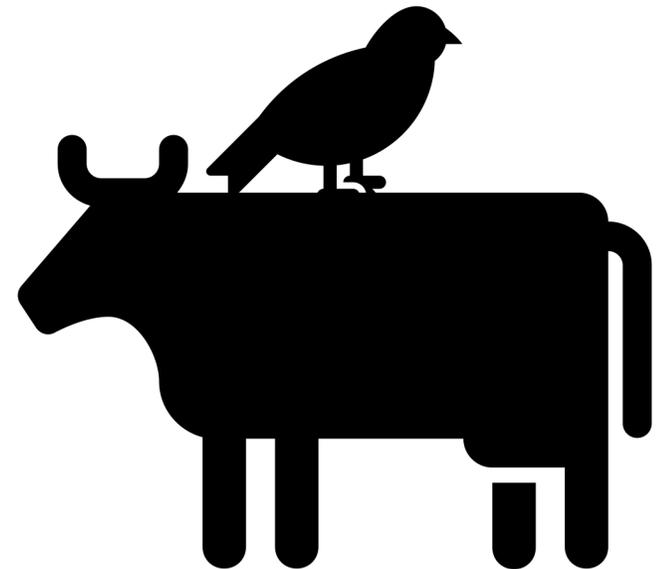
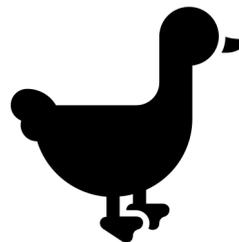


IDEAS Seminar: What to know about highly pathogenic avian influenza (H5N1) viruses

25 April 2024

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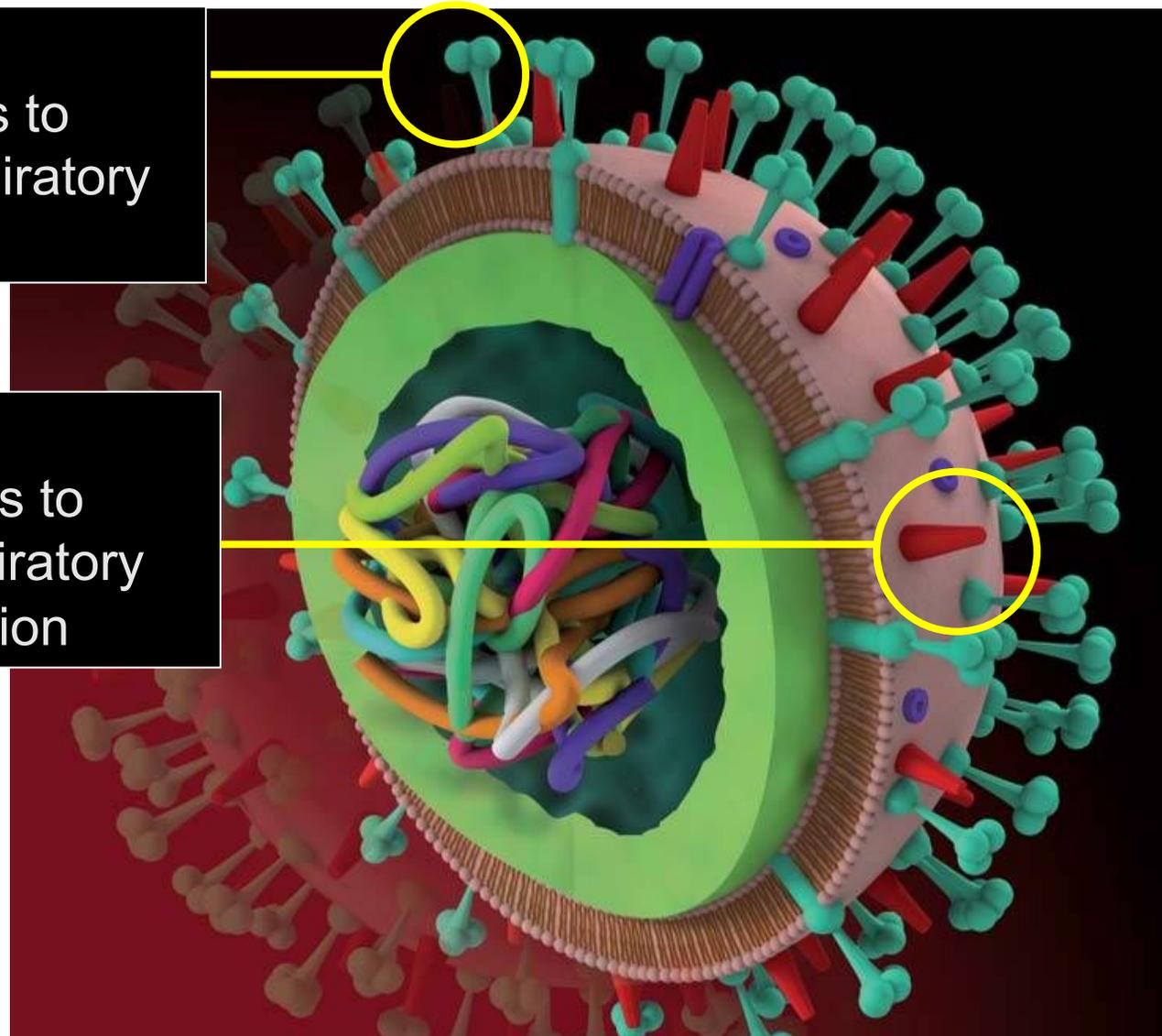
Two key proteins of influenza viruses

