Welcome

REGION 1
Regional Disaster Health Response System

RESPTC
REGION 1 EMERGING SPECIAL PATHOGENS TREATMENT CENTER

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Aileen Patel, MS, RN
Kathryne Tarnoff

The following speakers have reported no relevant financial relationships with an ineligible company:

Tim Uyeki, MD, MPH, MPP
David Banach, MD, MPH

The following speakers have reported a relevant financial relationship with an ineligible company:

None

MGH Center For Disaster Medicine Series 2023- 2024
Highly Pathogenic Avian Influenza: A Comprehensive Overview| Monday, October 23 | 12pm

Learning Objectives

Upon completion of this activity, participants will be able to:

1. Understand updated information of H5N1 viruses, the epidemiology of human cases of H5N1, and the associated risk to humans
2. Better understand the clinical characteristics of human cases of H5N1, testing, and recommended antiviral treatment
3. Apply the Identify/Isolate/Inform algorithm to patients presenting with signs/symptoms/epi risk for novel avian influenza, importance of alternative diagnoses considerations
4. Identify resources and current guidance on specimen collection and testing for patients with suspected infection with novel avian influenza

Target Audience

This activity is intended for Hospital and clinic administrators, emergency managers, nurses, providers, respiratory therapists and other leaders.

Course Director

Eileen F. Searle, PhD, RN
Director of Funded Projects,
Massachusetts General Hospital

Speaker/Faculty

Tim Uyeki, MD, MPH, MPP
David Banach, MD, MPH

SMS Code for Attendance: QUCHAK to 857-214-2277

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Mass General Brigham

Highly Pathogenic Avian Influenza: A Comprehensive Overview

David Banach MD, MPH
Tim Uyeki MD, MPH, MPP

October 23, 2023

Center for Disaster Medicine – Region 1 Disaster Health Response System and Regional Emerging Special Pathogens Treatment Center

Housekeeping

- The recording and slides for today's webinar will be made available on the Region 1 Disaster Health Response System website at https://www.rdhrs.org/regional-webinars/
- To limit background noise, your microphone has been muted for the duration of the webinar.
- We encourage your questions and comments! If you have a question or comment at any point during the webinar, you can type your questions into the Q&A box.
- Join the conversation on social media by following & tweeting @Region1RDHRS

Acknowledgement

This webinar is presented by the Region 1 Regional Emerging Special Pathogens Treatment Center (RESPTC) in collaboration with the Region 1 Disaster Health Response System (RDHRS). Both programs are funded by the Administration for Strategic Preparedness and Response (ASPR) within the US Department of Health and Human Services.

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Moderators & Speakers

Moderator:

Erica Shenoy, MD, PhD
Chief of Infection Control, Massachusetts General Hospital
Office of the Chief Medical Officer, Mass General Brigham

Speakers:

David Banach, MD, MPH
Associate Professor of Medicine
Hospital Epidemiologist at UConn Health

Tim Uyeki MD, MPH, MPP
Chief Medical Officer
Influenza Division
National Center for Immunization and Respiratory Diseases
Center for Disease Control and Prevention

