Intercontinental Spread and Strategies to Control Highly Pathogenic Avian Influenza Outbreaks

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Avian Influenza

• Orthomyxovirus with protein projections on the surface:
  – 16 hemagglutinin subtypes (i.e. H1-H16)
  – 9 neuraminidase subtypes (i.e. N1, N2, N3....N9)
  – Thus named: H5N1, H9N2, H5N2, etc.

• Vary in disease production (chickens):
  – Low pathogenicity (LP): local - mild respiratory disease and egg drop – (H1-16)
  – High pathogenicity (HP): systemic - deadly disease (some H5 & H7)

• Can infect a variety of poultry and wild birds species, depending on virus strain
1. Global Control for HPAI

Eradication is historical strategy for HPAI

Historical “Stamping-out” Program:

• Enhanced biosecurity → prevent HPAI introduction onto naïve farms or from leaving affected farms; movement control essential

• Diagnostics and surveillance → quickly find HPAI

• Elimination of infected poultry (culling) → stamp-out HPAI action plan

• Education → your individual responsibility and high compliance rate

• Decreasing host susceptibility (vaccines/vaccination) → temporary solution (5 of 40 outbreaks) (Preventative or Management of Diseases)
1.1 AIV Ecology/Epidemiology: Dogma

- Outdoor rearing
- Outdoor access
- Wild bird access to buildings
- Environmental exposure

LPAIV (H1-16)

Exposure

Adaptation

HA Mutation

HPAIV (H5/H7)

e.g.: H7N8 USA 2016
H5N2 USA (1983-84)
H7N3 Mexico (2012-)

e.g.: H9N2 Middle East, Asia, N. Africa
H5N2 Mexico & Central America
1.2. 40 HPAI Disease Events

<table>
<thead>
<tr>
<th>Year</th>
<th>Country</th>
<th>Virus Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>1959</td>
<td>Scotland</td>
<td>H5N1</td>
</tr>
<tr>
<td>1961</td>
<td>S. Africa</td>
<td>H5N3</td>
</tr>
<tr>
<td>1963</td>
<td>England</td>
<td>H7N3</td>
</tr>
<tr>
<td>1966</td>
<td>Canada</td>
<td>H5N9</td>
</tr>
<tr>
<td>1975</td>
<td>Australia</td>
<td>H7N7</td>
</tr>
<tr>
<td>1979</td>
<td>Germany</td>
<td>H7N7</td>
</tr>
<tr>
<td>1979</td>
<td>England</td>
<td>H7N7</td>
</tr>
<tr>
<td>1983-84</td>
<td>USA</td>
<td>H5N2</td>
</tr>
<tr>
<td>1983</td>
<td>Ireland</td>
<td>H5N8</td>
</tr>
<tr>
<td>1985</td>
<td>Australia</td>
<td>H7N7</td>
</tr>
<tr>
<td>1991</td>
<td>England</td>
<td>H5N1</td>
</tr>
<tr>
<td>1992</td>
<td>Australia</td>
<td>H7N3</td>
</tr>
<tr>
<td>1994</td>
<td>Australia</td>
<td>H7N3</td>
</tr>
<tr>
<td>1994-95</td>
<td>Mexico</td>
<td>H5N2</td>
</tr>
<tr>
<td>1995 &amp; 2004</td>
<td>Pakistan</td>
<td>H7N3</td>
</tr>
<tr>
<td>1997</td>
<td>Australia</td>
<td>H7N4</td>
</tr>
<tr>
<td>1997</td>
<td>Italy</td>
<td>H5N2</td>
</tr>
<tr>
<td>1996-present</td>
<td>Eurasia/Afr./N.</td>
<td>H5Nx (including N1, N2, N3, N5, N6, N8 reassortants)</td>
</tr>
<tr>
<td>1999-2000</td>
<td>Italy</td>
<td>H7N1</td>
</tr>
<tr>
<td>2002</td>
<td>Chile</td>
<td>H7N3</td>
</tr>
<tr>
<td>2003</td>
<td>Netherlands</td>
<td>H7N7</td>
</tr>
<tr>
<td>2004</td>
<td>USA</td>
<td>H5N2</td>
</tr>
<tr>
<td>2004</td>
<td>Canada</td>
<td>H7N3</td>
</tr>
<tr>
<td>2004</td>
<td>S. Africa</td>
<td>H5N2 (ostriches)</td>
</tr>
<tr>
<td>2006</td>
<td>S. Africa</td>
<td>H5N2 (ostriches)</td>
</tr>
<tr>
<td>2005</td>
<td>N. Korea</td>
<td>H7N7</td>
</tr>
<tr>
<td>2007</td>
<td>Canada</td>
<td>H7N3</td>
</tr>
<tr>
<td>2008</td>
<td>England</td>
<td>H7N7</td>
</tr>
<tr>
<td>2009</td>
<td>Spain</td>
<td>H7N7</td>
</tr>
<tr>
<td>2011-3</td>
<td>S. Africa</td>
<td>H5N2 (Ostriches)</td>
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<tr>
<td>2012</td>
<td>Chinese Taipei</td>
<td>H5N2</td>
</tr>
<tr>
<td>2012-present</td>
<td>Mexico</td>
<td>H7N3</td>
</tr>
<tr>
<td>2012</td>
<td>Australia</td>
<td>H7N7</td>
</tr>
<tr>
<td>2013</td>
<td>Italy</td>
<td>H7N7</td>
</tr>
<tr>
<td>2013</td>
<td>Australia</td>
<td>H7N2</td>
</tr>
<tr>
<td>2015</td>
<td>England</td>
<td>H7N7</td>
</tr>
<tr>
<td>2015</td>
<td>Germany</td>
<td>H7N7</td>
</tr>
<tr>
<td>2015</td>
<td>France</td>
<td>H5Nx</td>
</tr>
<tr>
<td>2016</td>
<td>USA</td>
<td>H7N8</td>
</tr>
<tr>
<td>2016</td>
<td>Italy</td>
<td>H7N7</td>
</tr>
</tbody>
</table>