Hemagglutinin

Allows the flu virus to adhere to the respiratory tract

Neuraminidase

Allows the flu virus to escape from respiratory cells after replication

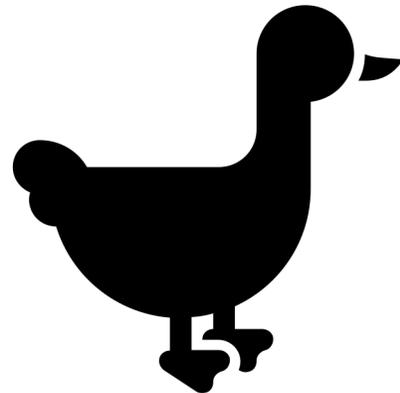


Wild waterfowl, aquatic ducks are a natural reservoir for nearly all influenza A virus subtypes

Avian Influenza A Viruses

H1 - H16

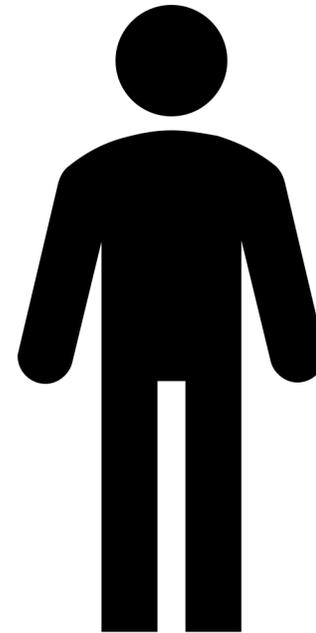
N1 - N9



Human Influenza A Viruses

H1 - H3

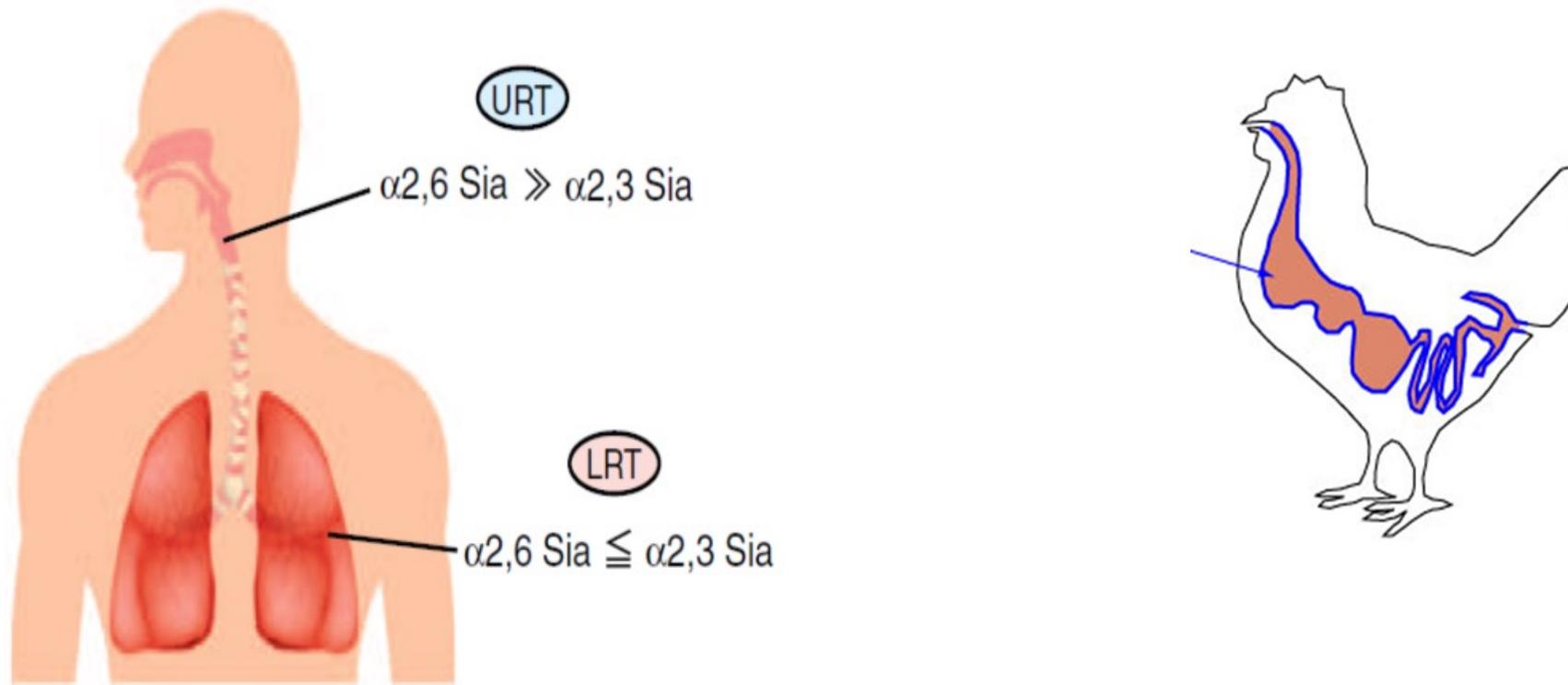
N1 - N2



Influenza A HA and NA Subtypes

H1	  	
H2	 	
H3	  	Other Animals
H4	 	Other Animals
H5	  	Other Animals
H6		
H7	 	Other Animals
H8		
H9	  	
H10		
H11		
H12		
H13		
H14		
H15		
H16		
N1	  	
N2	  	
N3		
N4		
N5		
N6		
N7		Other Animals
N8		Other Animals
N9		

Human and Avian Influenza A viruses and tropism



- *Seasonal influenza A viruses bind primarily to receptors in the **upper respiratory tract of humans**