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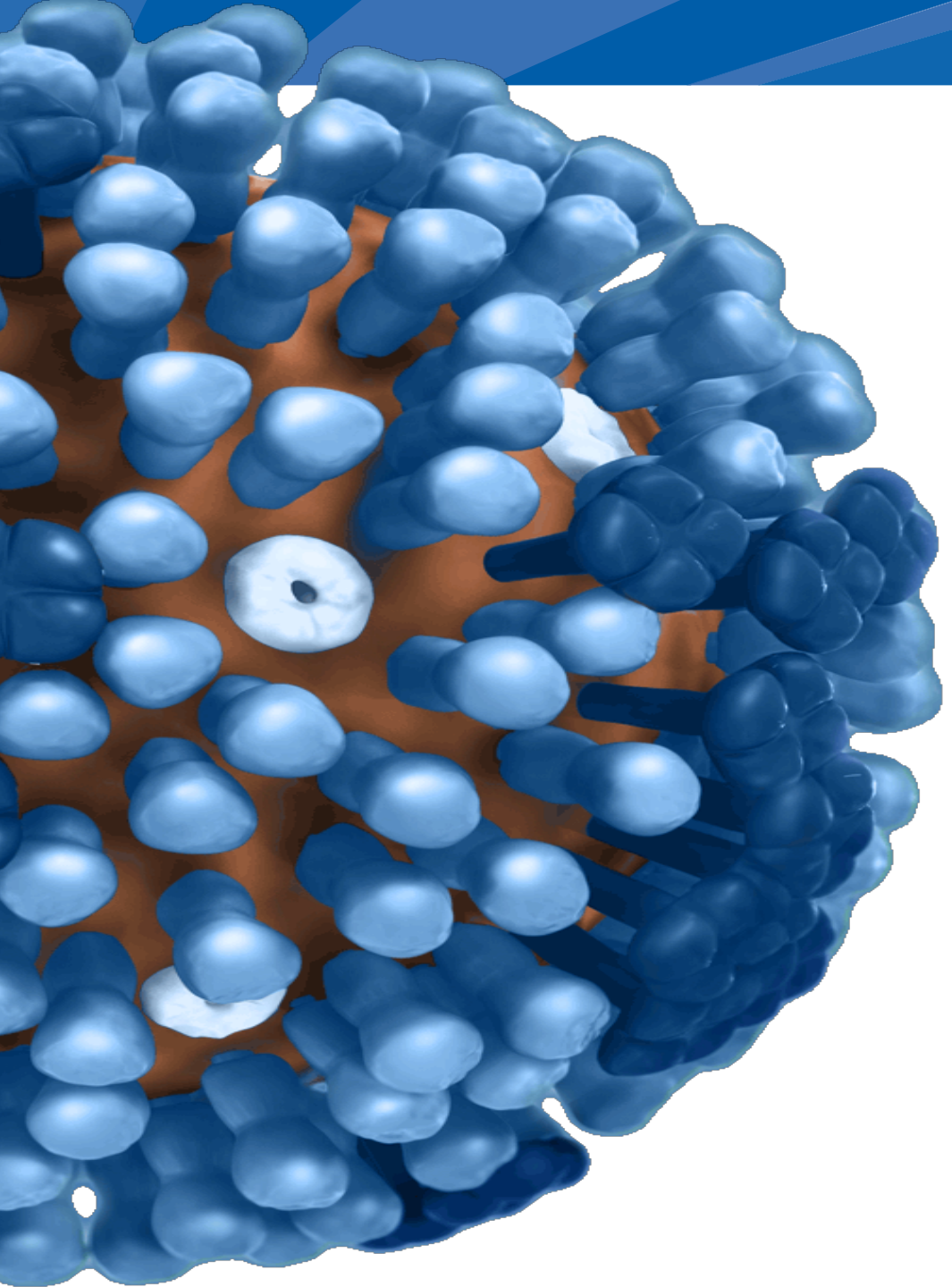


Human Infections with Highly Pathogenic Avian Influenza A(H5N1) Virus Epidemiology and Clinical Aspects

