
- Decrease in feed and water consumption
- Ocular discharge
- Diarrhea
- Drops in egg production
- Mild increase in mortality
LPAI outbreaks reported to the OIE 2012-2014

H5 and H7 avian influenza in its low pathogenic form in poultry is a notifiable disease as per Chapter 10.4. on avian influenza of the Terrestrial Animal Health Code (2010)
Highly Pathogenic Avian Influenza

*Chickens and turkeys*

Severe systemic disease. Highly contagious

- High mortality. Rapid spread
- Severe decrease in feed and water consumption
- +/- nervous signs
- Edema of head and legs
- Pulmonary edema, congestion and hemorrhage
- Visceral hemorrhage
37 HPAI Disease Events

1890’s-1950’s numerous outbreaks, subtypes not known
1924-25, North east US H7N7?
1. 1959-Scotland, H5N1
2. 1961-S. Africa, H5N3
3. 1963-England, H7N3
4. 1966-Canadada, H5N9
5. 1975-Australia, H7N7
6. 1979-England, H7N7
7. 1979-England, H7N7
8. 1983-84 - USA, H5N2
9. 1983-Ireland, H5N8
10. 1985-Australia, H7N7
11. 1991-England, H5N1
12. 1992-Australia, H7N3
13. 1994-Australia, H7N3
14. 1994-95-Mexico, H5N2
15. 1995 and 2004 -Pakistan, H7N3
16. 1997-Australia, H7N4
17. 1997-Italy, H5N2

*LPAIV ⇒HPAIV

**Largest epizootic on record

**18. 1996-present – Asia/Europe/Africa, H5N1

*19. 1999-2000 - Italy, H7N1
*20. 2002 - Chile, H7N3
*21. 2003 – Netherlands, H7N7
*22. 2004 – USA, H5N2
*23. 2004 – Canada, H7N3
25. 2005? – N. Korea, H7N7
*26. 2007 – Canada, H7N3
27. 2008 – England, H7N7
28. 2009- Spain, H7N7
29. 2011- South, Africa H5N2
30. 2012- Taipei, H5N2
31. 2012- South Africa, H7N1
32. 2012. Mexico, H7N3
33. 2012: Australia, H7N7
34. 2013: Italy, H7N7
35. 2013: Australia, H7N2
36. 2014: S. Korea and Europe, H5N8
37. 2014: Canada, H5N2
H5 and H7 avian influenza in its low pathogenic form in poultry is a notifiable disease as per Chapter 10.4. on avian influenza of the Terrestrial Animal Health Code (2010)
HPAI (7/1/2012-2/7/2014): 18 countries

H5N1 HPAI
12 countries – poultry, wild birds, humans

H5N2 HPAI
S. Africa – ostriches
Chinese Taipei – native chicken

H5N8 HPAI
S. Korea – ducks and other poultry

H7N2 HPAI
Australia - layers

H7N7 HPAI
Italy – poultry

H7N3 HPAI
Australia - layers

Mexico - layers
Early this year, China, Japan and South Korea reported outbreaks of H5N8 in poultry farms as well as findings in migratory birds.

South Korea: 26+ outbreaks: breeding ducks, meat ducks, layer chickens, broilers, breeders. 15,114 deaths and 494,346 culled.

Since early November 2014, H5N8 HPAI was reported at poultry farms in Germany (1 farm), Netherlands (3 farms), and the UK (1 farm).

A sample collected from an wild Common Teal legally hunted in Germany tested positive for HPAI H5N8.
H7N3 HPAI in Mexico

• Reported to OIE 6/21/2012 – Jalisco
  • 44 farms
  • 10.6 million chickens affected– all layers
  • 11 million culled in outbreak zone
• Temporary vaccination authorized: 165.9 m doses used by Jan/2013
• Limiting factors in control:
  • Large number of diagnostic testing: 730 premises in Jalisco
  • Labor intensive depopulation of individual layers
• Resurgence in 2013 (central Mexico):
  12/1/2013 to 31/8/2013 – 64 outbreaks in Jalisco, Aguascalientes, Guanajuato and Puebla
  • 550,322 deaths, 6,230,022 culled
  • Layers, broiler breeders, backyard poultry and broilers
• H7N3 total – 110 outbreaks, 20 million poultry
H5N2 HPAI in Canada

- Canadian health officials confirmed H5N2 HPAI in two of the four H5-related poultry outbreaks in British Columbia's Fraser Valley near Vancouver.

