

# Invasive Species Advisory Committee October 2015



## Overview of the Viral Ecology and Epidemiology, Of the Eurasian HPAI H5 Viruses in the United States and Outbreak Response: 2014-2015

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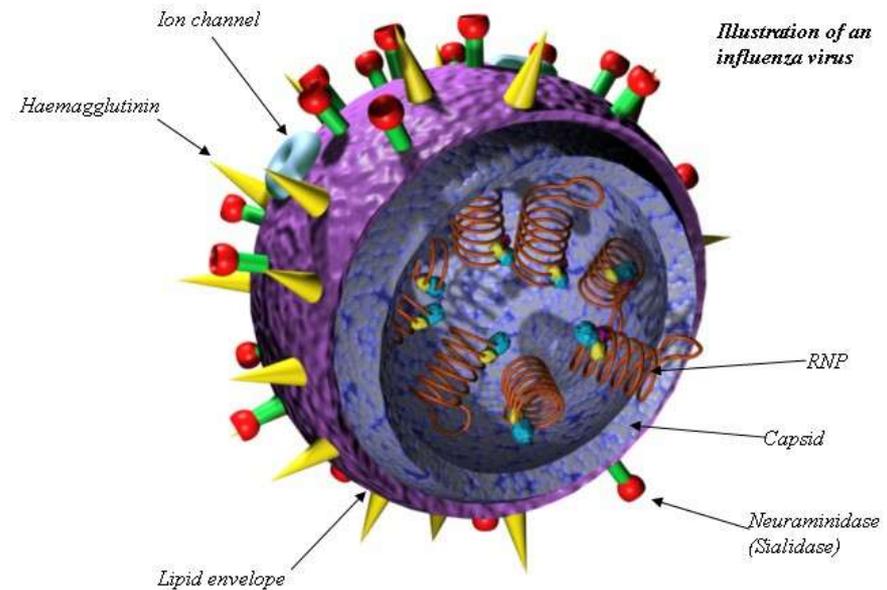
Safeguarding Animal Health



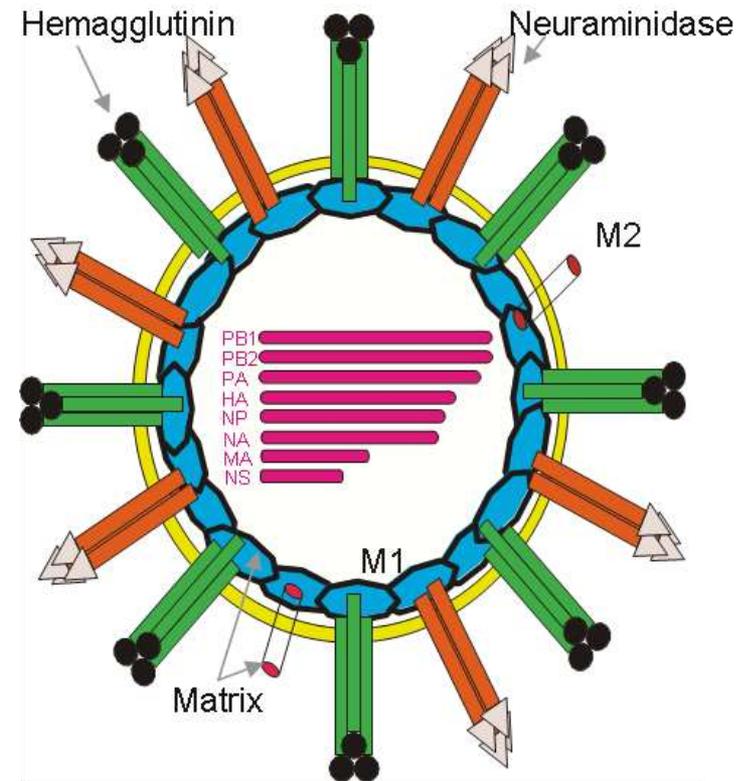
- Three types of influenza viruses: A, B, C & D
- Type A infects birds, humans, swine, and other mammals
- Type A classified into subtypes by its surface proteins:
  - Hemagglutinin (H)
  - Neuraminidase (N)
- Type B infects primarily humans, but detected in dogs and swine
- Type C infects primarily 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

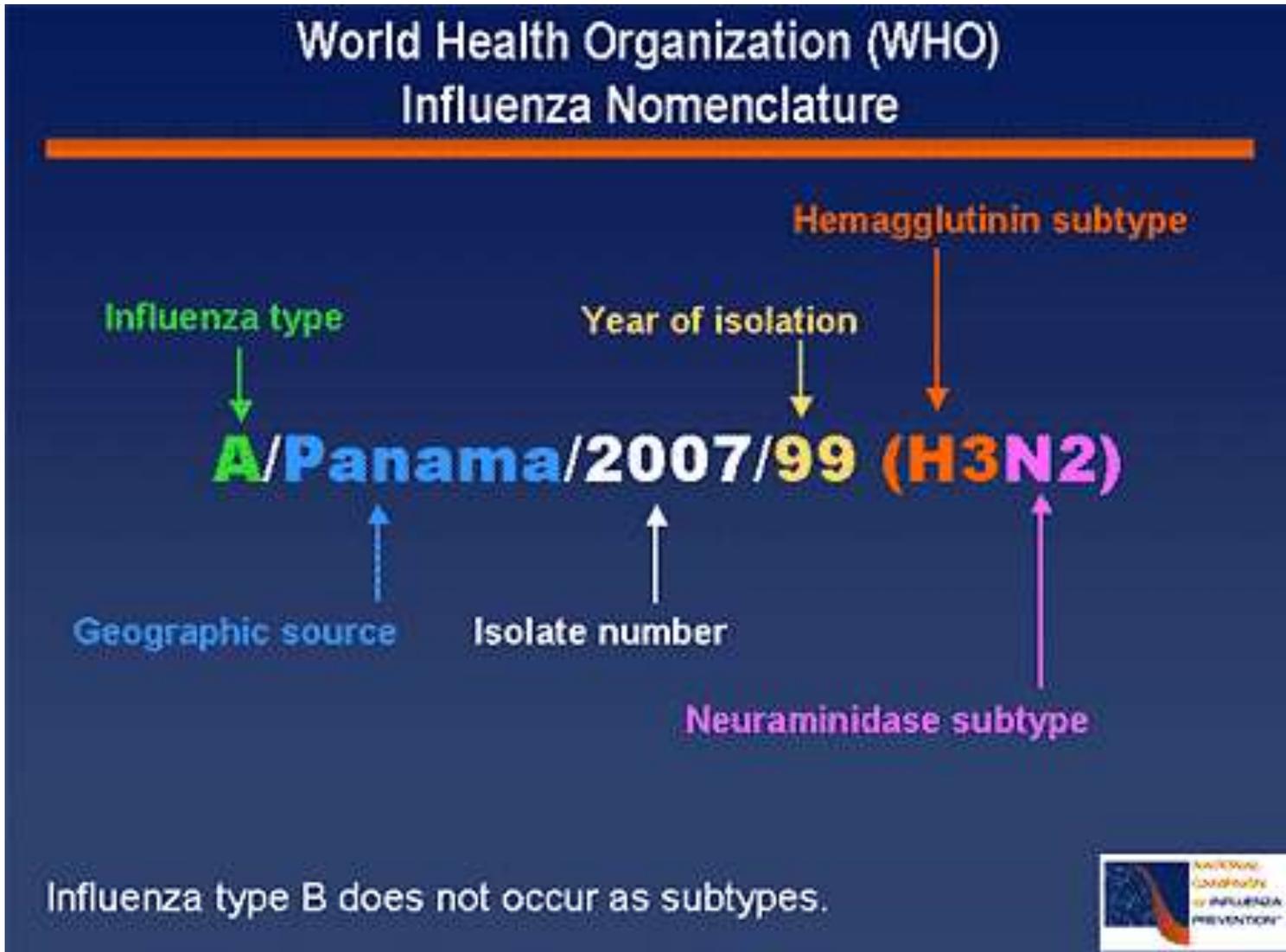
# Influenza: Biology - Type A

- 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)

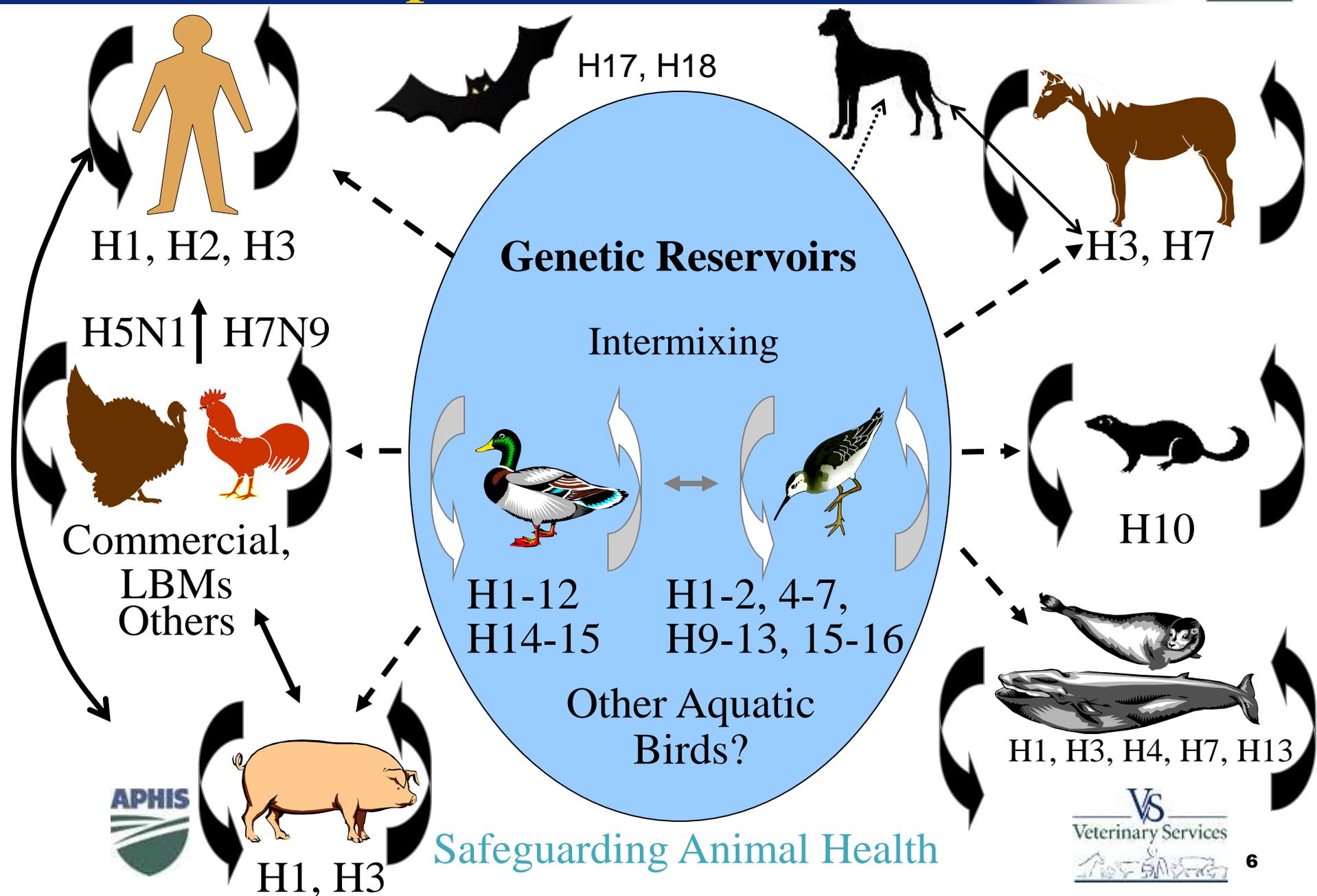


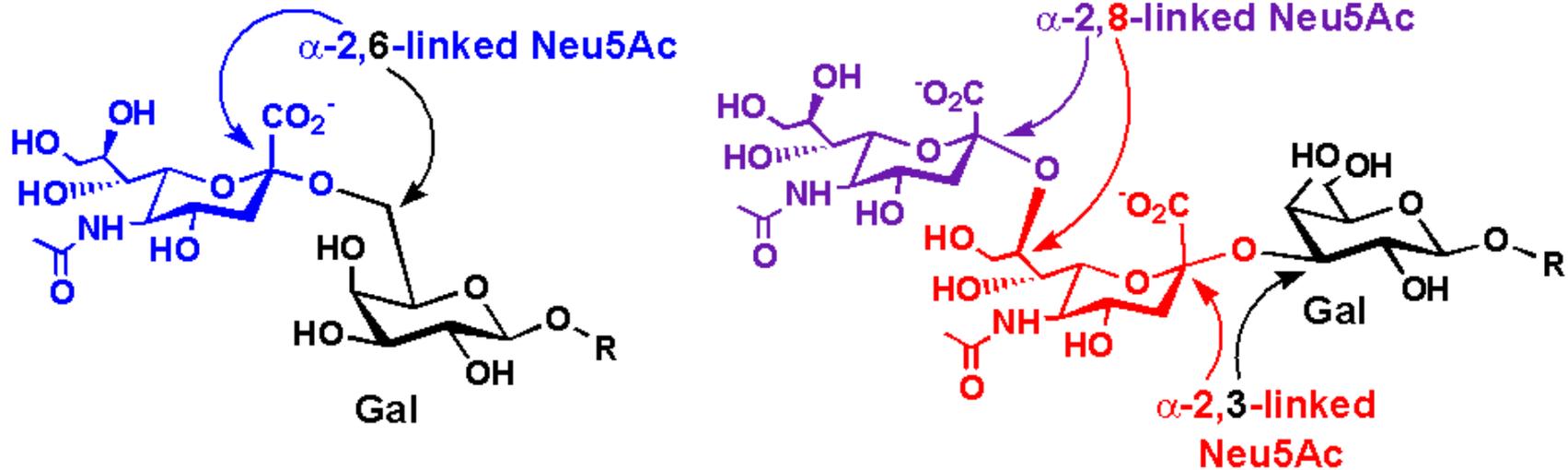
- Enveloped virus
- Segmented genome
- Single-stranded (-) sense RNA
- 8 genes coding for 11 proteins