Tim Uyeki MD, MPH, MPP

Chief Medical Officer, Influenza Division

National Center for Immunization and Respiratory Diseases, CDC

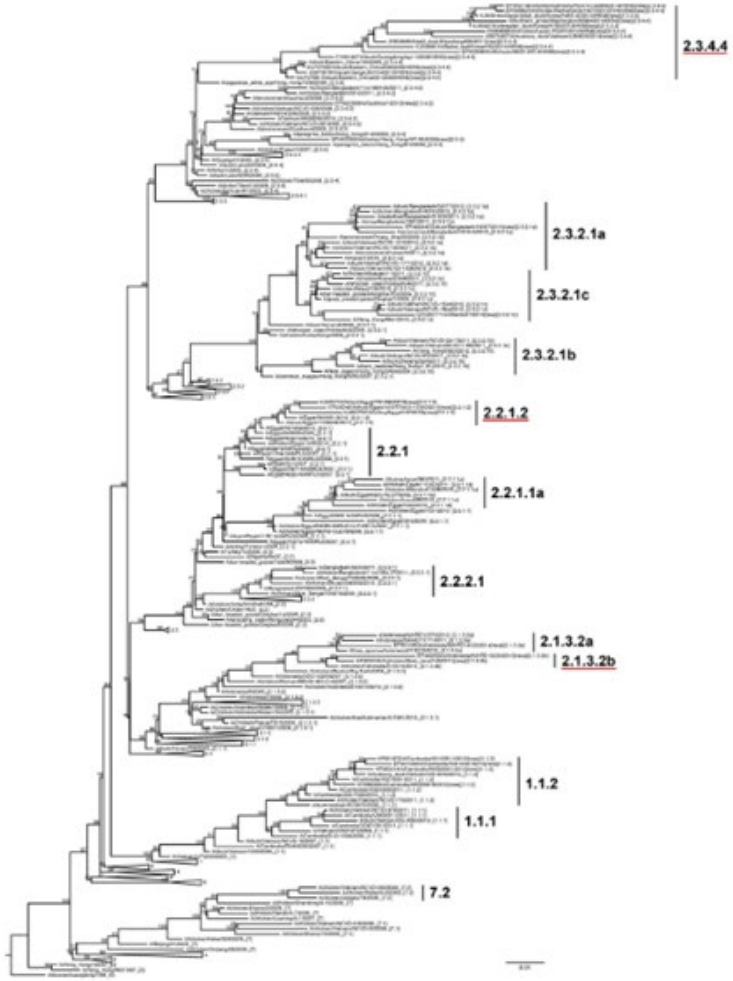
October 23, 2023

Overview

- Background on highly pathogenic avian influenza A(H5N1) viruses
- Wild bird infections, poultry outbreaks, spillover to mammals
- Human cases
  - Epidemiology, risk factors for infection
- Clinical characteristics
- Clinical management
  - Testing, treatment
  - Infection control and prevention recommendations

Highly Pathogenic Avian Influenza A(H5N1) Virus

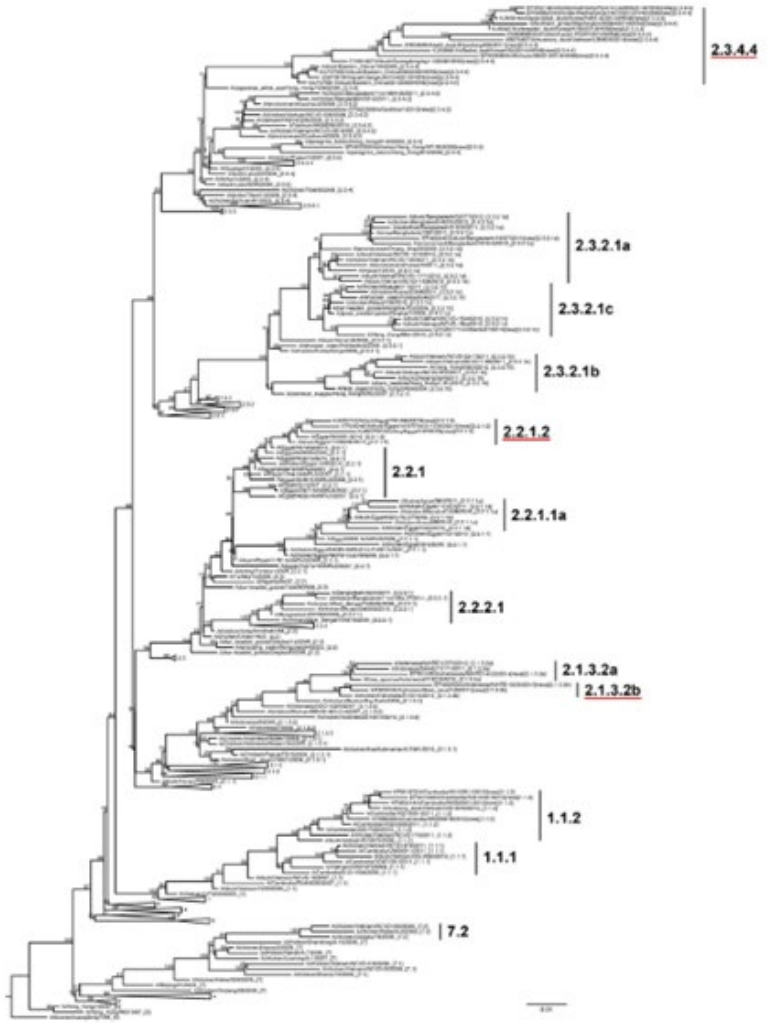
- First identified in 1959 during a poultry outbreak in Scotland
- Identified in a goose from southern China in 1996 (Guangdong Province)
- HPAI A(H5N1) virus evolution
  - Since 1996, H5N1 viruses have continued to evolve into distinct antigenic clades and subclades
    - Spread in wild birds and poultry in Asia, and >60 countries during 2004-2007 (Europe, Africa, Middle East)
    - Endemic circulation (enzootic) among poultry in some countries



