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Safeguarding Animal Health
Influenza: Biology

- Three types of influenza viruses: A, B, C & D
- Type A infects birds, humans, swine, and other mammals
- Type A classified into subtypes by its surface proteins:
  - Hemagglutinin (H)
  - Neuraminidase (N)
- Type B infects primarily humans, but detected in dogs and swine
- Type C infects primarily humans
- Type A may cause outbreaks, epidemics, & pandemics;
- Type B may cause outbreaks and epidemics but not pandemics;
- Type C rarely causes either but results in outbreaks
- Type D has only been detected in cattle and swine
Influenza: Biology - Type A

- Surface proteins (antigens):
  - H or HA – Hemagglutinin
  - N or NA – Neuraminidase
- 16 HA subtypes (avian)
- 9 NA subtypes (avian)
- 144 known characterizations
- H17N10 and H18N11 (bats)
Enveloped virus
Segmented genome
Single-stranded (-) sense RNA
8 genes coding for 11 proteins
Influenza Nomenclature

World Health Organization (WHO) Influenza Nomenclature

Influenza type

Year of isolation

Hemagglutinin subtype

Geographic source

Isolate number

Neuraminidase subtype

A/Panama/2007/99 (H3N2)

Influenza type B does not occur as subtypes.
Species Affected

Genetic Reservoirs

Intermixing

H1, H2, H3

H1, H3, H4, H7, H13

H10

H3, H7

H5N1 \textarrow{} H7N9

Commercial, LBMs Others

H17, H18

H1-12

H14-15

H1-2, 4-7, H9-13, 15-16

Other Aquatic Birds?

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Host Preference – Receptor Biology

Mammalian respiratory epithelium has α-2,6 linkages preferred by Mammalian influenza viruses

Avian gastrointestinal epithelium has α-2,3 linkages preferred by avian influenza viruses

Swine (quail?) respiratory epithelium has a mixture of α-2,3 and α-2,6 linkages, so both avian and mammalian strains can infect; quail also have α-2,3 and α-2,6 links and are thought to adapt strains
Influenza: Antigenic Drift

- Small, modest changes in viral characteristics at a predictable rate
- Point mutations in the viral RNA (e.g. hemagglutinin gene)
- Accumulate in the normal process of viral replication
- Mutation rates for RNA viruses high (RNA polymerase)
Influenza: Antigenic Drift

Point mutation analogy:
“The reading was incorrect for the instrument”
“The reeding was incorrect for the instrument”
Influenza: Antigenic Shift

- Radical change in antigens or host preference
- Three mechanisms of antigenic shift:
  1. Reassortment – gene exchange occurs between two differing influenza viruses co-infecting the same host
  2. Direct transfer – a virus adapted to one species jumps directly into another (e.g. avian HPAI H5N1 -> Humans or equine H3N8 -> dogs)
  3. Re-emergence - a previously prevalent influenza virus infects a now naïve host population (H1N1 Russian lab strain escape outbreak)
Influenza: Antigenic Shift - Reassortment

2. Antigenic Shift

H3N2

H5N1

HA

NA

8 RNA segments

membrane

cell

possible new virus from genetic reassortment

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Influenza: Antigenic Shift - Reassortment

History of Antigenic Shift

SEROARCHEOLOGY 1933  VIRUS ISOLATION

1933

1889 H2N2 1900 H3N8 1918 SPANISH H1N1 1950

1957 ASIAN H2N2 1968 HONG KONG H2N2

1977 RUSSIAN H1N1

Influenza virus first isolated

1933 - 1950

1977

1889 H2N2 1900 H3N8 1918 SPANISH H1N1

1957 ASIAN H2N2 1968 HONG KONG H2N2

RUSSIAN H1N1

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Avian Influenza Classification

- Based on behavior in land-based poultry:
  1. Highly pathogenic avian influenza (HPAI)
  2. Low pathogenicity avian influenza (LPAI)

- **HPAI** – severe illness with high mortality
- **LPAI** – mild/subclinical illness and production loss with low mortality
Interspecies Transmission in Birds