# Species Affected





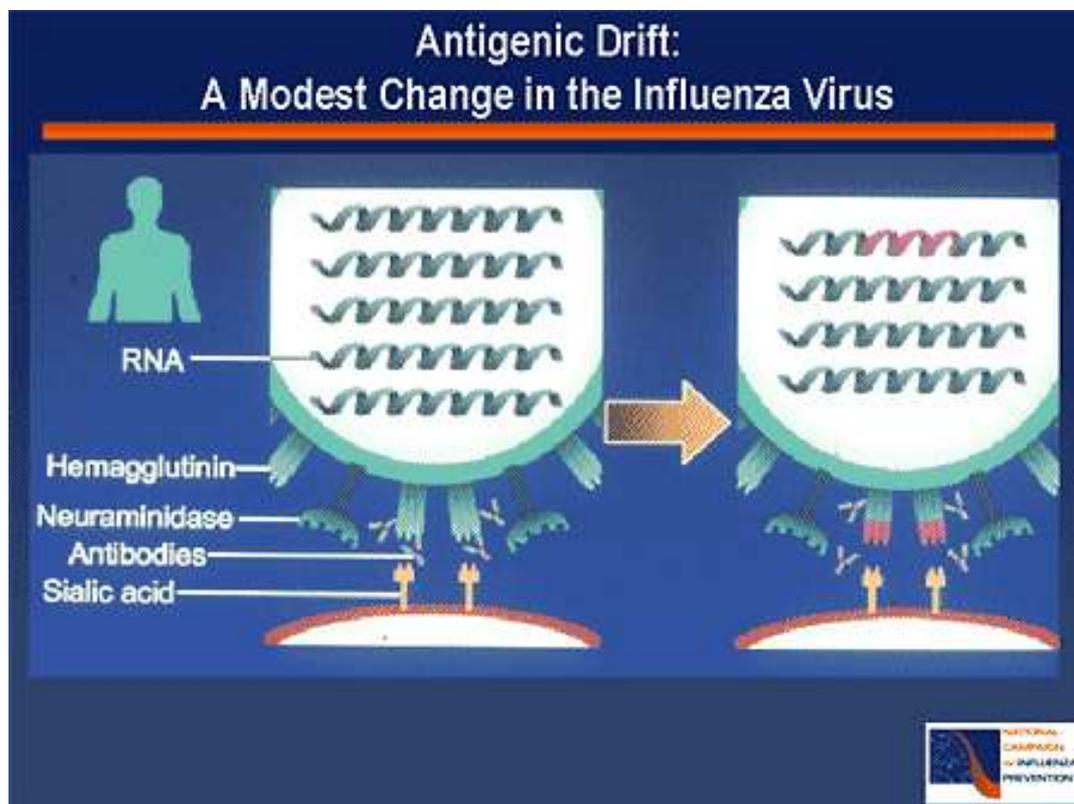
Mammalian respiratory epithelium has  $\alpha$ -2,6 linkages preferred by Mammalian influenza viruses

Avian gastrointestinal epithelium has  $\alpha$ -2,3 linkages preferred by avian influenza viruses

Swine (quail?) respiratory epithelium has a mixture of  $\alpha$ -2,3 and  $\alpha$ -2,6 linkages, so both avian and mammalian strains can infect; quail also have  $\alpha$ -2,3 and  $\alpha$ -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)



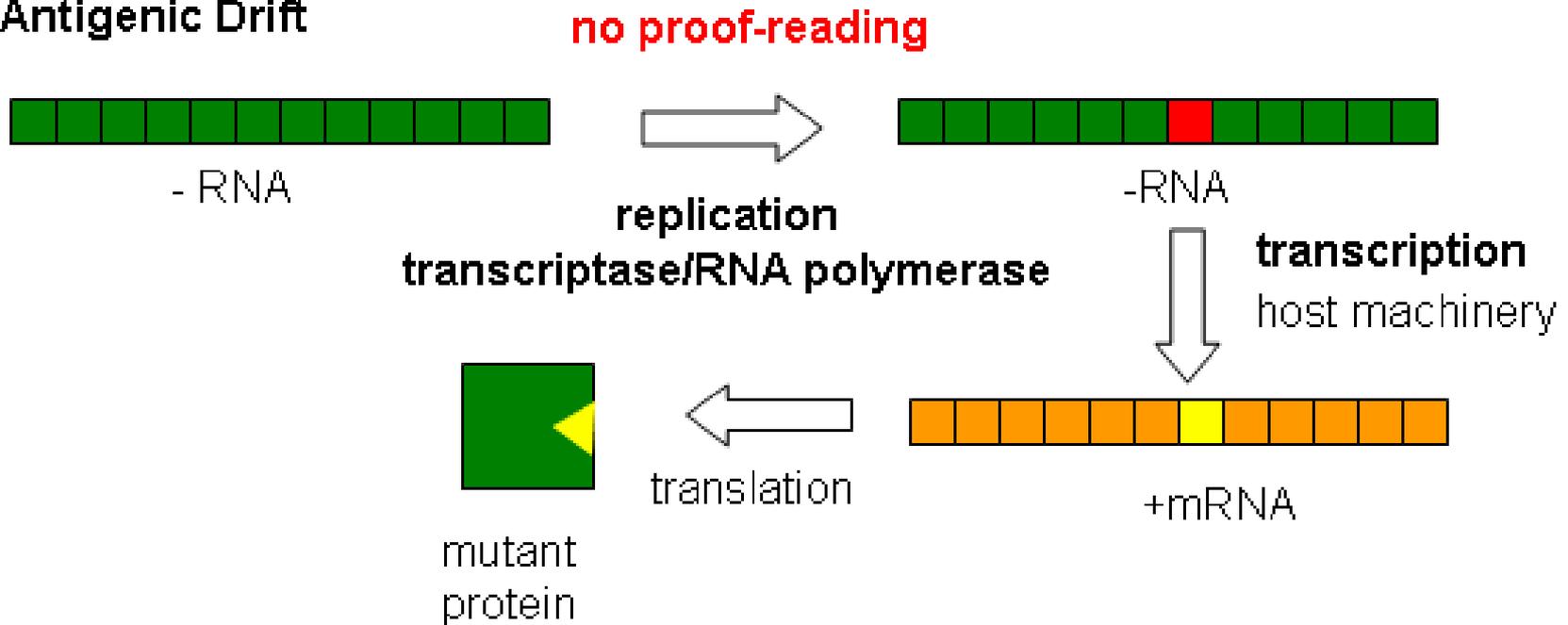
# Influenza: Antigenic Drift

Point mutation analogy:

“The **re**ading was incorrect for the instrument”

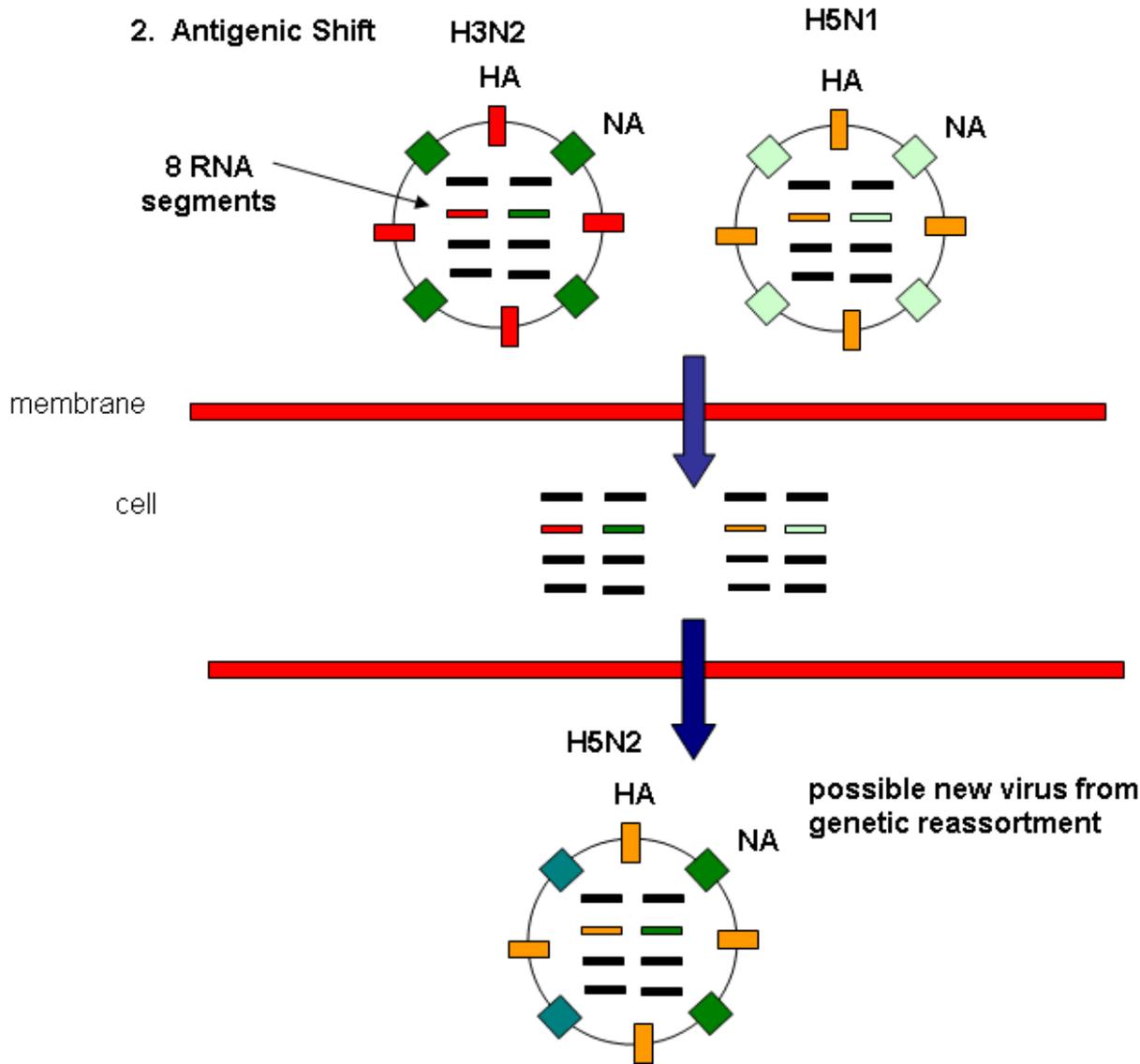
“The **re**eding was incorrect for the instrument”