Smith and Donis Influenza Other Resp Viruses 2015

Highly Pathogenic Avian Influenza A(H5N1) Virus

- **Spread in recent years by wild birds**
  - **Since 2020: clade 2.3.4.4b H5N1 viruses have spread via migratory birds in Africa, Asia, and Europe**
  - **Late 2021-2022: spread to North America: poultry outbreaks, wild bird detections (hawks, eagles, owls, vultures, raven, crows, geese, ducks, grebes, pelicans, swans, shovelers, teal, cormorants, kestrels, gulls, California condors, etc.)**
    - **Detected in wild birds in 49 states to date**
  - **Late 2022-2023: spread to South America**
  - **Wild bird detections, poultry outbreaks**
  - **Not all birds are equally susceptible to H5N1 virus**
    - **Some ducks can have asymptomatic infection**



Smith and Donis Influenza Other Resp Viruses 2015

HPAI 2022/2023 Confirmed Detections

as of October 19, 2023
Last reported detection Tuesday, October 17, 2023
Data updated weekdays by 12pm Eastern

Download Data

856 Confirmed Flocks

16 confirmed last 30 days
Birds tested and confirmed having HPAI

47 Affected States

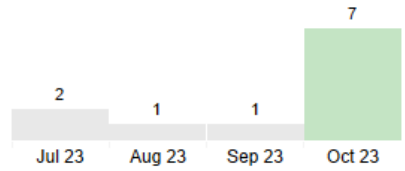
9 states last 30 days
States with at least one confirmed infected flock

Commercial Flocks

333

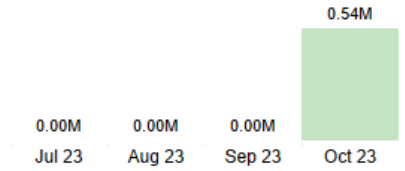
Backyard Flocks

523



Birds Affected*

59.34M

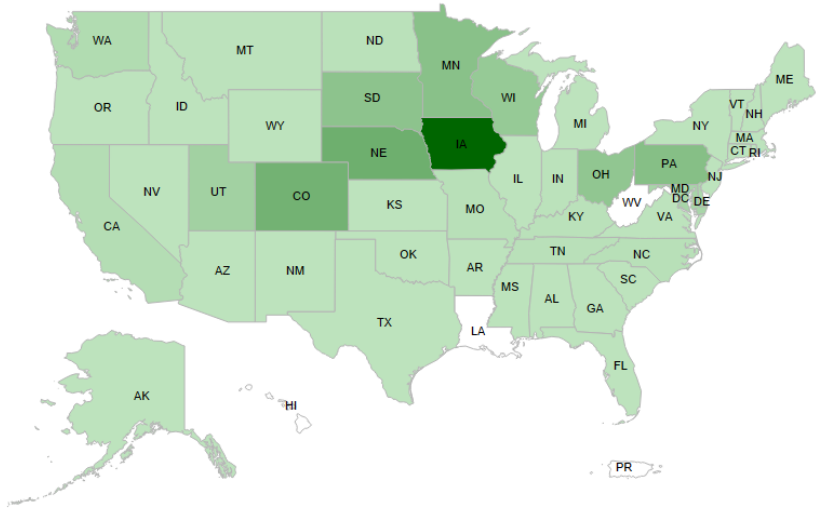


*Number of birds on confirmed infected premises.
Bars reflect most recent 4 months (numbers may not add up to total).