- LPAI viruses are host adapted to waterfowl
- LPAIVs usually replicate poorly in new hosts (chickens, turkeys)
- LPAI viruses require adaptation to new hosts to sustain transmission

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Frequently associated with mutation of the hemagglutinin precursor (pantropism)
Other viral proteins may convey increased pathogenicity (e.g. NS1)
All HPAI viruses to date have been H5 or H7 subtypes (H9 may act like HPAI)
**However,** not all H5 or H7 subtypes are HPAIs, many are LPAIs
HA Cleavage Site for LPAI and HPAI

HA0: Whole Hemagglutinin Protein

- LPAIs have single basic amino acid cleavage points
- HPAIs have multiple basic amino acid cleavage points

- HA0 whole protein cleaved by host cellular proteases or furins (enzymes)
- Human influenza viruses and LPAIs have single cleavage points
- Each cell type (respiratory or intestinal epithelium) has a unique protease capable of cleaving at that single point, so the virus only replicates efficiently in that cell type
- HPAIs have multiple cleavage points that convey “pantropism”, or the ability to replicate in multiple atypical cell types (e.g. liver, spleen, kidney, etc.)
- Therefore, the virus can achieve systemic replication
Multiple cleavage points in the H0 precursor protein or any genetic resemblance to previously described HPAI viruses

High pathogenicity with virus challenge of chicks – IVPI or intravenous pathogenicity index: infect ten 4-8 week old SPF chicks and observe for 10 days – HPAI if IVPI ≥ 1.2 or ≥ 75% of birds die
Movements paths of wildfowl species (no. of birds) monitored by satellite telemetry during 2006–2009 over three main wildfowl migratory flyways (Black Sea-Mediterranean, Central Asian and East Asian flyways) and the inter-tropical African region. For a detailed list of birds monitored see Table S1 (Supporting information). *Afro-tropical ducks: spur-winged goose, comb duck, white-faced and fulvous whistling ducks; Egypt ducks: common teal, Northern pintail and Northern shoveler; Kazakhstan ducks: common teal, gadwall, mallard, Northern shoveler; India ducks: common teal, Eurasian wigeon, gadwall, garganey, Northern pintail and Northern shoveler; Hong Kong ducks: Eurasian wigeon and Northern pintail; Poyang Ducks: Baikal teal, Chinese spotbill duck, common teal, Eurasian wigeon, falcated teal, garganey, mallard and Northern pintail. (Map by M. Ge´ly ©)
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• First reported 1996 - Quiescent after 1997 - Re-emerged 2003 (Lake Quinghai)
• Multiple clades/subclades - More virulent and adapted to land-based poultry
• 1\textsuperscript{st} time HPAI isolated from wild birds in significant numbers
• Showing potential to adapt to waterfowl (Russia – Siberia, 2015)
Transmission/Reservoirs in Southeast Asia

- Domestic waterfowl are kept on open ponds and “herded” to glean rice chaff; one likely reservoir
- Commercial chickens appear to be key in movement of virus and transmission
- Backyard poultry a “symptom” of the problem, serve to infect humans but not really viral movement
- Both vaccinated and unvaccinated birds may harbor virus
AI – Movement & Maintenance

- Chicken & ducks/products key in large distances
- Commercial poultry key in movement and maintenance
- Local outbreaks in migratory and select domestic birds
- Adapted strains can move long distance in wild waterfowl
- Species/Strain Adaptation and Re-Transmission
- LPAI data shows delayed migration; shorter flights
Chronology of Evolution of Eurasian HPAI H5N8

- Eurasian HPAI H5N1 is the progenitor virus of reassortants H5N2, H5N3, H5N5, H5N6, and H5N8
- H5N8 progenitor reported in China in 2010 in domestic ducks
- JAN 2014, H5N8 precipitated outbreaks in South Korea and effectively eradicated by MAY 2014
- Catastrophic mortality in poultry and some wild bird species (Baikal teal)
- H5N8 precipitates outbreaks in poultry in Germany, The Netherlands, and the UK in fall 2014
- Late NOV 2014, turkeys in British Columbia, Canada began to die due to infection by an H5 virus of Eurasian origin
- Canadian virus determined to a reassortant between Eurasian H5N8 and an endemic North American LPAI N2 virus creating Eurasian/North American HPAI H5N2
- DEC 2014, waterfowl in Whatcom Country, Washington State; dying from Aspergillosis secondary to lead intoxication; found incidentally infected with EA H5N8 and EA/NA H5N2
H5 HPAI reports from East Asia
September 2014 through February 2015 (OIE)

Reports of H5 HPAI subsided in the region during summer 2014. Then in September, outbreaks of H5N1, H5N2, H5N6, H5N8 HPAI occurred in China.