- *Avian influenza A viruses bind to receptors in the **respiratory and gastrointestinal tracts of birds**

Background

- Avian influenza is categorized into highly pathogenic and low pathogenicity
- Highly pathogenic avian influenza (HPAI) strains are deadly to domestic poultry and can wipe out entire flocks within a matter of days.
- Low pathogenicity avian influenza strains typically cause few or no signs of illness.

Background

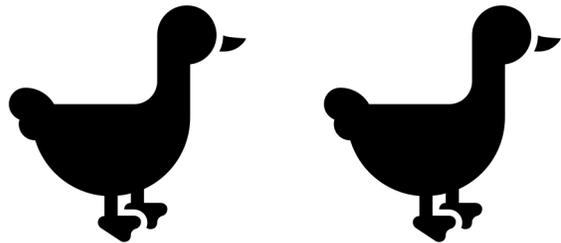
- While rare, mammals can be infected with HPAI A(H5N1) (“H5N1 bird flu”) viruses.
- Reports of these sporadic infections in mammals have occurred globally amid widespread outbreaks of bird flu infections in wild birds and poultry.
- Mammals can be infected with H5N1 bird flu viruses when they eat infected birds, poultry, or other animals and/or if they are exposed to environments contaminated with virus.
- Spread of H5N1 bird flu viruses from mammal to mammal is generally thought to be rare.