Choose variable: Birds Affected
Choose time period: Total Outbreak

Birds Affected by State

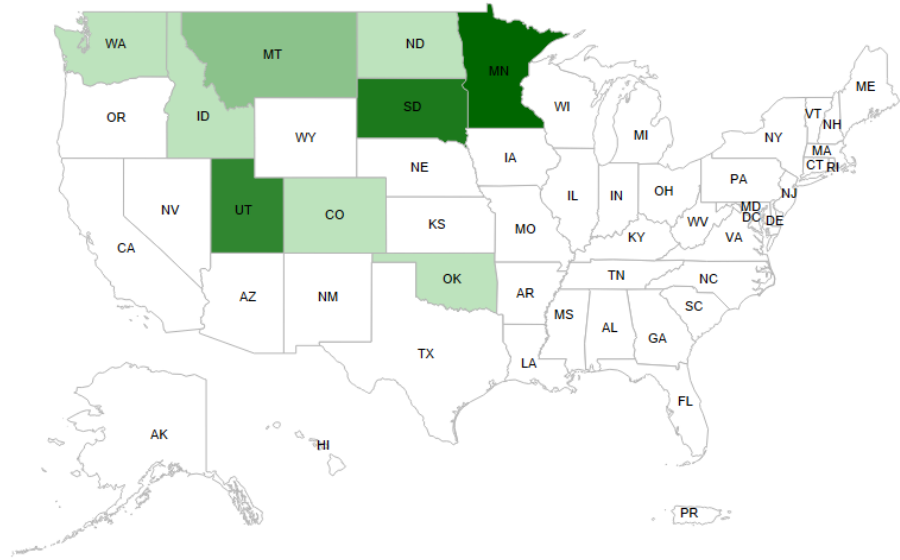
Legend: 0 – 15,951,724



Choose variable: Birds Affected
Choose time period: Last 30 Days

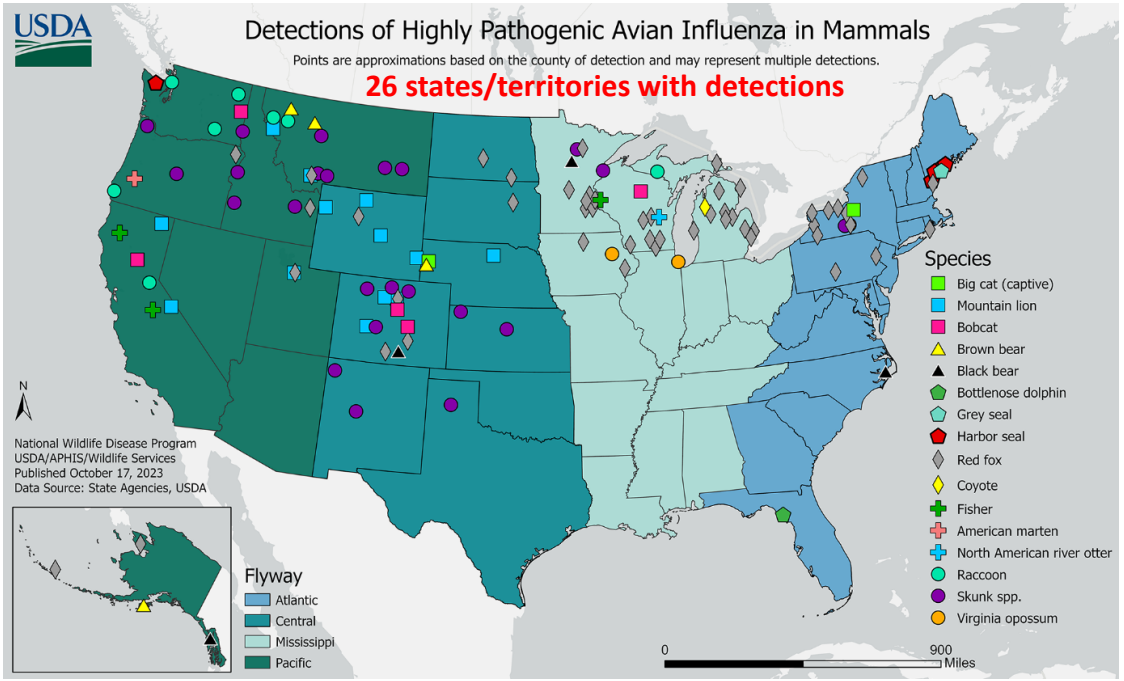
Birds Affected by State

Legend: 0 – 189,800



Highly Pathogenic Avian Influenza A(H5N1) Virus in Mammals

- **Transmission to mammals reported since 2003** (neurologic & respiratory disease, fatal outcomes)
  - **Terrestrial mammals:** tigers, leopards in a zoo; dogs, cats, other animals during 2003-2004, cats (multiple countries 2022-2023: France, U.S., Poland, South Korea)
    - **Examples:** red fox, raccoon dog, coyote, otter, badger, polecat, ferret, farmed mink, lynx, mountain lion, bobcat, fisher cat, amur leopard, raccoon, skunk, black bear, brown bear, grizzly bear, opossum
      - **Farmed animals:** mink (Spain 2022), arctic foxes (Finland 2023)
  - **Marine mammals:** seals, sea lions, porpoise, dolphin
    - Unclear if mammal-to-mammal transmission is occurring, some markers of mammalian adaptation reported
    - Harbor and gray seals (New England 2022; environment-to-seal transmission), sea lions (Peru 2023), sea elephants