Original H5N8 outbreak occurred January-April, 2014, most intensely in S. Korea and Japan. After 5 months with no reported cases, H5N8 was detected again, 24 September, in S. Korean commercial poultry. It was detected again in Japan in November.

H5N2, H5N3, H5N8 outbreaks occurred in Taiwan in early 2015.
H5 HPAI reports from Europe, Middle East, and Africa
November 2014 through February 2015 (OIE)

Western Europe

H5N8 was first isolated 4 November 2014 from commercial poultry in Germany; also isolated in November from a wild duck.

By mid-December, H5N8 was isolated from commercial poultry in The Netherlands, United Kingdom, and Italy.

Eastern Asia

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Migratory aquatic birds – likely mode for H5N8 HPAI virus
spread to Europe in fall 2014

Several migratory flyways overlap extensively in northern Eurasia during
the breeding season. H5N8 virus carried there from East Asia in the
spring could have been transferred to other birds that migrate south into
Europe in the fall.

H5N8 may be better suited for long-distance dispersal than most strains of
HPAI.

Developed by Matt Sandbulte, PhD, CFSPH

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H5 HPAI reports from North America
November 2014 through February 2015 (OIE)

North America
- **H5N2** first isolated 30 November 2014 from commercial poultry in British Columbia; outbreak continues into 2015.
- **H5N8** first isolated 10 December 2014 from captive wild birds in Washington; later isolated from backyard poultry in Oregon. Similarly, **H5N2** identified in US wild birds and backyard poultry.
- **H5N1** first isolated 29 December 2014 from wild duck in Washington.
- **H5N8** isolated 19 January 2015 from commercial turkey farm in California.
- **H5N2** detected in poultry in Minnesota, Missouri, Arkansas & Kansas in March 2015.

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Eastern Asia
- Reports of H5 HPAI subsided in the region during summer 2014. Then in September, outbreaks of **H5N1**, **H5N2**, **H5N6**, **H5N8** HPAI occurred in China.
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H5 HPAI reports from North America
November 2014 through February 2015 (OIE)

Migratory aquatic birds – also the likely mode for H5N8 HPAI virus spread to North America

Eurasian (EA) H5N8 was likely carried to Alaska by infected birds migrating on the East Asia / Australia flyway. Within 3 months, HPAI viruses were detected in the Pacific Americas flyway and the Mississippi/Central Americas flyway.

EA H5N8 underwent gene reassortment with low pathogenicity avian influenza (LPAI) strains endemic to North American wild birds. This means a bird was co-infected at some point with the H5N8 and an American (AM) LPAI strain, enabling the 8 gene segments to be mixed and matched in new combinations.

EA/AM H5N1 and EA/AM H5N2 isolates in the western and central US were reassortants that contained genes of North American and Eurasian origin.
Asian-origin H5N1 HPAI clade 2.3.4 – Eurasian virus
Eurasian H5N8 clade 2.3.4.4
aka “Transcontinental” EA-H5N8
EA/AM H5N2-reassortant
EA-H5N8 (5 genes) / AM (3 genes)
A/Northern pintail/Washington/40964/2014 (H5N2) Genbank 1589662

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EA/AM H5N1-reassortant
EA-H5N8 (4 genes) / AM (4 genes)
A/American green winged teal/195750/Washington/2014(H5N1)
EA-H5 2.3.4.4* reassortants in North America (AM)

*All H5 2.3.4.4 viruses to date are considered highly pathogenic in poultry

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Outbreak Dynamics Winter 2014/2015