Global Summary

- Globally, sporadic HPAI A(H5N1) virus infections in mammals have been reported across the continents of Asia, North America, South America, and Europe.
- Specifically, recent HPAI A(H5N1) infections in mammals have been detected in sea lions in Peru and Chile, sea elephants in Argentina, and foxes in Canada, France, and other countries.
- Since 2022, USDA has reported HPAI A(H5N1) virus detections in more than 200 mammals in the United States.
- Sporadic human A(H5N1) virus infections have a >50% case fatality proportion, primarily associated with exposures to sick or dead infected poultry, have been reported in 23 countries

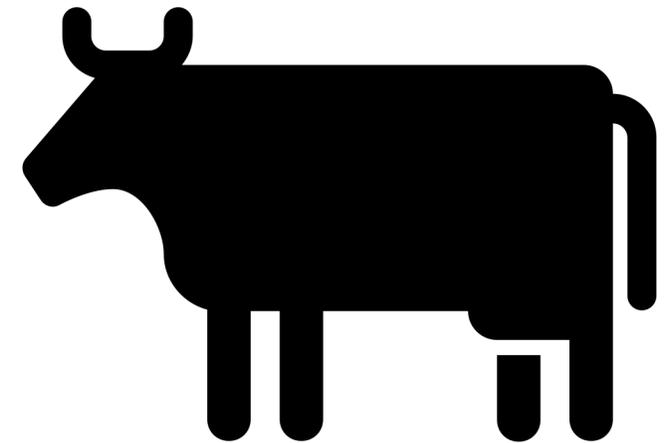
US Poultry

- Since 2022, more than 90 million birds, mostly egg-laying hens and turkeys, in U.S. commercial flocks have either died from the virus or been killed to try to prevent the spread of bird flu.



On March 25, 2024, a multi-state outbreak of HPAI A(H5N1) bird flu in dairy cows was first reported

- This is the first time that H5N1 influenza viruses were found in cattle.
- This likely traces to a single spillover event from wild birds, based on an analysis of genetic sequences collected from sick cattle.



US dairy cows

- According to USDA influenza A(H5N1) been found in nearly three dozen herds in eight states.
- On April 23, 2024, health officials said they had detected inactivated remnants of the virus in samples taken from milk during processing and from store shelves. They stressed that such remnants pose no known risk to people or the milk supply.
- On April 24, 2024, U.S. agriculture officials said that every lactating cow must be tested and post a negative result before moving to a new state from April 29th.

US dairy cows

- Initially, bird flu viruses in the current outbreak had been found in raw milk and the cows udders that produced it.
- Officials think the virus may have spread between cows during the milking process on farms, through surfaces contaminated with infected raw milk.
- Recently, H5N1 virus was detected in lung tissue of a dairy cow that had been culled and sent to slaughter in Kansas. The cow was condemned by USDA inspectors and did not enter the food supply.

US dairy cows

- The one dairy cow with bird flu in the lung tissue so far appears to be an isolated event.
- More generally, cows mostly have been recovering from the virus without dying.
- That's different from the mass die-offs seen in birds and some other species that were infected with the same clade of influenza A(H5N1) viruses.
- Dairy industry officials have previously said some cows have yet to recover their ability to produce milk, raising concerns of long-term issues for some cattle.

US egg supply

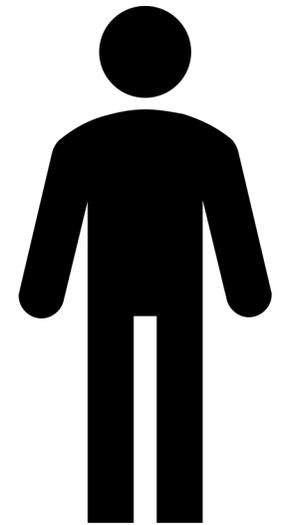
- Egg farms from Texas and Michigan are also suspected to have been infected by virus that spread from cows, adding to millions of poultry culled because of infections from wild birds.
- Those farms have been in close proximity to affected dairy farms.
- There is potential lateral flow from the dairy farms to these poultry operations, to these egg laying operations.