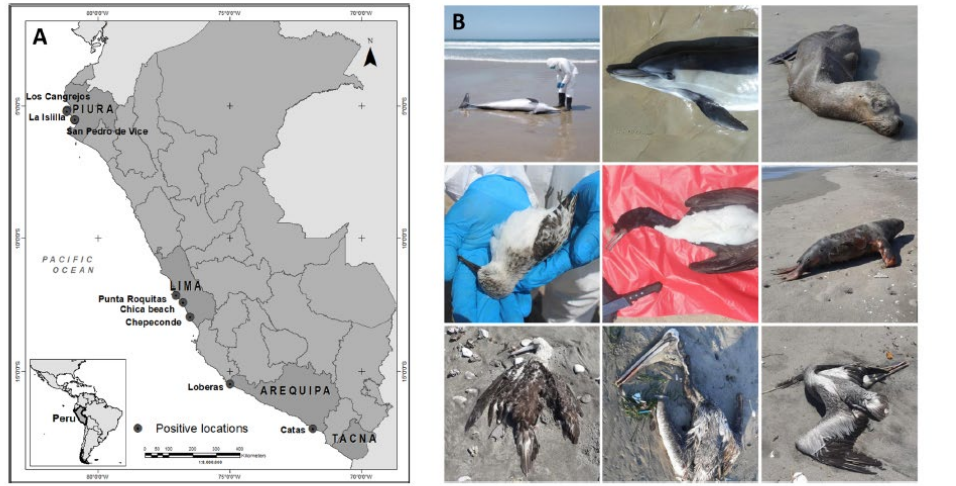
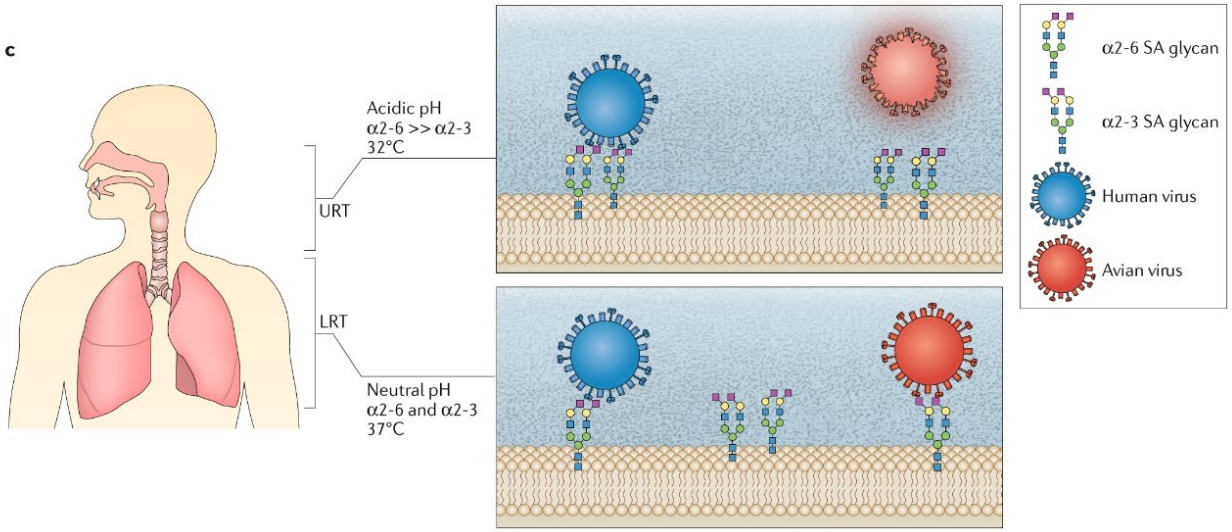


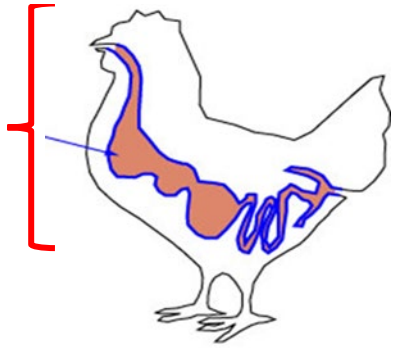
Fig. 1 | Collection sites and animals sampled. A Map of Peru showing collection sites representative of the northern, central and southern regions. Mass die-offs of both birds and mammals occurred along the entire coast of Peru, but map only shows positive locations of animals samples in this study. B Photographic record of animals sampled, including common dolphin, South American sea lion, sanderling, Guanay cormorant, Peruvian booby and Peruvian pelican.