Up to 140,000 chickens and turkeys culled in B.C. as officials try to contain outbreak of highly-contagious avian flu

T. Hopper | December 7, 2014. The National Post
Asian lineage H5N1 HPAI
H5N1 HPAI – The bird Flu
H5N1 HPAI

- H5N1 HPAI viruses continue to circulate in poultry and cause disease, and remain a threat to human and animal health (OIE-FAO-WHO)
- Outbreaks in poultry have seriously impacted livelihoods, the economy and international trade in affected countries
Ecology and Epidemiology - H5N1 HPAI

Exposure Adaptation

LPAIV (H1-16)

Asian H5N1 HPAIV Re-adaptation

Mammals

D. E. Swayne, 2007
H5N1 HPAI Epizootics

2. Local extension - Hong Kong: 1997, 2001-3
3. SE Asian Regional Extension
   - S. Korea: 2003-4
   - Vietnam: 2004-6
   - Japan: 2004
   - Thailand: 2004-6
   - Cambodia: 2004-6
   - Laos: 2004-6
   - Taiwan (smuggled ducks): 2003
   - Indonesia: 2003-6
   - Malaysia: 2004

4. Central Asia & E. Europe, wild bird –
   - Mid-2005: China (Qinghai Lake), Russia, Mongolia, Kazakhstan
   - Late-2005: Turkey, Romania, Kuwait, Croatia, Ukraine, Cyprus

D. E. Swayne, 2007
• +55 countries with cases in wild birds and/or poultry
• Over 220 million birds dead or culled 2004-2008 (FAO)
H5N1 HPAI

Endemic in poultry in Egypt, China, Bangladesh, Indonesia, India and Vietnam
H5N1 HPAI in Vietnam
H5N1 HPAI viruses continue evolving

**Evolution of the Asian H5 Hemagglutinin**

When discrete monophyletic groups begin to appear within a specific clade and those groups meet the nucleotide divergence criteria (as well as having bootstrap values >60), they are split into second order clades (but still considered part of the original first order clade). As a second order clade continues to evolve, it may reach a similar level of genetic diversity at which point it may be split into third order clades and so on. The same clade designation criteria apply to first, second, and any higher order clade designations.
H5N1 HPAI viruses continue evolving

The evolution of H5N1 viruses impacts vaccine and diagnostic test development for both humans and birds.

Reassortant viruses with the H5 and different NA genes are more prevalent: H5N2 in China, H5N6 in China, Laos and Vietnam, and H5N8 in South Korea and Japan.
## H5N1 HPAI and Public Health

### Cumulative Number of Confirmed Human Cases of H5N1. Reported to WHO. 2003-2014

<table>
<thead>
<tr>
<th>Country</th>
<th>Total 2003-2014</th>
<th></th>
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<tbody>
<tr>
<td></td>
<td>cases</td>
<td>deaths</td>
</tr>
<tr>
<td>Azerbaijan</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Bangladesh</td>
<td>7</td>
<td>1</td>
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<tr>
<td>Cambodia</td>
<td>56</td>
<td>37</td>
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<tr>
<td>China</td>
<td>47</td>
<td>30</td>
</tr>
<tr>
<td>Djibouti</td>
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<td>0</td>
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<tr>
<td>Egypt</td>
<td>177</td>
<td>63</td>
</tr>
<tr>
<td>Indonesia</td>
<td>197</td>
<td>165</td>
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<tr>
<td>Iraq</td>
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<td>2</td>
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<tr>
<td>Lao</td>
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<td>2</td>
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<tr>
<td>Myanmar</td>
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<td>0</td>
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<td>1</td>
</tr>
<tr>
<td>Pakistan</td>
<td>3</td>
<td>1</td>
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<td>Thailand</td>
<td>25</td>
<td>17</td>
</tr>
<tr>
<td>Turkey</td>
<td>12</td>
<td>4</td>
</tr>
<tr>
<td>Viet Nam</td>
<td>127</td>
<td>64</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>668</strong></td>
<td><strong>393</strong></td>
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H5N1 HPAI and Public Health

- Human cases of H5N1 infection are rare and sporadic events, occurring mostly in areas where the virus is circulating endemically in poultry
- Exposure risks for human infection
  - Exposure one week before illness to poultry, especially direct handling of sick or dead poultry
  - Women - preparers of food
  - Limited human-to-human transmission
- H5N1 HPAI has not been a Food Safety issue
  - Virus is killed by pasteurization and cooking
### Natural Human AI Virus Infections

<table>
<thead>
<tr>
<th>Year</th>
<th>Country</th>
<th>Subtype</th>
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<td>USA</td>
<td>H7N7 HPAI</td>
<td>1</td>
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<td>1978-9</td>
<td>USA</td>
<td>H7N7 LPAI</td>
<td>?</td>
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<td>U. Kingdom</td>
<td>H7N7 LPAI</td>
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<td>0</td>
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<td>1999-2011</td>
<td>China-Hong Kong</td>
<td>H9N2 LPAI</td>
<td>7+</td>
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<td>0</td>
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<td>2003</td>
<td>Netherlands</td>
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<td>2004</td>
<td>Canada</td>
<td>H7N3 LP/HPAI</td>
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<td>2006</td>
<td>U. Kingdom</td>
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<td>2003-2014</td>
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<td>2013-2014</td>
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<td>2013-2014</td>
<td>China</td>
<td>H10N8 LPAI</td>
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</table>
H7N9 influenza in China