§ Vaccine used in the control strategy
- H5 Gs/GD largest & longest running since 1920-30
- 1996-2014: 68 countries in poultry, wild birds or humans
- >500m poultry died/culled by mid-2005, >$10B in losses
- Focused in Old World, Northern Hemisphere
1.3 Ecology/Epidemiology: Gs/GD HPAIV

- Outdoor rearing
- Outdoor access
- Wild bird access to buildings
- Environmental exposure

LPAIV (H1-16)

Exposure
Adaptation

HA Mutation

HPAIV (H5/H7)

A/goose/Guangdong/1/1996 lineage is unique in affecting domestic poultry (including waterfowl) and wild aquatic birds
1.4 H5N1 Gs/GD HPAI

- Triad: wild aquatic birds with smallholder and commercial integrated poultry
- Asymptomatic HPAIV-infected domestic ducks have become a major player, and in some locations a reservoir of HPAIV
  - Free-ranging production creates challenges:
    - Minimal movement controls
    - Intermixing with wild waterfowl
    - Short window of availability for vaccination
    - Difficulty in giving 2 immunizations
  - Vaccination has become problematic – lack of consistent disease has reduced farmer support of vaccination
H5 GS/GD HPAIV EPIDEMIOLOGY

Infected Poultry (most HPAIV)

Naïve Commercial Poultry

Periurban birds

Village Poultry

Wild or Domestic Waterfowl

Fomites (clothing, shoes & equipment - mechanical)
1.5 Gs/GD HPAIV

- Three episodes of transboundary H5Nx Gs/GD lineage HPAIV introduction by wild birds
  - 2005: Spread westward from Quinghai Lake China to Europe
  - 2010: Central Asia to Japan and Korea
  - 2014-15: China to Korea/Japan to Russia, Europe and North America

- Denial of the major contribution of HPAIV spread in country from agricultural systems
  - Blame on wild birds for majority of HPAIV spread
  - Legal and illegal movement/trade of live poultry main risk factor in spread
  - Blame all legal trade on meat as high risk even with OIE code mitigations for risk reduction
1.6. NDV - historical surrogate global poultry disease, but without severe public health concern