## 1. Antigenic Drift

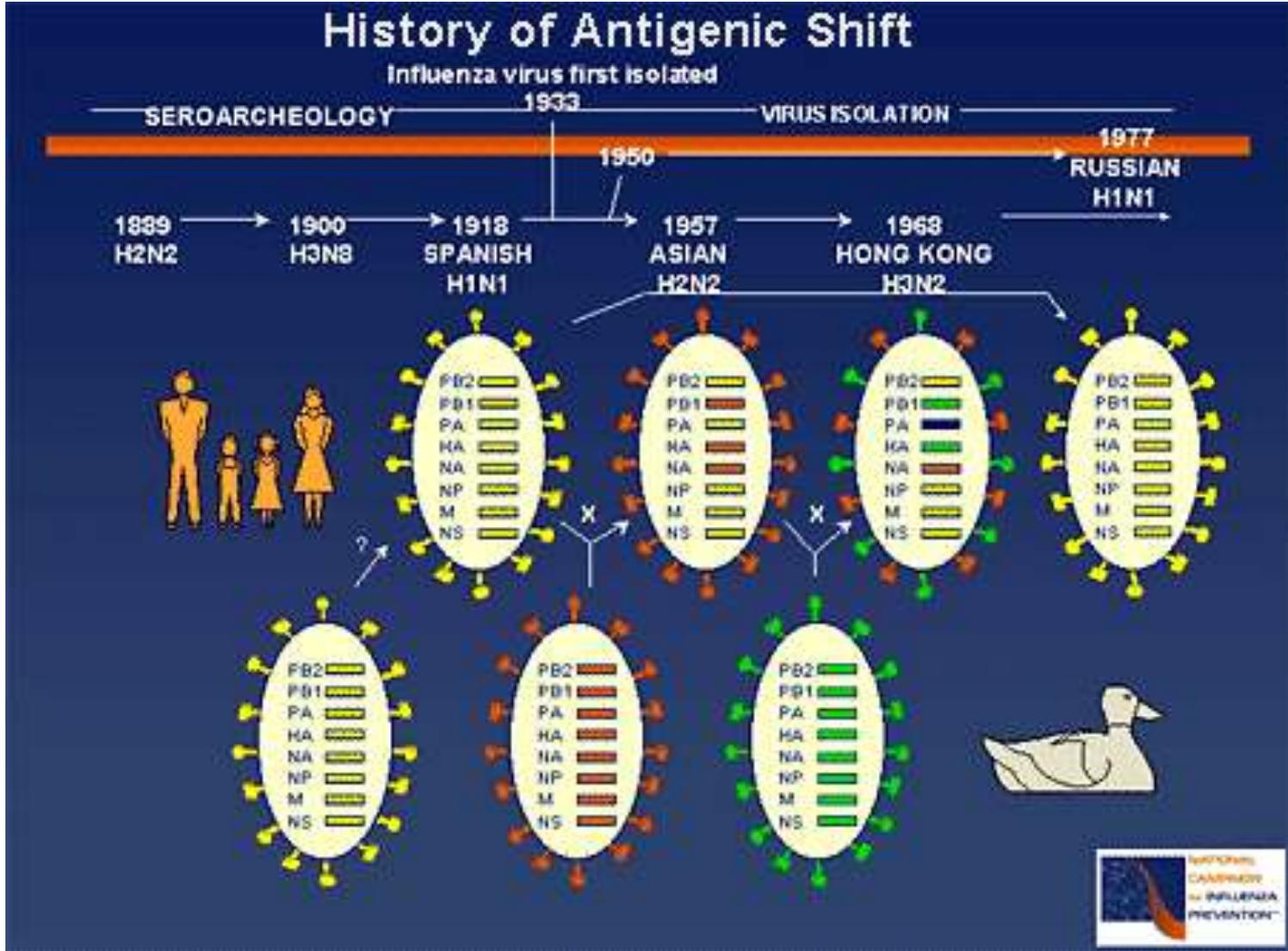


- Radical change in antigens or host preference
- Three mechanisms of antigenic shift:
  1. Reassortment – gene exchange occurs between two differing influenza viruses co-infecting the same host
  2. Direct transfer – a virus adapted to one species jumps directly into another (e.g. avian HPAI H5N1 -> 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



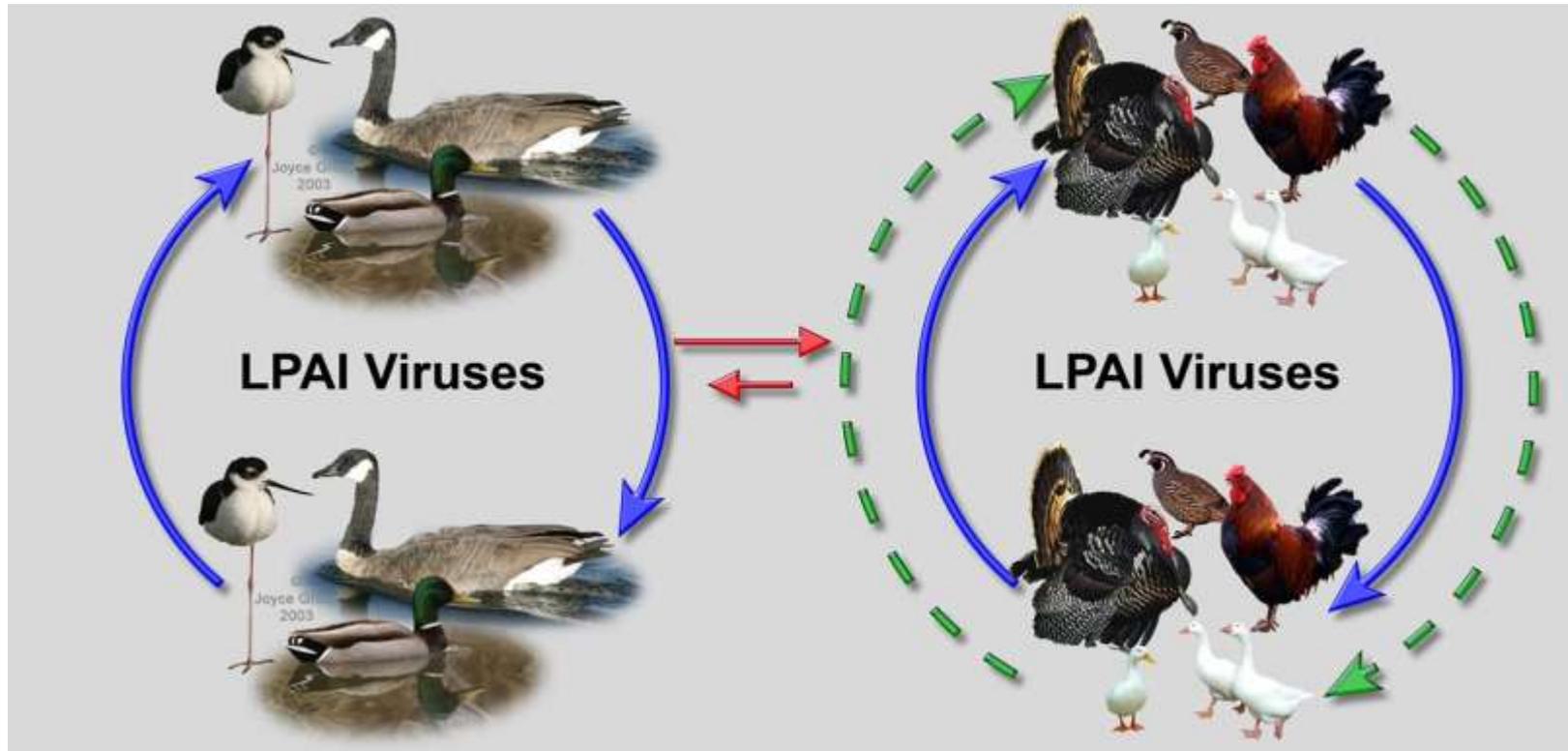
# Influenza: Antigenic Shift - Reassortment



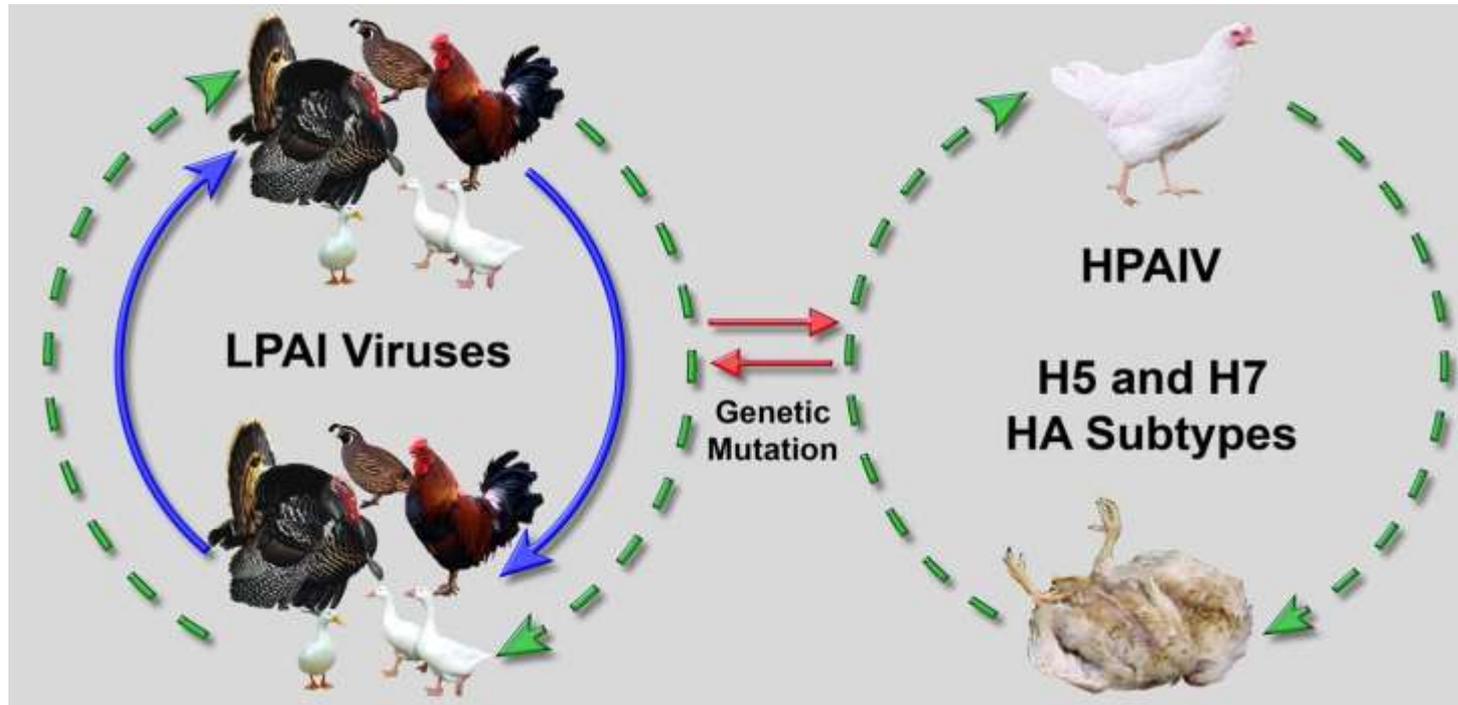
# Avian Influenza Classification

- 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





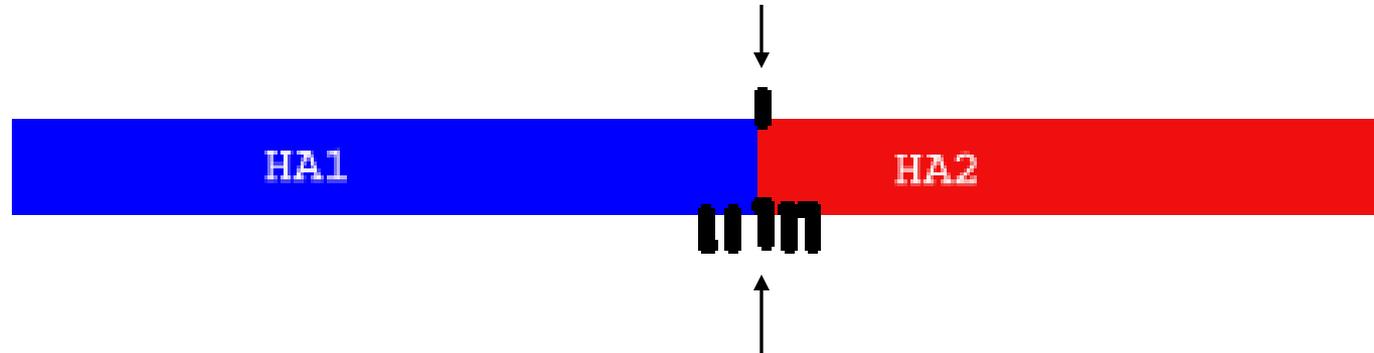
- LPAI viruses are host adapted to waterfowl
- LPAIVs usually replicate poorly in new hosts (chickens, turkeys)
- LPAI viruses require adaptation to new hosts to sustain transmission