- A novel H7N9 influenza A virus emerged in humans eastern China in February of 2013. Cases were often severe and the case fatality rate approximately 32%.
- The viral genome was rapidly characterized and was found to be a novel combination of genes from avian influenza viruses.
- An avian reservoir was immediately suspected as a likely origin of human infections because of the genes of the virus were of avian origin and because recent contact with poultry was documented with numerous human cases.
H7N9 influenza in China

- Chinese veterinary officials quickly started testing poultry associated with live poultry markets (LPM’s), commercial poultry operations, and wild birds in the regions where human infections were being reported.
- H7N9 viruses were detected in avian species in the LPM’s including chickens, pigeons, ducks, and the environment.
- Therefore LPM’s were suspected of being a major source of human infections, and Chinese officials required closure of LPM’s resulting in the reduction of human cases.

It’s a LPAI
Location of H7N9 Influenza in China (8/4/14)*

<table>
<thead>
<tr>
<th>Province/City</th>
<th>Number of Cases</th>
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<tbody>
<tr>
<td>Anhui</td>
<td>18</td>
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<tr>
<td>Beijing</td>
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<tr>
<td>Fujian</td>
<td>22</td>
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<tr>
<td>Guangdong</td>
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<td>Guangxi</td>
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<td>Hebei</td>
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<td>Jiangxi</td>
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<td>Jilin</td>
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<td>Shandong</td>
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<tr>
<td>Shanghai</td>
<td>42</td>
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<tr>
<td>Zhejiang</td>
<td>140</td>
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</tbody>
</table>

*452 total cases/124 deaths
Since 2 December 3 new human cases have been reported in Guangdong and Fujian Provinces and Shanghai City
http://empres-i.fao.org/eipws3g/
Role of LPM’s

• Retail LPMs provide a mixing ground for the emergence of novel strains of influenza
  – The closure of 780 LPM’s in the Chinese cities of Shanghai, Hangzhou, Huzhou and Nanjing in April 2013 reduced the daily number of H7N9 infections by more than 97 percent (Cowling et al, The Lancet 2014)
  – Losses associated with the closures have been estimated at about 57 billion yuan (about $9 billion/7 billion euros)

• The findings confirm that LPM closure, though a huge economic setback, is a highly effective intervention to prevent human disease and protect public health
Avian Influenza: Prevention and Control
Avian Influenza

Animal Health Risk and Impact

- Economics: Treatment costs and production impacts
- Animal suffering and welfare
- Negative impact on human nutrition and livelihoods (i.e. Food Security)
- Trade impact: real-risk and pseudo-risk with outcome of trade barriers
Avian Influenza

Economic losses from AI result from:

• Direct losses:
  – Depopulation and disposal
  – High morbidity and mortality
  – Quarantine and surveillance
  – Indemnities

• Indirect losses:
  – Loss of consumer confidence in poultry products
  – Costs to prevent, manage or eradicate the disease
  – Effect on trade

• HPAI negatively impacts the livelihoods of millions of people especially the rural poor

• Early and successful control of AI requires an accurate and rapid diagnosis
Control of Avian Influenza

• In most counties, LPAI and HPAI are not common so prevention is the primary goal
• Surveillance and diagnostics

• When AI occurs, eradication is the overall objective
  – Quarantine, depopulation, cleaning and disinfection

• Appropriate biosecurity
  – Control human traffic
  – Introduction of new birds into flock
  – Avoid open range rearing in waterfowl prevalent areas

• Vaccination can be used as part of a control program during an outbreak

• Wide variation among countries in regards to veterinary diagnostics and animal health infrastructure
In the USA

- HPAI is rare
  - 1924-25: Classic Fowl Plague (H7N7?), New England and upper Midwest states
  - 1929: Classic Fowl Plague (H7N7?), New Jersey
  - 1983-84: H5N2, Pennsylvania, Virginia and Maryland
  - 2004: H5N2, Texas

- H5/H7 LPAI – historically handled by companies and states; since 2005, national control program (prevent H5/7 LPNAIV $\rightarrow$ HPAIV)

- Other LPAI (H1-4, H6, H8-16) – no federal program but handled by companies and states
Summary

• Avian Influenza viruses are constantly emerging and changing, and will always be a threat to animal and human health

• Both animal and public health sectors at the national, regional and international levels should maintain vigilance in regularly detecting, reporting, and characterizing animal influenza viruses, and in assessing and managing existing and evolving health risks associated with these viruses
Thanks for your attention!