US egg and dairy testing

- Health authorities think pasteurization kills bird flu based off previous work done pasteurizing eggs for HPAI H5N1 and milk for other viruses, however continued verification is ongoing.
- Further, a positive PCR test does not necessarily mean that the sample contains an intact infectious pathogen.
- The FDA "gold standard" for checking if the virus that they found is potentially infectious is to take the H5N1 HPAI particles they found and see if it grows in chicken eggs.
- Research backed by the NIH has also found H5N1 HPAI fragments in milk. Early testing of those samples suggests the virus in the pasteurized milk was not infectious, by trying to grow the virus in cells and chicken eggs.

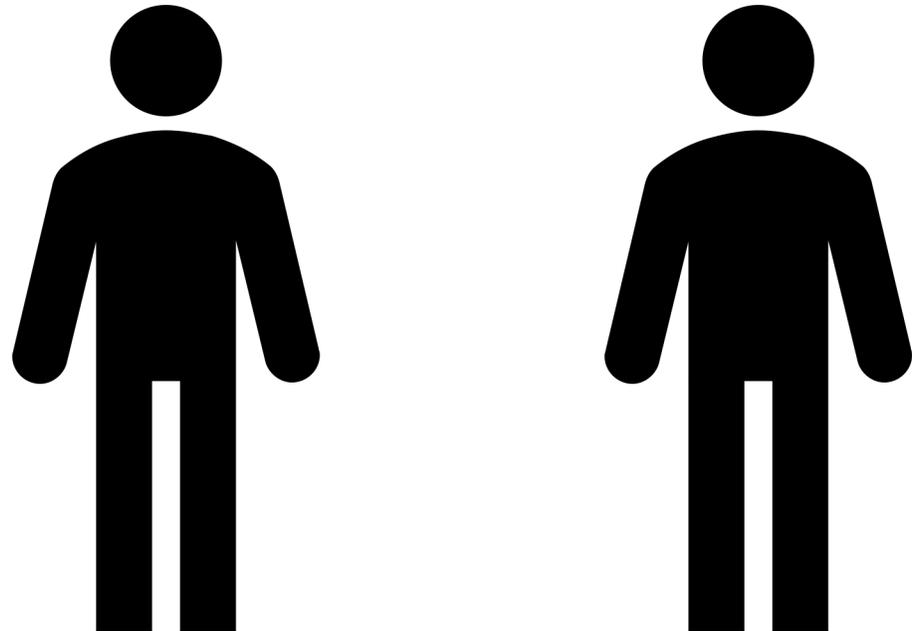
Human Case in Texas among a U.S. dairy worker

- On April 1st, CDC confirmed one human HPAI A(H5N1) infection among a dairy worker in Texas.
- While thought to be rare, this exposure to HPAI A(H5N1) bird flu virus is the first instance of likely mammal to human transmission.
- The patient had conjunctivitis
- He was treated with influenza antivirals
- Has been recovering



When is it a problem

- If HPAI A(H5N1) starts to spread from human-to-human
- Could cause an epidemic or even another pandemic



Risk to Humans

- Health officials said 23 people have been tested for bird flu to date and 44 people exposed to infected animals are being monitored
- The wide geographic spread of HPAI A(H5N1) viruses in wild birds, poultry, and some other mammals, including in cows, create additional opportunity for exposure.
- People who have job-related or recreational exposure to infected birds or animals, including cows, are at greater risk of contracting HPAI A(H5N1) virus.
- CDC believes the current risk to the general public from bird flu viruses is low.

US economic threat

- Total poultry sector sales in 2022 were \$76.9 billion.
- The egg and turkey sectors being particularly impacted by the highly pathogenic avian influenza (HPAI) outbreak.
- U.S. milk production, was measured to be \$59.2 billion in 2022 according to data from the USDA.