- EA H5N8 and EA/NA H5N2 appeared to be confined to the Pacific flyway
- Wild bird surveillance was extensive
- Both viruses precipitated outbreaks in domestic poultry (both backyard and commercial)
- EA H5N8 resulted in the death of captive wild avian species (gyrfalcons)
- EA H5N8 was detected throughout the Pacific flyway
- EA/NA H5N2 was largely detected in the northern portion of the Pacific flyway
- Detections in ended in poultry in FEB 2015, and wild bird surveillance was halted due to logistics of sample acquisition
Outbreak Dynamics Spring 2015

- Beginning in MAR 2015, outbreaks occurred in the Midwest and concentrated in the upper Midwest
- Outbreak pattern coincided with northward spring migration of wild waterfowl
- EA/NA H5N2 causing outbreaks
- Outbreaks largely limited to commercial turkeys and layer chickens
- Backyard poultry largely unaffected
- Wild bird detection rare
- Presumably EA/NA H5N2 emerged earlier in season that previously thought
- H5N2 detected in Pacific flyway but went undetected in the Central and Mississippi flyways until Spring 2015
- Epidemiology of poultry outbreaks not yet well elucidated
- EA H5 viruses have not yet been detected in the Atlantic flyway
Figure 9. HPAI Detections by Subtype in All Birds, as of 7/16/2015
(as reported on www.aphis.usda.gov) *one or more detections may have occurred in county
Total Number of Cases, as of 10/6/15

- Premises confirmed positive for HPAI: 232
  - 211 commercial (including 7 dangerous contact premises)
    - MN-108, IA-71, SD-10, WI-9, NE-5, CA-2, MO-2, ND-2, and AR-1
  - 21 backyard
Total Cost, as of 10/6/15

- Total indemnity commitments for flocks appraised: $200,515,123

- Total indemnity paid: $195,884,243

- Obligations for response operations on positive premises: $596,814,445
Costs and Impacts

• Direct Losses:
  • About $1.6 billion

• Economy-Wide Impact:
  • $3.3 billion

• Trade Impact:
  • 17 Trading Partners, including
    • China - $391 million
    • Russia - $153 million
    • South Korea - $123 million
Eurasian H5 Viral Ecology in Wild Birds

- Eurasian H5 viruses of clade 2.3.4.4 appear to be uniquely adapted to dabbling ducks, members of the family Anatidae, genus Anas
- Examples include mallards in their relatives, such as teal and pintail
- EA H5 viruses result in subclinical infections in these species and they shed high titers of virus for long periods of time
- The EA H5 virus outbreak epidemiology in domestic poultry is correlated with the movements of wild migratory waterfowl
- Three EA H5 viruses have been detected in North America, EA H5N8, EA/NA H5N1, EA/NA H5N2
- Waterfowl other than the Anatidae do not appear to be readily infected (4 Canada Geese; 4 Snowy Geese)
- Raptors are highly susceptible (1 peregrine falcon; ~9 gyrfalcons; 2 Cooper’s hawks; 2 Red Tailed hawks; 1 Bald eagle; 1 Snowy owl; 1 Great-horned owl)
- A single passerine (chickadee) reported in July 2015; epidemiology not yet elucidated
- National wild bird surveillance begins JUL 2015
- Focus of surveillance on hydrologic unit codes (HUCs) associated with dabbling ducks
Preparing for the 2015 Autumn and 2016 Spring Migrations

• We have to speculate about, yet prepare for the future
• EA LPAI virus genes typically diluted southward migration – unknown about EA HPAI H5
• EA H5 viruses may persist in the wild migratory waterfowl population
• Migration traditional start AUG/SEP – delayed this year due to warmer weather
• Over 15K samples tested to date in wild birds and only 1 detection in waterfowl (mallard, Utah, 31JULY)
Watersheds or HUCs to be monitored for HPAI in Wild Waterfowl

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Wild Bird Surveillance for EA H5

- Passive Ongoing
  - Bird Die-offs
- Focus dabbling ducks
  - Anatidae
- Banding sampling
  - Live birds pre-migration
- Hunter kill surveillance
  - Fall – February (depending on State)
- Estimated prevalence

Northern Pintail Ducks
QUESTIONS?