Puryear EID 2023; Leguia Nature Communications 2023

Seasonal Influenza A viruses and Avian Influenza A(H5N1) Viruses Have Different Receptor Binding Tropism



- Seasonal influenza A viruses bind preferentially to sialic acid receptors attached to galactose by **α2,6 linkages** expressed on epithelial cells that are primarily found in the ***upper respiratory tract in humans***
- Some influenza viruses can bind to **α2,3 sialic acid receptors** that are primarily found in the ***lower respiratory tract in humans***



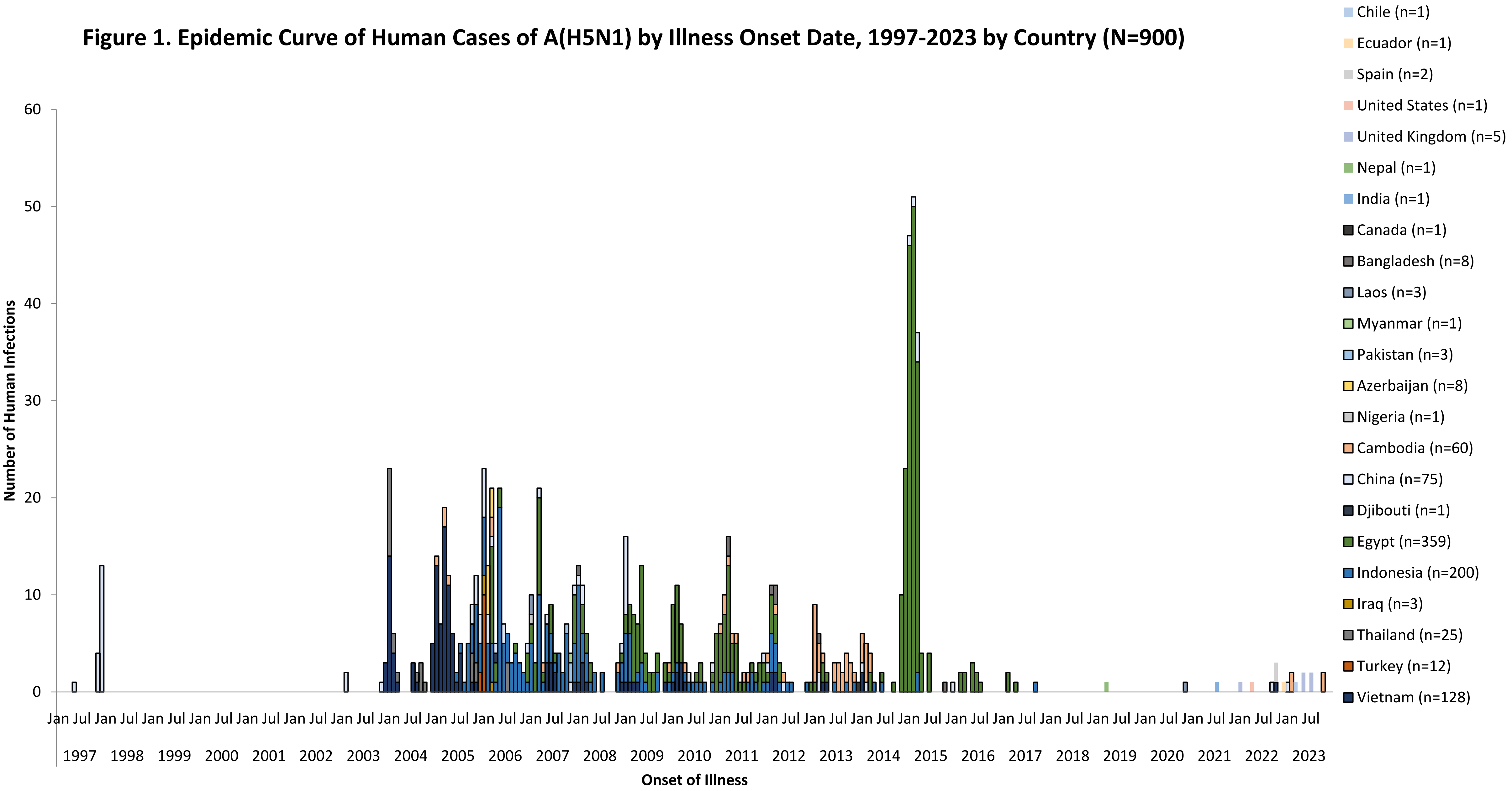
- Highly Pathogenic avian Influenza A(H5N1) viruses bind to sialic acid receptors attached to galactose by **α2,3 linkages expressed in the respiratory and gastrointestinal tracts in birds**