Novel influenza A viruses and pandemic threat

- A novel influenza A virus is an influenza A virus that is antigenically and genetically distinct from currently circulating seasonal influenza A viruses and has infected at least one human

Public Health Impact of Novel Influenza A viruses

- Pandemic influenza
 - Adaptation of an avian or swine-origin virus
 - 1918 H1N1 virus
 - 2009 H1N1 virus
 - Human-animal reassortment virus
 - 1957 H2N2 virus
 - 1968 H3N2 virus
- Zoonotic influenza (sporadic infections)
 - Low pathogenic avian influenza A viruses
 - Highly pathogenic avian influenza A viruses
 - Swine influenza A viruses (variant viruses)



Estimated Impact of Influenza Pandemics

1918-19 Spanish Flu (H1N1)

- 50-100 million estimated deaths worldwide
- >675,000 U.S. deaths
- Estimated mortality = 2%

1957-58 Asian Flu (H2N2)

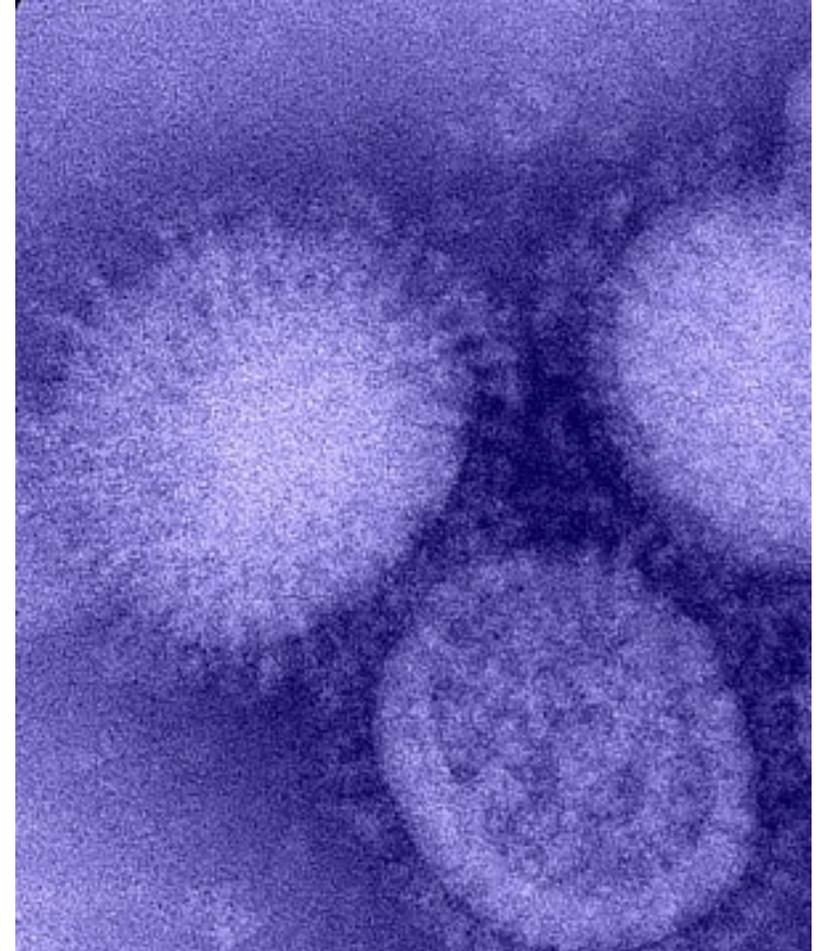
- 70,000 excess U.S. deaths

1968-69 Hong Kong Flu (H3N2)

- 34,000 excess U.S. deaths

2009 H1N1 (H1N1pdm09)

- Estimated 12,500 U.S. deaths



Global Impact of 2009 H1N1 Pandemic

Mortality estimates

- Two modeling efforts*
 - 123,000 - 203,000 respiratory deaths (April-Dec 2009)
 - 62-85% aged <65 years
 - 105,700 - 395,600 respiratory deaths (April 2009 - August 2010)
 - 80% aged <65 years; 51% occurred in SE Asia and Africa
 - 46,000 - 179,900 cardiovascular deaths (April 2009 - August 2010)
- H1N1pdm09 virus continues to circulate worldwide as a seasonal influenza A virus
 - Limited “antigenic drift”: virus has not changed significantly since emergence in 2009
 - Continues to cause severe illness and deaths worldwide
- Influenza pandemics introduce new influenza A virus subtypes that continue to circulate among humans