Jan-June 2015

July-Dec 2015

80 countries: NDV; active, suspect or unresolved

(75 poultry or wild birds & poultry, 5 wild birds only)
Summary 1

• Traditional Stamping-out Programs have not eliminated/eradicated H5 Gs/GD HPAIV from the globe, and its “persistence” has changed all control paradigms
  – Some countries have eliminated/eradicated but a reservoir in other countries maintains the virus for resurgences, including reintroductions
  – Staging for global elimination/eradication: risk reduction and control strategies
  – Maintain food security – vaccination stop gap measure
  – Upgrading production systems or HPAIV will become as NDV has since 1920’s
• Since 1996 – H5N1 hemagglutinin gradual changes – e.g. DRIFT (like seen with human seasonal flu)
2.1. Distribution of H5 Gs/GD Subclades

H5N1 HPAI (22)

Bangladesh  Japan
Bhutan        N. & S. Korea
Cambodia      Laos
Canada        Libya
China         Nepal
Egypt         Netherlands
Germany       Russia
Hong Kong     United Kingdom
India         USA
Indonesia     Vietnam
Italy

6 genetic clades
1.1.2, 2.1.3.2, 2.2.1, 2.3.2.1, 2.3.4.4, 7.2

Epicenter – S. Central & SE Asia, & NE Africa

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2.1. One Predictable Issue About Avian Influenza Viruses – They Change

**Drift**

<table>
<thead>
<tr>
<th>Subclade</th>
<th>Poultry/Wild Birds Infections</th>
<th>Human Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1.2</td>
<td>Cambodia, Viet Nam</td>
<td>Cambodia (7)</td>
</tr>
<tr>
<td>2.1.3.2a</td>
<td>Indonesia</td>
<td></td>
</tr>
<tr>
<td>2.2.1</td>
<td>Egypt, Libya</td>
<td>Egypt (4)</td>
</tr>
<tr>
<td>2.3.2.1a</td>
<td>Bangladesh, India</td>
<td>Cambodia</td>
</tr>
<tr>
<td>2.3.2.1c</td>
<td>China, Indonesia, Lao, Viet Nam</td>
<td>Indonesia (1)</td>
</tr>
<tr>
<td>2.3.4.4</td>
<td>China (H5N1/N6/N8), Japan &amp; Korea (Rep.) (H5N8); Lao (H5N6), Viet Nam (H5N6/N1), Canada Chinese Taipei, USA</td>
<td>China (H5N6) (1)</td>
</tr>
<tr>
<td>Unknown</td>
<td>Korea (Dem. Peoples Republic)</td>
<td>Indonesia (1)</td>
</tr>
</tbody>
</table>

**Shift**

**Reassortment of Genes**

- H5N1 (2.3.4.4)
- H5N2 (2.3.4.4)
- H5N3 (2.3.4.4)
- H5N5 (2.3.4.4)
- H5N6 (2.3.4.4)
- H5N8 (2.3.4.4)

**Outcome:** Gene reassortment (e.g. Shift) with H5N2, H5N3, H5N5, H5N6, H5N8 emerging in Asia and North America

**Avian Influenza Viruses from Wild Birds and Live Poultry Markets**
Recent:

- H5N8 HPAI outbreaks in poultry and wild birds – S. Korea & Japan, winter 2014
- Spring 2014 virus moved to Siberia and west Alaska
- Fall 2014: H5N8 appeared Europe (IcA1), North America (IcA2)
- Fall 2014: Reassortant H5N2 and H5N1 in North America
12/8/2015 to 6/17/2015 – H5 HPAIV in wild bird, backyard poultry and commercial poultry

Midwest: Central/MS flyways

• 311 detections (4 captive wild bird; 21 backyard; 211 commercial flocks, 75 wild birds)
  • 21 states affected (AR, CA, IA, ID, IN, KS, KY, MI, MN, MO, MT, NE, ND, NM, NV, OR, SD, UT, WA, WI, WY)
  • ~48.6 million commercial birds: Turkeys ~7.5 million (n=153), Chickens ~41.1 million (n=47)
Lesser Snow Goose (Chen caerulescens)
Northern Shoveler (Anas clypeata)
Ring-necked Duck (Aythya collaris)

Cinnamon Teal (Anas cyanoptera)
H5Nx North America

Infectivity assess: via BID50

<table>
<thead>
<tr>
<th>Species</th>
<th>log_{10} EID50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mallards</td>
<td>&lt;2</td>
</tr>
<tr>
<td>Ducks (D.)</td>
<td>3</td>
</tr>
<tr>
<td>Chickens</td>
<td>4.3</td>
</tr>
<tr>
<td>Turkeys</td>
<td>5.0</td>
</tr>
</tbody>
</table>