- 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 HPAs, many are LPAs**

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

# OIE HPAI Designation



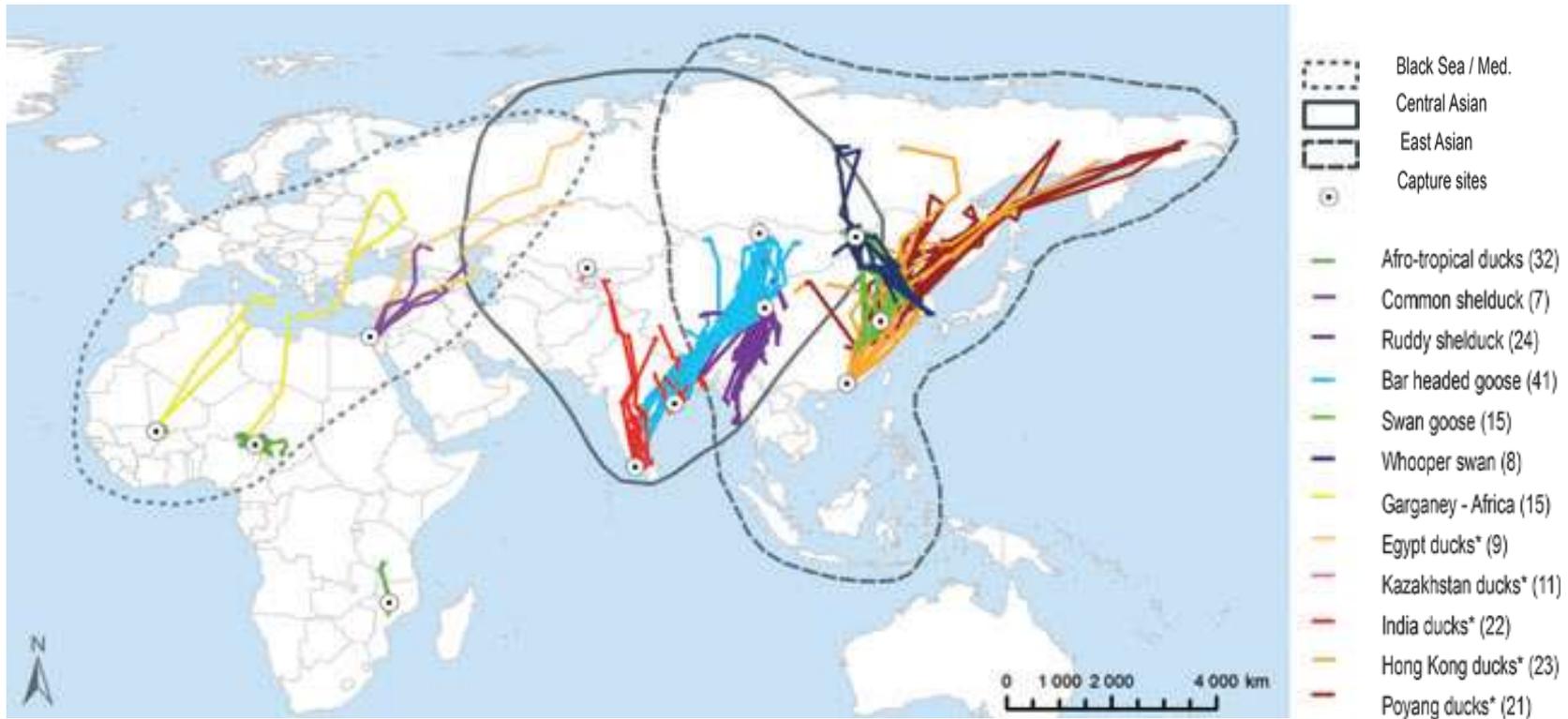
- Multiple cleavage points in the H0 precursor protein or any genetic resemblance to previously described HPAI viruses
- High pathogenicity with virus challenge of chicks – IVPI or intravenous pathogenicity index: infect ten 4-8 week old SPF chicks and observe for 10 days – HPAI if  $IVPI \geq 1.2$  or  $\geq 75\%$  of birds die



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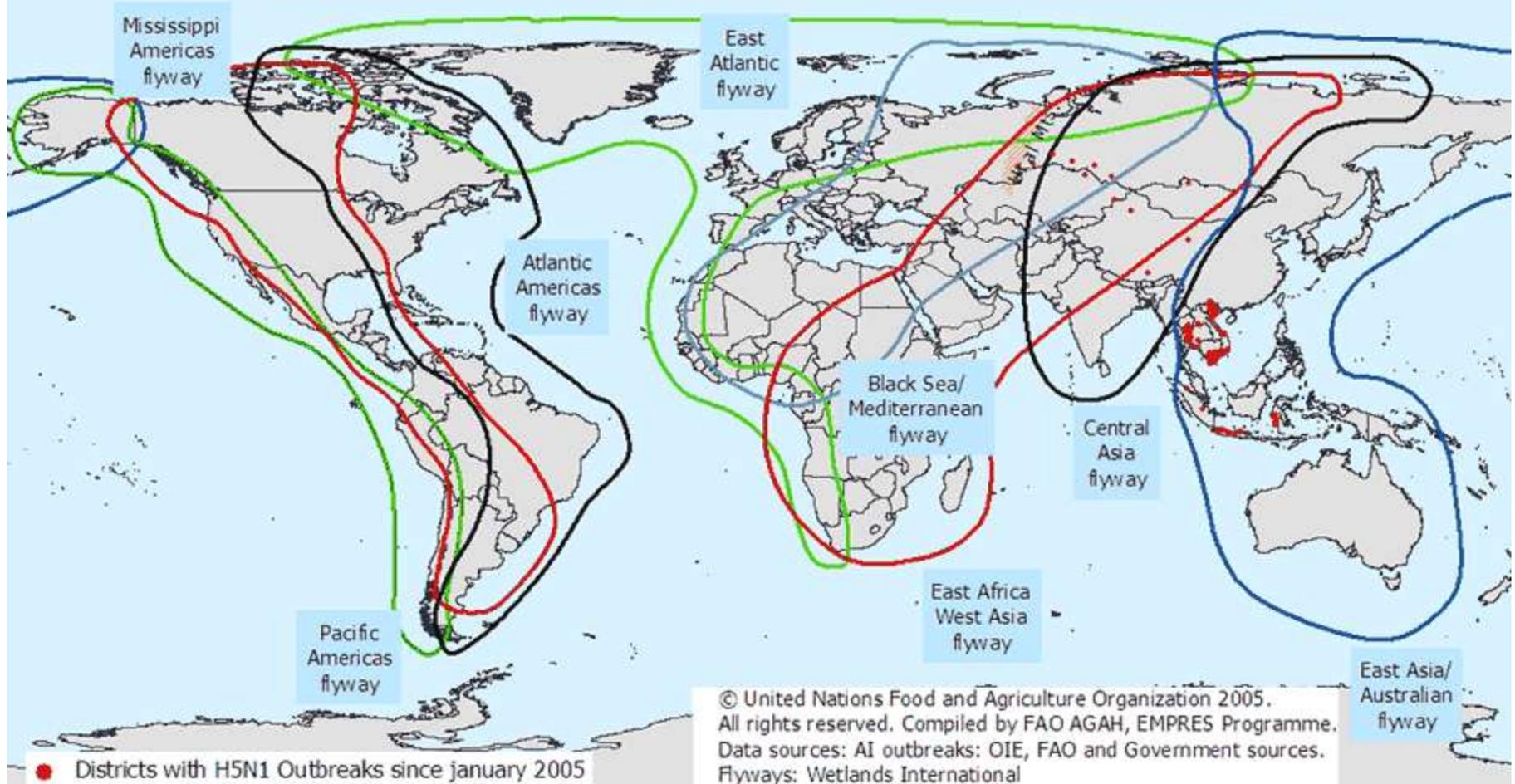
# Eurasian HPAI H5N1: a new paradigm



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 ©)

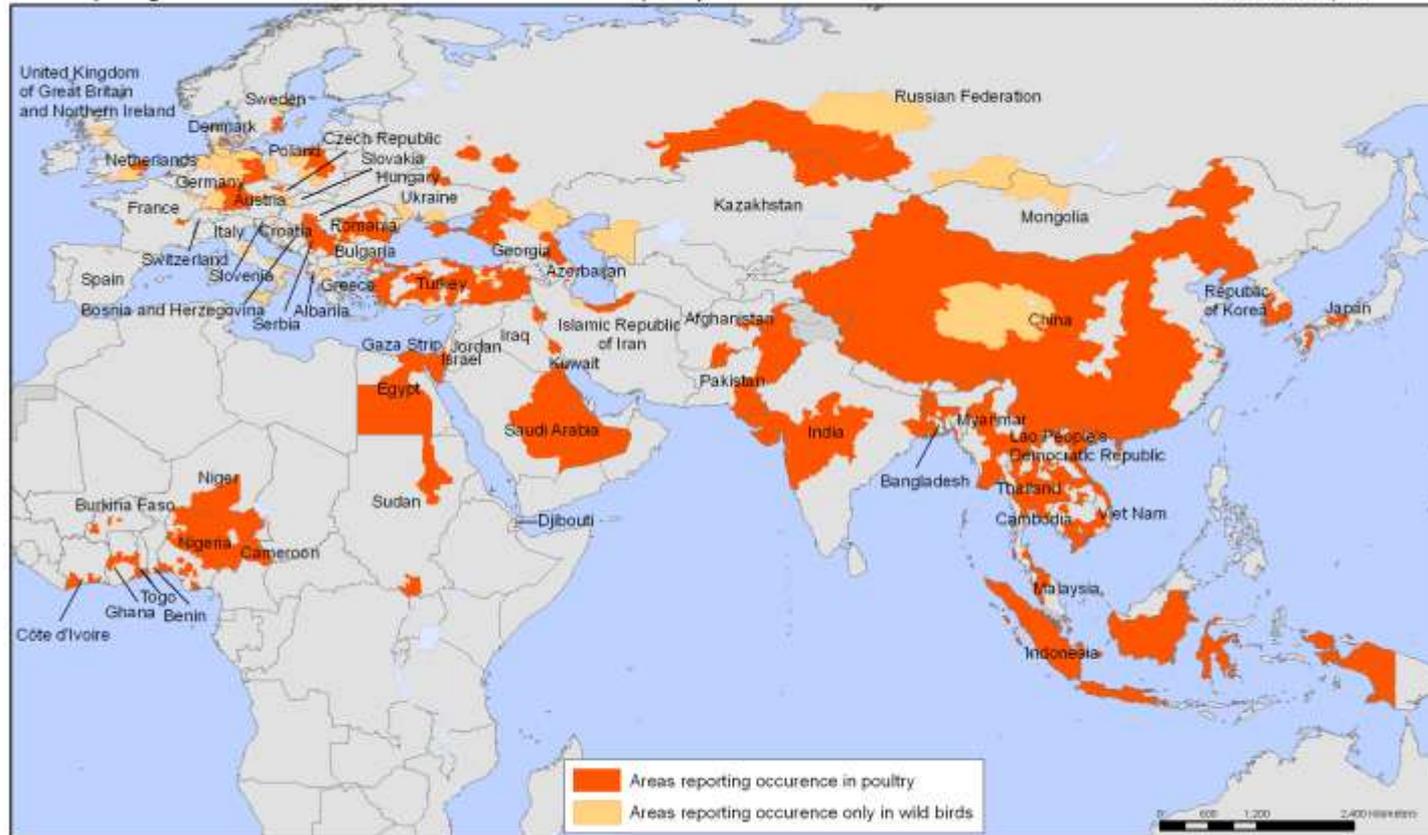
# EA H5 Transmission Wild Birds and Poultry

**H5N1 outbreaks in 2005 and major flyways of migratory birds**  
Situation on 30 August 2005



Areas reporting confirmed occurrence of H5N1 avian influenza in poultry and wild birds since 2003

Status as of 21 February 2009  
Latest available update



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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.