Human infections with Avian Influenza A Viruses

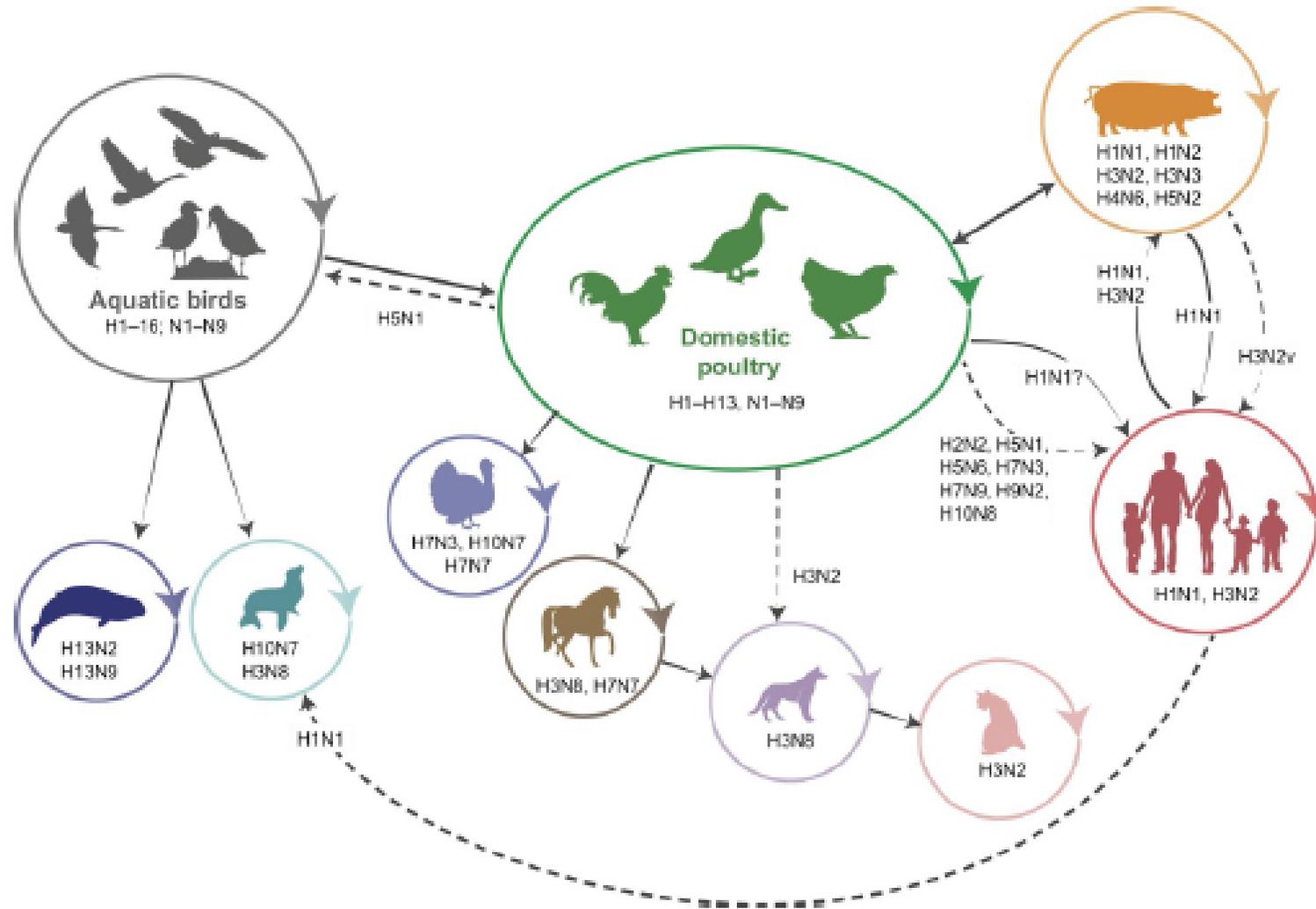
Sporadic poultry-to-human transmission

- [incubation period: 2-7 days (up to 10 days)]
 - Risk factors: direct or close exposure to infected poultry (sick/dead/well-appearing), visiting live poultry markets

Case Clusters (incubation period: 2-9 days)

- Blood-related family members
- Usually common poultry exposures
 - Limited, non-sustained human-to-human transmission (H7N9, H5N1)

Interspecies transmission of influenza A viruses



Thank you!