3 genes (HA, M, PB2)
H5Nx North America

• Initial spread by wild waterfowl
• Later, farm-to-farm human activity

269 viruses, 3 genes (HA, M, PB2)
• 35 epizootics used stamping-out alone, but 5 epizootics added vaccination as a additional control component
• Vaccination - immediate positive impact on HPAI prevention & management (disease & mortality)
• But stamping-out alone was associated with shorter eradication times than stamping-out + vaccination programs (Pavade et al. OIE Sci Tech Rev 30:661-671, 2011)
• HPAI vaccination can be associated with complacency
14 countries vaccinated poultry against HPAI (2002-2010)

- Preventive (<0.2%): Mongolia, Kazakhstan, France, The Netherlands
- Emergency (<0.8%): Cote d’Ivoire, Sudan, PDR Korea, Israel, Russia, Pakistan
- National/routine (>99%): China (including HK), Egypt, Indonesia and Vietnam, plus added Bangladesh and Mexico
What Can Vaccines Do?

Increase resistance to AIV infection
Reduce replication of AIV in respiratory & GI tract
Prevent illness and death in poultry

Result: Vaccines manage disease

Negative: Makes diagnosis and surveillance difficult
What is needed to have effective LPAI or HPAI vaccination program?

1) High potency vaccine
2) Antigenically relevant vaccine seed strains
3) Proper vaccination program
4) Adequate number of vaccinations
5) Monitor vaccinated populations for protective titers
6) Survey vaccinated populations to find vaccine resistant AIV (‘DIVA’)
Risk Factors for Delayed Eradication

OIE Performance of Veterinary Services (PVS) tool: Higher critical competencies associated with better HPAI control:

• Staffing of veterinarians and paraveterinarians
• Professional competencies & continuing education of vets
• Emergency funding
• Veterinary laboratory diagnosis
• Epidemiological surveillance
• Availability of veterinary medicines and biologicals
• Transparency
• Disease prevention, control and eradication measures

Outcome:

• Higher PVS scores were associated with shorter time to eradication, fewer outbreaks, lower mortality rate, and higher culling rate
Summary 2

• What is limiting elimination/eradication
  – Low biosecurity/movement control of small
    holder/live poultry market system
  – Lack transparency & lapses in biosecurity of
    commercial integrated production system
  – Lack of effective compensation system
  – Inadequate national, Provincial/State and/or local
    veterinary services
  – Limited outside resource funding long term: e.g.
    donor fatigue
  – Need for effective restructuring of national
    poultry production systems (long-term)
  – Inadequate/inflexible vaccination programs
Global Improvements in Last 10 Years

- Rapid Diagnosis – RRT-PCR accelerated speed and accuracy
- Increased usage of indemnification
- Rapid depopulation – CO2 (whole house and plastic tent methods) and foam
- Safe Disposal – composting or burial
- Re-invigorated veterinary infrastructure
- Partnerships (trust): government/academia/industry
- Improved surveillance methods (poultry & wild birds)
- Emergency response plans and exercising
- Regionalization of poultry trade
Challenges for Future

• Consistent practice of biosecurity: Are we doomed to repeat the mistakes of the past?
  – Economics
  – Social structure
  – Low education of workers and farmers

• Vaccines for emergency verses routine use – when & how

• Resurgence of outdoor rearing in developed and developing countries: Partnership, trust and education in outdoor rearing systems for risk reduction and early detection

• Movement controls and LPM system

• Early warning system in wild bird detections
Conclusions

• Biosecurity is critical in control and eradication
• Eradication requires strong veterinary services, movement controls, and high level of buy-in and observance by growers
• Eradication HPAI is not achievable in immediate future in developing world
  – Large number of small producers
  – Lack of fair and fast compensation system
  – Live market systems disfavors movement control system and biosecure production
• Prevention is critical in non-affected countries
Conclusion

Prevention

• Enhance biosecurity on farms after audits on each farm to prevent introduction
• Movement controls/restrictions
• Increased surveillance for earlier detection, quarantine and stamping-out
• Quick depopulation of infected premises (24hr)
• Safe disposal of carcasses and litter
• Vaccine bank for high risk areas
Merci Beaucoup!