Data Source: World Organisation for Animal Health (OIE) and national governments  
Map Production: Public Health Mapping and GIS  
World Health Organization

- First reported 1996 - Quiescent after 1997 - Re-emerged 2003 (Lake Quinghai)
- Multiple clades/subclades - More virulent and adapted to land-based poultry
- 1<sup>st</sup> 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



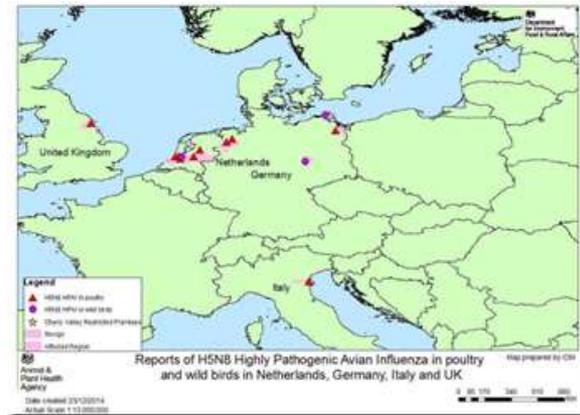
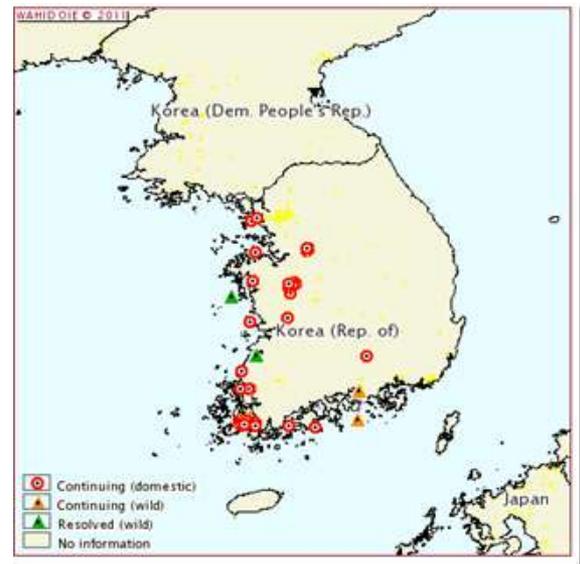
# AI – Movement & Maintenance

- 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)



**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.

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.

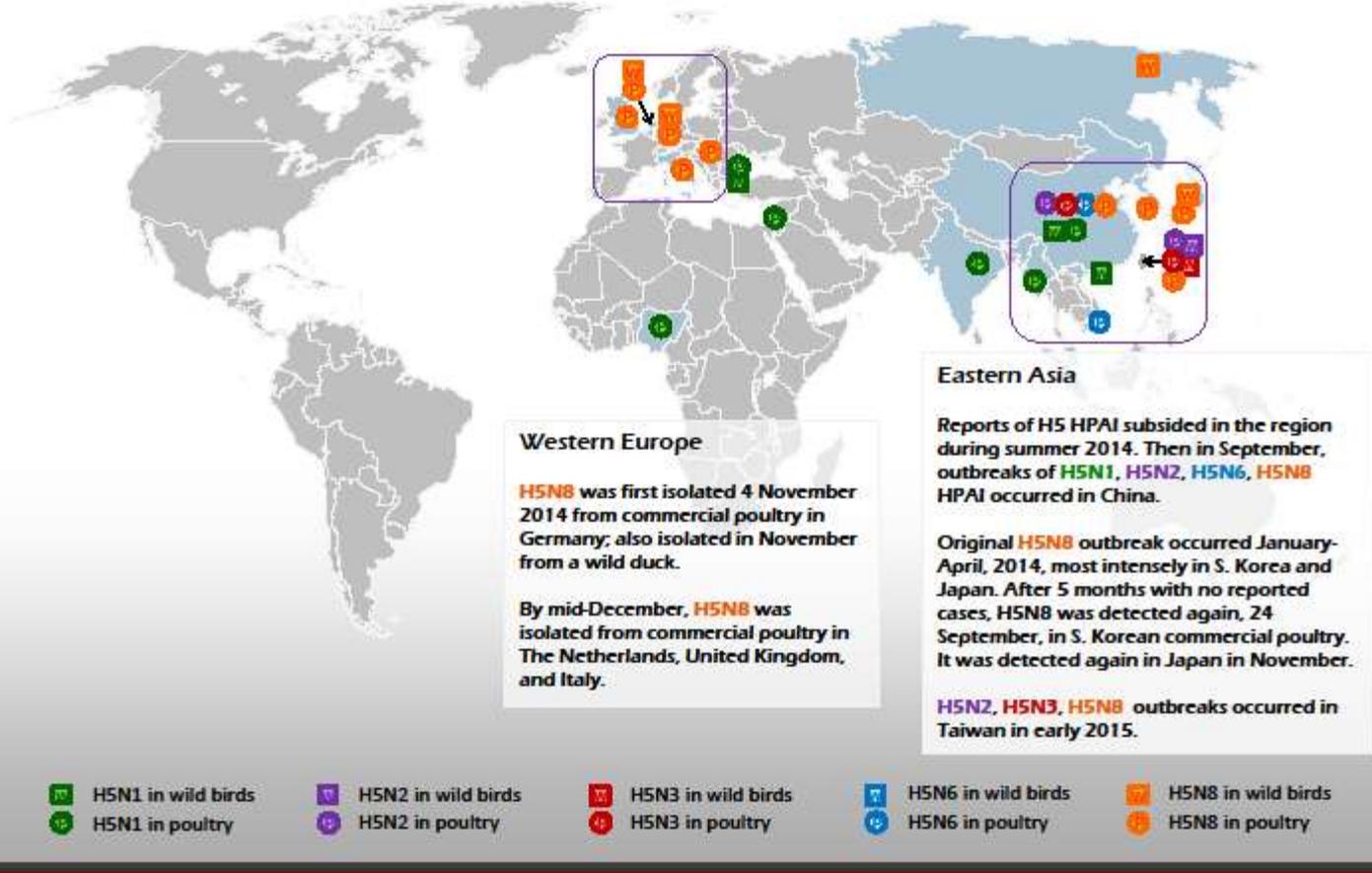
**H5N2**, **H5N3**, **H5N8** outbreaks occurred in Taiwan in early 2015.

- H5N1 in wild birds  
● H5N1 in poultry
- H5N2 in wild birds  
● H5N2 in poultry
- H5N3 in wild birds  
● H5N3 in poultry
- H5N6 in wild birds  
● H5N6 in poultry
- H5N8 in wild birds  
● H5N8 in poultry

Developed by Matt Sandbulte, PhD, CFSPH



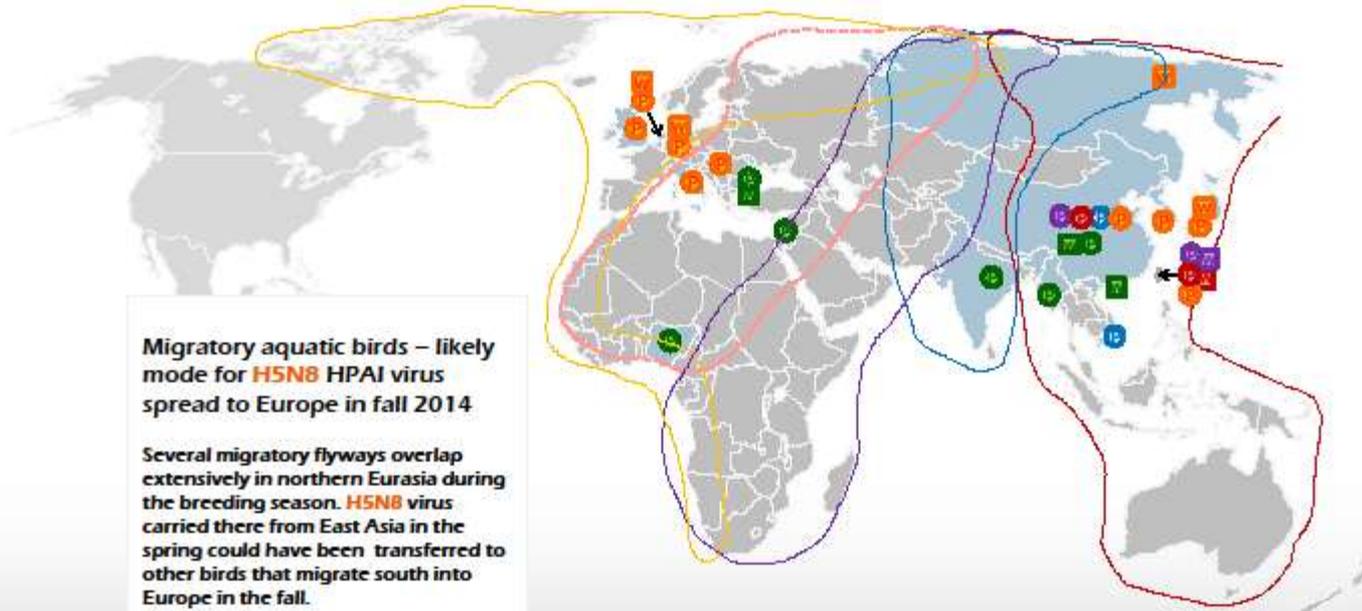
## H5 HPAI reports from Europe, Middle East, and Africa November 2014 through February 2015 (OIE)



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## H5 HPAI reports from Europe, Middle East, and Africa November 2014 through February 2015 (OIE)



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.

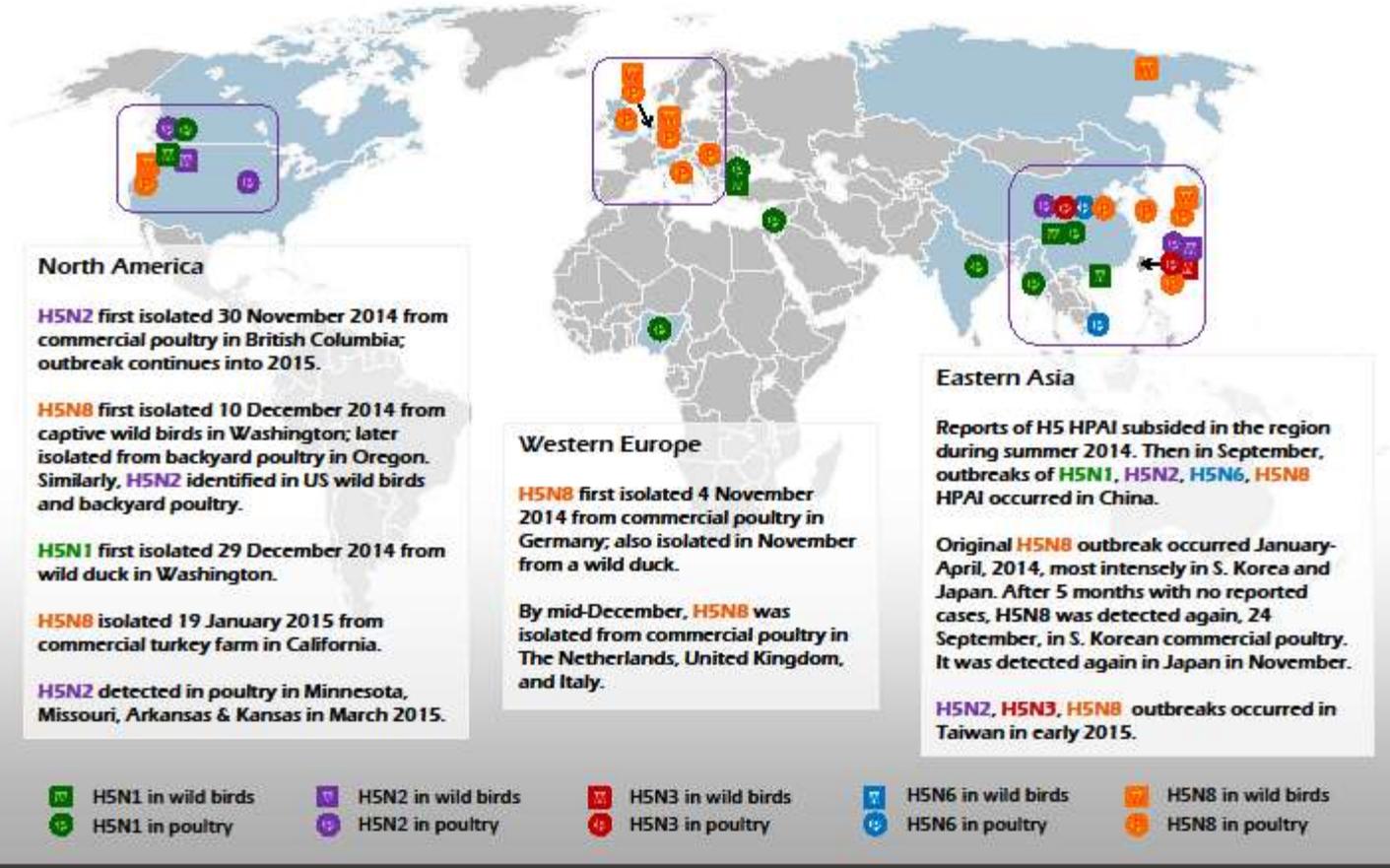
**H5N8** may be better suited for long-distance dispersal than most strains of HPAI.

- |                    |                    |                    |                    |                    |
|--------------------|--------------------|--------------------|--------------------|--------------------|
| H5N1 in wild birds | H5N2 in wild birds | H5N3 in wild birds | H5N6 in wild birds | H5N8 in wild birds |
| H5N1 in poultry    | H5N2 in poultry    | H5N3 in poultry    | H5N6 in poultry    | H5N8 in poultry    |

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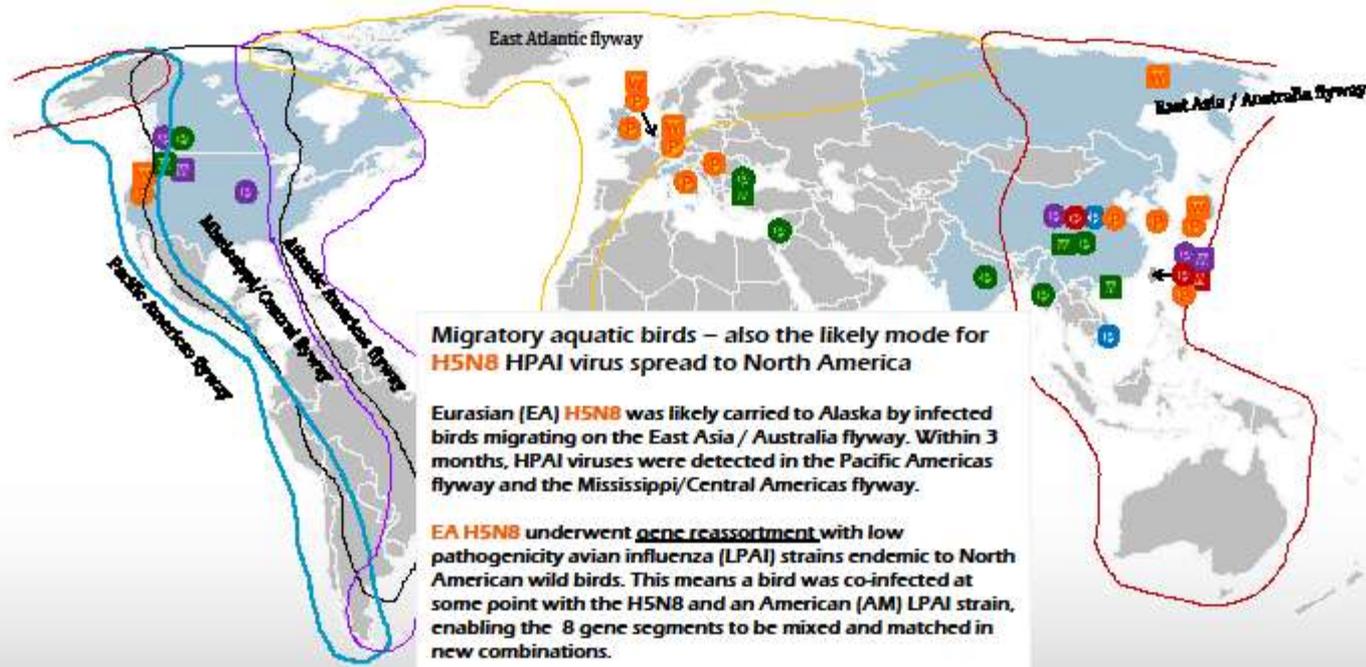
## H5 HPAI reports from North America November 2014 through February 2015 (OIE)



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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.

- H5N1 in wild birds  
● H5N1 in poultry
- H5N2 in wild birds  
● H5N2 in poultry
- H5N3 in wild birds  
● H5N3 in poultry
- H5N6 in wild birds  
● H5N6 in poultry
- H5N8 in wild birds  
● H5N8 in poultry

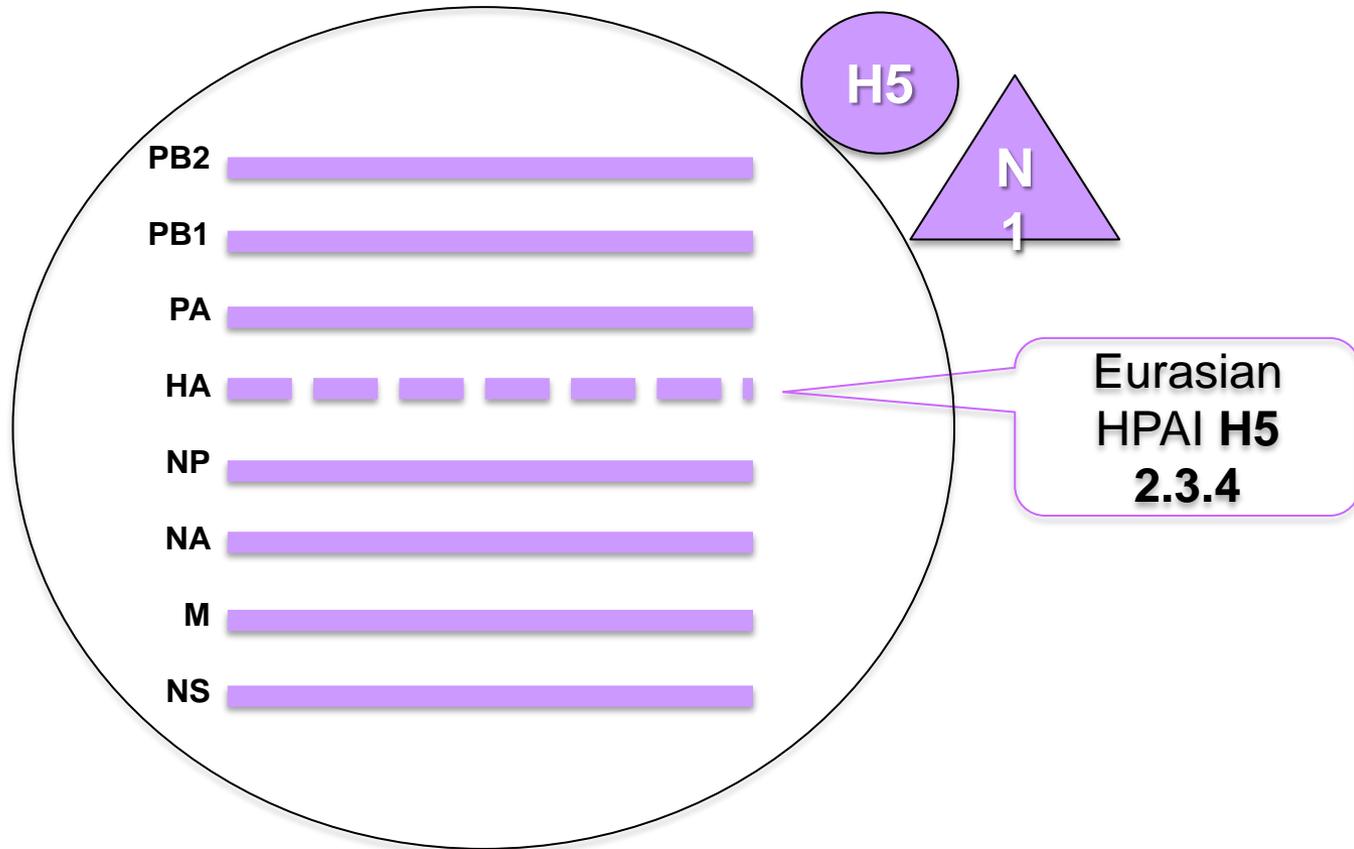
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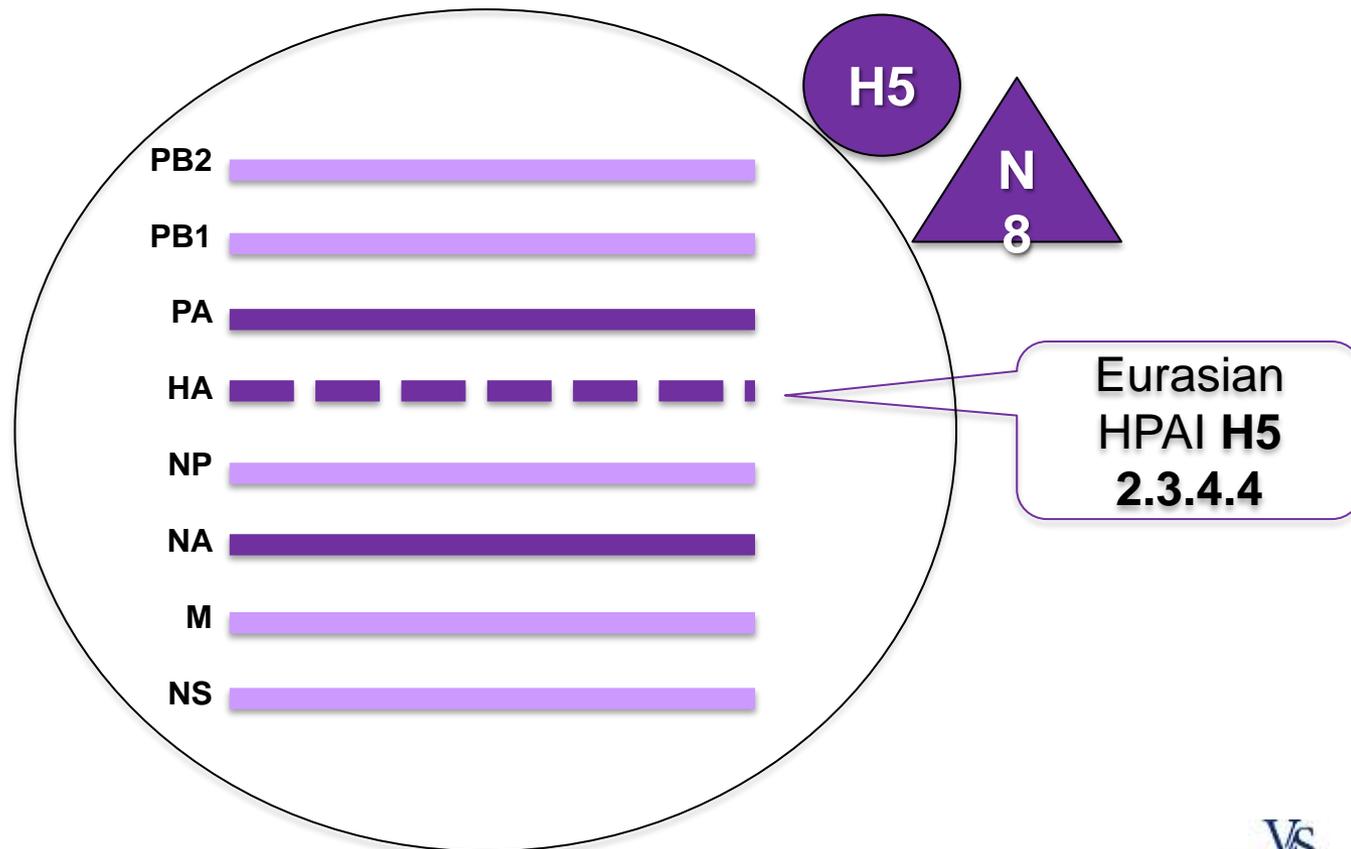
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# Asian-origin H5N1 HPAI clade 2.3.4 – Eurasian virus



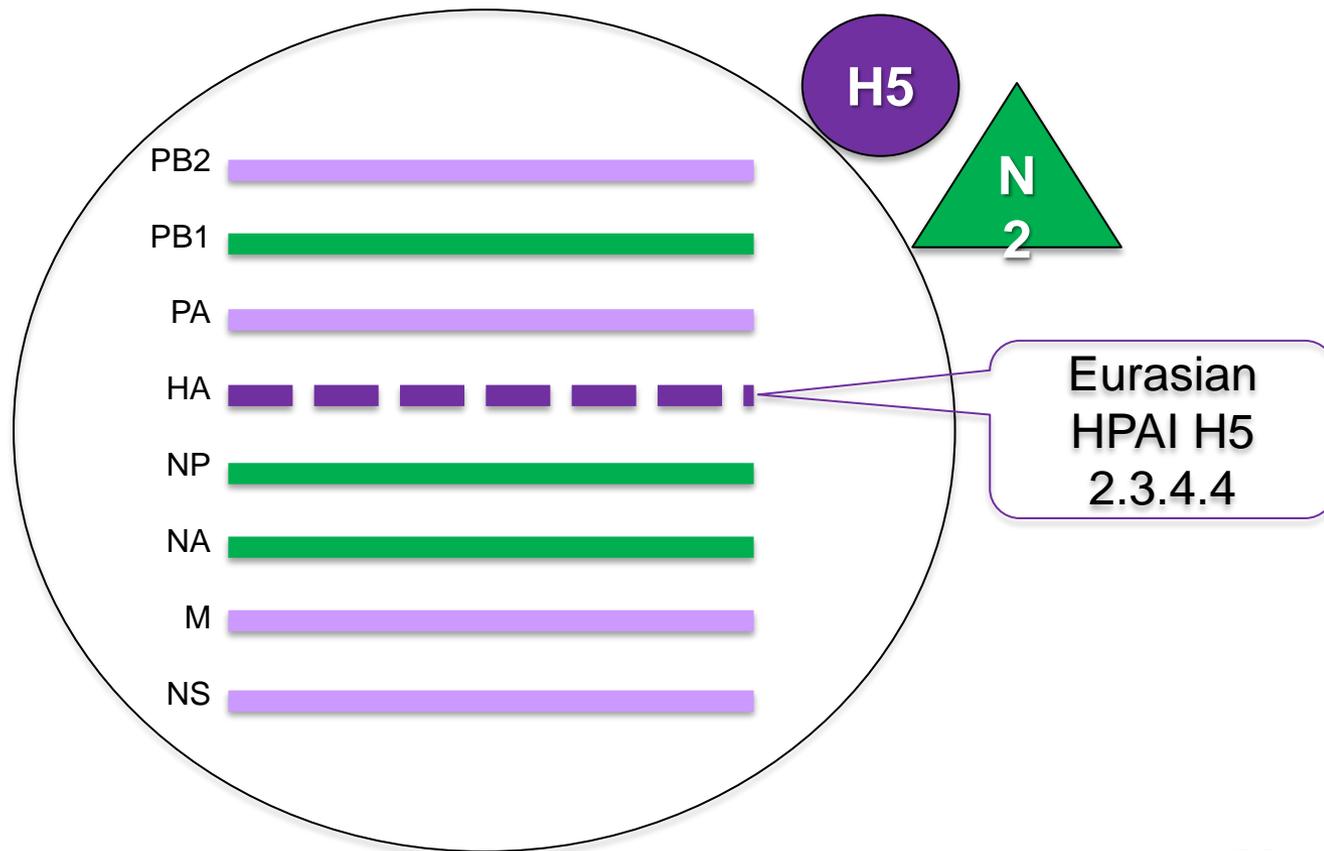
# Eurasian H5N8 clade 2.3.4.4 *aka* “Transcontinental” EA-H5N8



# EA/AM H5N2-reassortant

## EA-H5N8 (5 genes) / AM (3 genes)

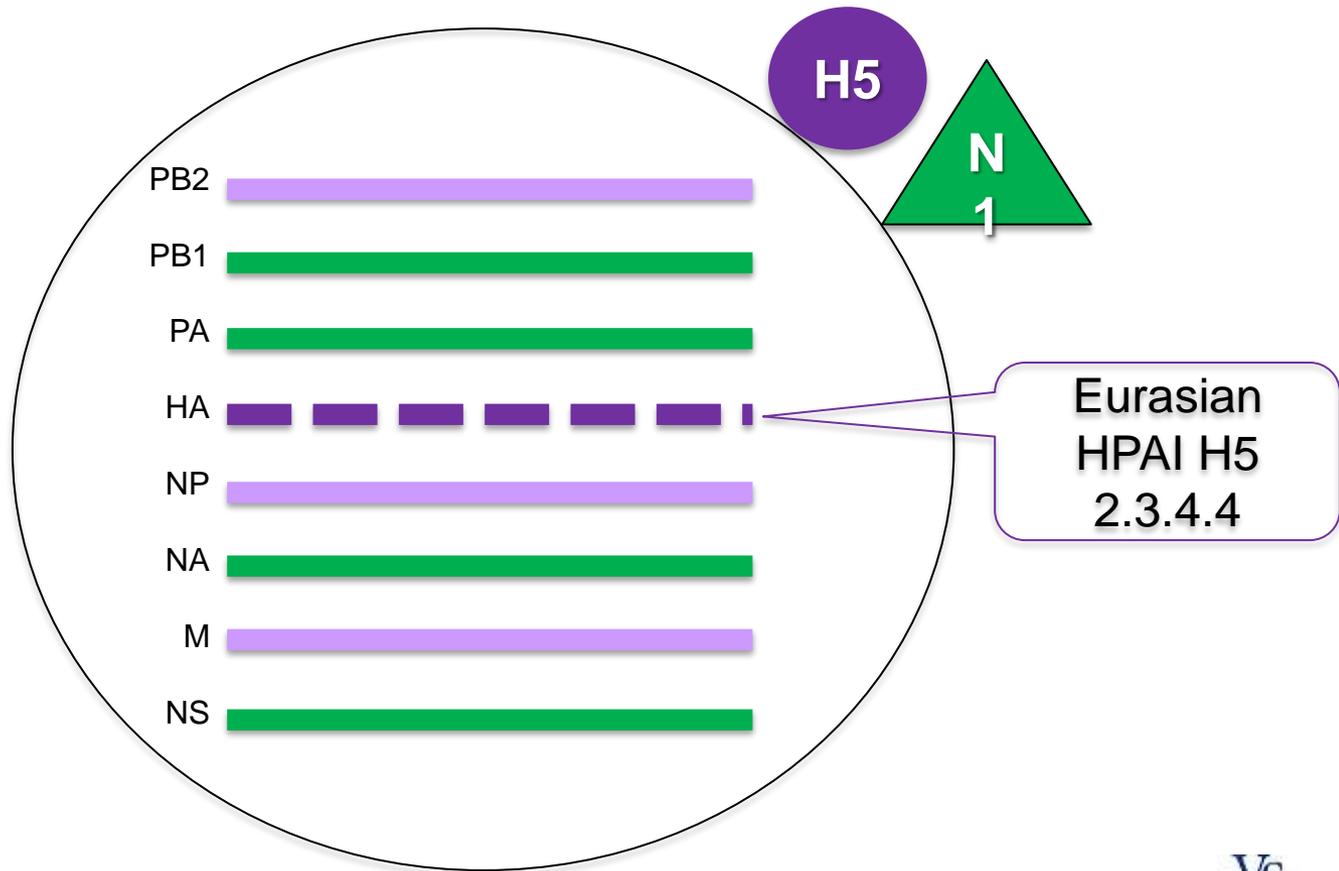
A/Northern pintail/Washington/40964/2014 (H5N2) Genbank 1589662



# EA/AM H5N1-reassortant

## EA-H5N8 (4 genes) / AM (4 genes)

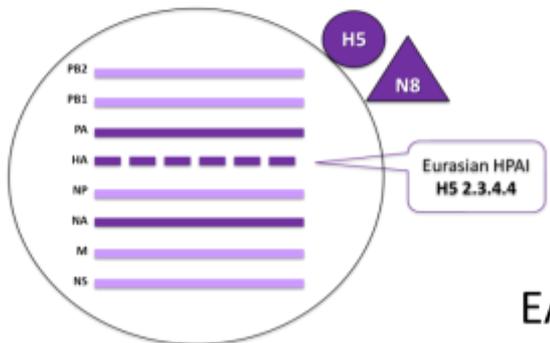
A/American green winged teal/195750/Washington/2014(H5N1)



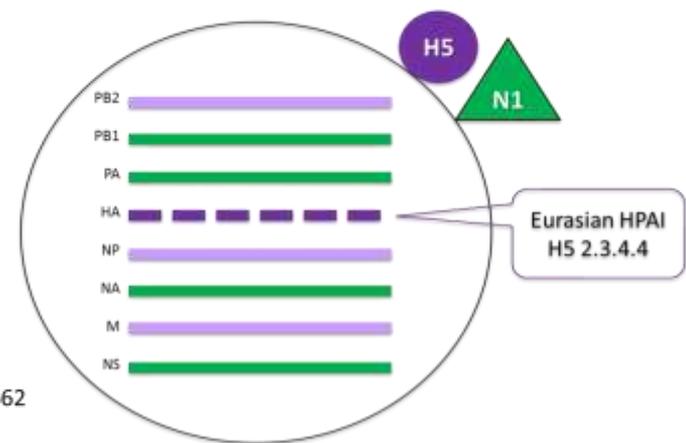
# EA-H5 2.3.4.4\* reassortants in North America (AM)

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

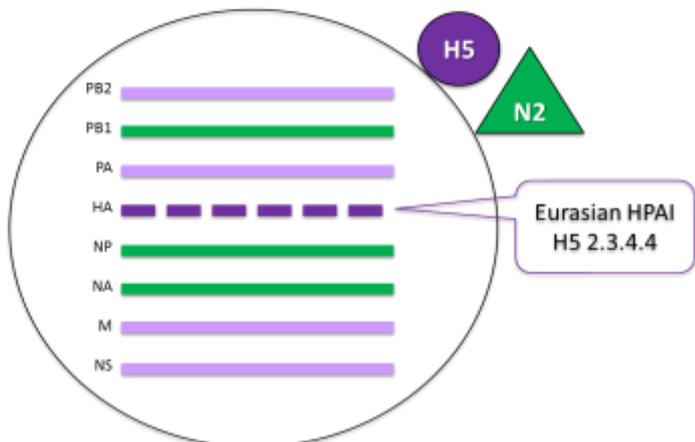
Eurasian H5N8 clade 2.3.4.4  
aka "Transcontinental" EA-H5N8



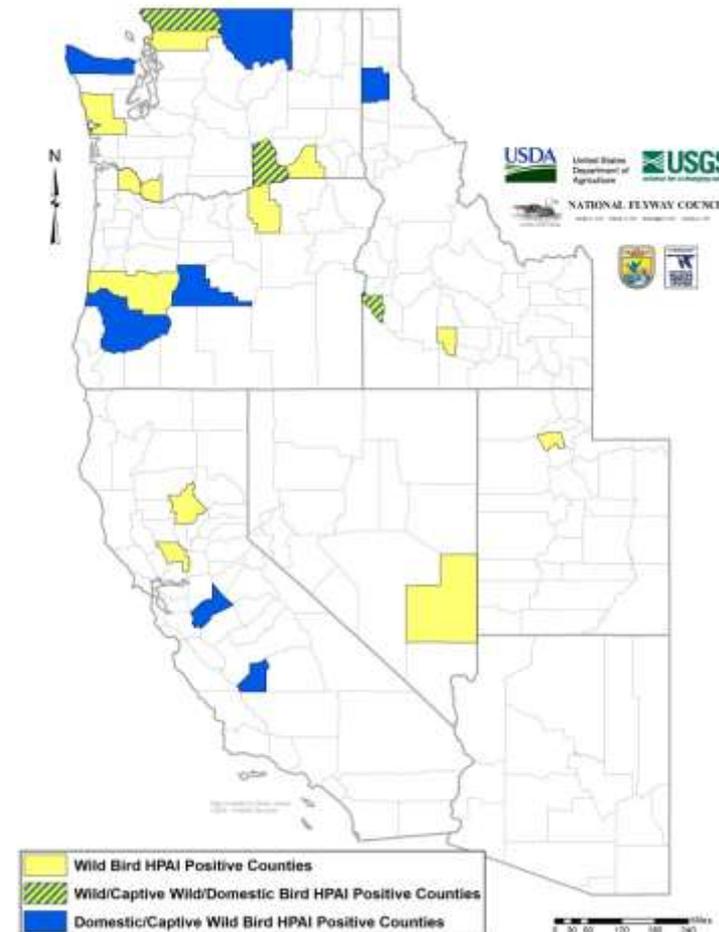
EA/AM H5N1-reassortant  
EA-H5N8 (4 genes) / AM (4 genes)  
A/American green winged teal/195750/Washington/2014(H5N1)



EA/AM H5N2-reassortant  
EA-H5N8 (5 genes) / AM (3 genes)  
A/Northern pintail/Washington/40964/2014 (H5N2) Genbank 1589662



- 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



- 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 than 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

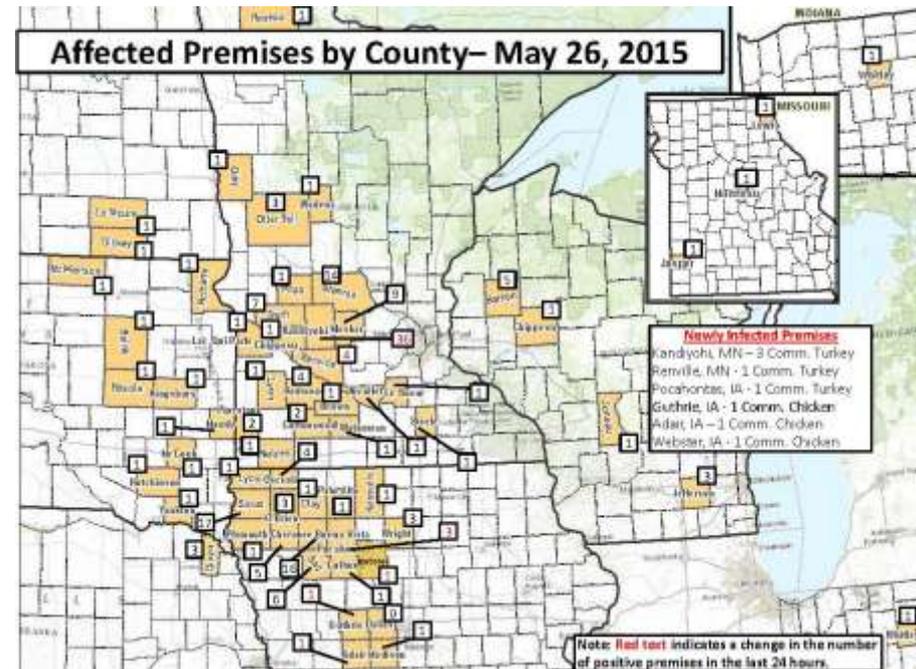
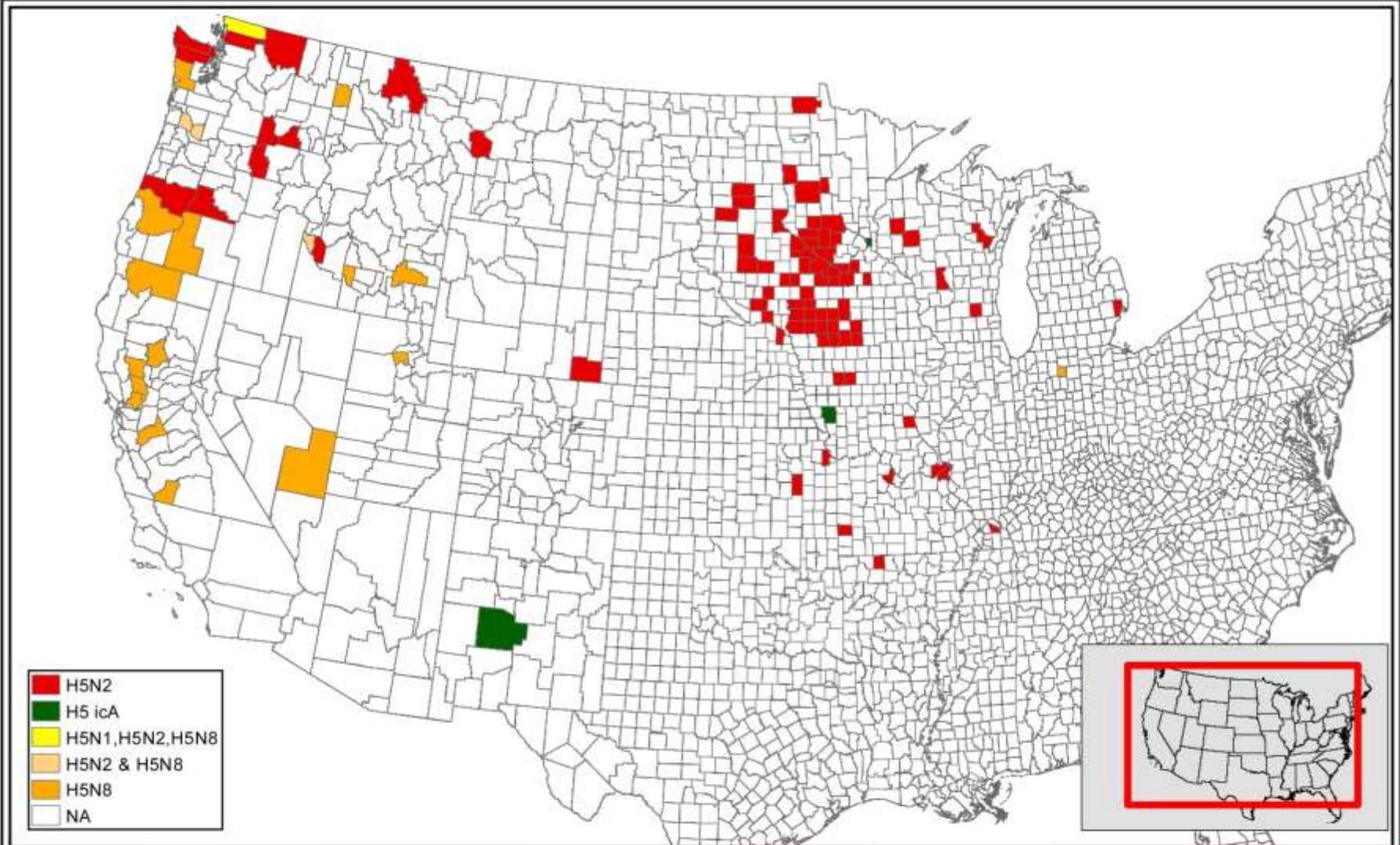


Figure 9. HPAI Detections by Subtype in All Birds, as of 7/16/2015  
 (as reported on [ww.aphis.usda.gov](http://ww.aphis.usda.gov)) \*one or more detections may have occurred in county



- H5N2
- H5 icA
- H5N1, H5N2, H5N8
- H5N2 & H5N8
- H5N8
- NA



## 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

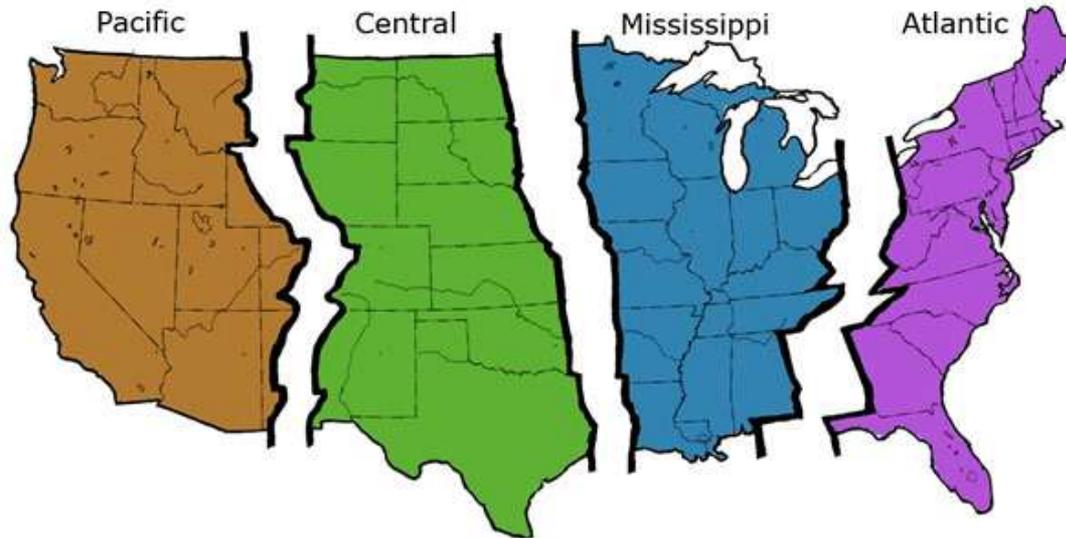
- **Direct Losses:**
  - About \$1.6 billion
- **Economy-Wide Impact:**
  - \$3.3 billion
- **Trade Impact:**
  - 17 Trading Partners, including
    - ❖ China - \$391 million
    - ❖ Russia - \$153 million
    - ❖ South Korea - \$123 million



# Eurasian H5 Viral Ecology in Wild Birds

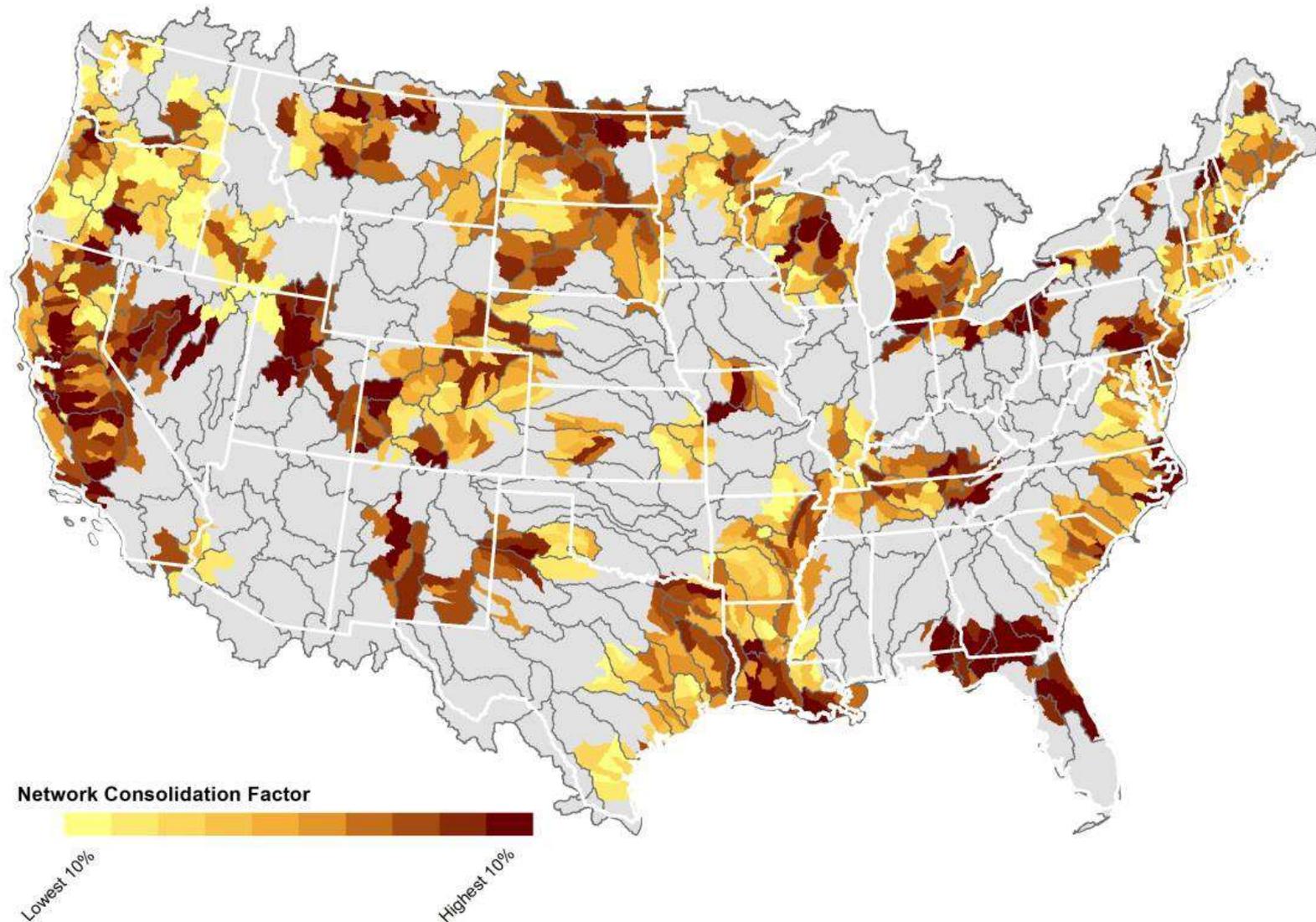
- Eurasian H5 viruses of clade 2.3.4.4 appear to be uniquely adapted to dabbling ducks, members of the family *Anatidae*, genus *Anas*
- Examples include mallards in their relatives, such as teal and pintail
- EA H5 viruses result in subclinical infections in these species and they shed high titers of 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





U.S. Migratory Bird Flyways

- 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)



# 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?