Long et al. Nature Reviews Microbiology 2019; Rajao et al. Frontiers in Veterinary Science 2019

Epidemiology of Human Cases of H5N1 Virus Infection

- First infections identified in Hong Kong, 1997 (18 cases, 6 deaths)
- Re-emergence in humans: 2003-2005 (China, Southeast Asia)
- Cases identified in other regions since 2006 (Middle East, Europe, Africa)
- 1997-2023: 900 cases with >50% case fatality proportion (22 countries)
  - Most cases had severe pneumonia (young adults, some children), few cases since 2015-2016
    - Mostly sporadic avian-to-human H5N1 virus transmission from poultry exposures
- Some clusters of epidemiologically-linked cases
  - Most clusters represent common poultry exposures in family members
  - Small number of clusters: probable limited, non-sustained human-to-human transmission among blood-related family members

Figure 1. Epidemic Curve of Human Cases of A(H5N1) by Illness Onset Date, 1997-2023 by Country (N=900)



Risk Factors for Human Infection with H5N1 Virus

- **Sporadic avian-to-human transmission from poultry exposures**
  - **Direct/close unprotected exposure to sick/dead infected poultry, raising backyard poultry**
  - **Visiting a live poultry market**
- **Exposure to infected wild birds**
  - **Defeathering wild swans that died (2 clusters of cases, Azerbaijan, 2006)**
- **Small number of cases with unknown source of infection**
  - **(e.g., one returned traveler, Canada Dec. 2013)**
- **Small number of clusters with probable limited, non-sustained human-to-human transmission among blood-related family members**
  - **Prolonged, unprotected, close exposure to a symptomatic case (household or hospital exposures in blood-related family members)**
  - **No cases of human-to-human H5N1 virus transmission reported since 2007**

➢ **No cases of mammal-to-human transmission reported**

WHO NEJM 2008; Zhou J Infect Dis 2009; Mounts J Infect Dis 1999; Gilsdorf Eurosurveillance 2006; Ungchusak NEJM 2005; Wang Lancet 2007

Clinical Spectrum of H5N1 Virus Infection

- Wide clinical spectrum (asymptomatic infection to fulminant critical illness)
- Most case-finding has focused on hospitalized patients with severe pneumonia
- Surveillance of close contacts of cases or routine surveillance for influenza-like illness has identified a small number of H5N1 virus infections with mild illness
  - Mild illness with upper respiratory tract symptoms has been reported (especially in children)
- Asymptomatic H5N1 virus infection reported
  - Some asymptomatic cases with virologic and serologic confirmation of H5N1 virus infection have been reported
  - However - some reported cases may not represent true infection
    - Transient detection of H5N1 viral particles deposited in the upper respiratory tract

Uyeki Clin Infect Dis 2009

Clinical Presentation

- **Incubation period (poultry exposure to symptom onset): mean 3 days (2-7 days)**
- **Patients with severe disease: median time onset to hospitalization: @6 days**
  - **Clinical progression:**
    - **Fever or feverishness, nonproductive cough, muscle aches, malaise, headache, sore throat, myalgia, abdominal pain, vomiting and diarrhea can occur**
    - **Progression to lower respiratory tract disease: difficulty breathing, shortness of breath, chest pain, tachypnea**
  - **Hospital admission findings:**
    - **Clinical: hypoxia, signs of pneumonia**
    - **Laboratory: leukopenia, lymphopenia, mild-to-moderate thrombocytopenia**
    - **Radiographic findings: patchy, interstitial, lobar, and/or diffuse infiltrates and opacities, consolidation, pleural effusion**

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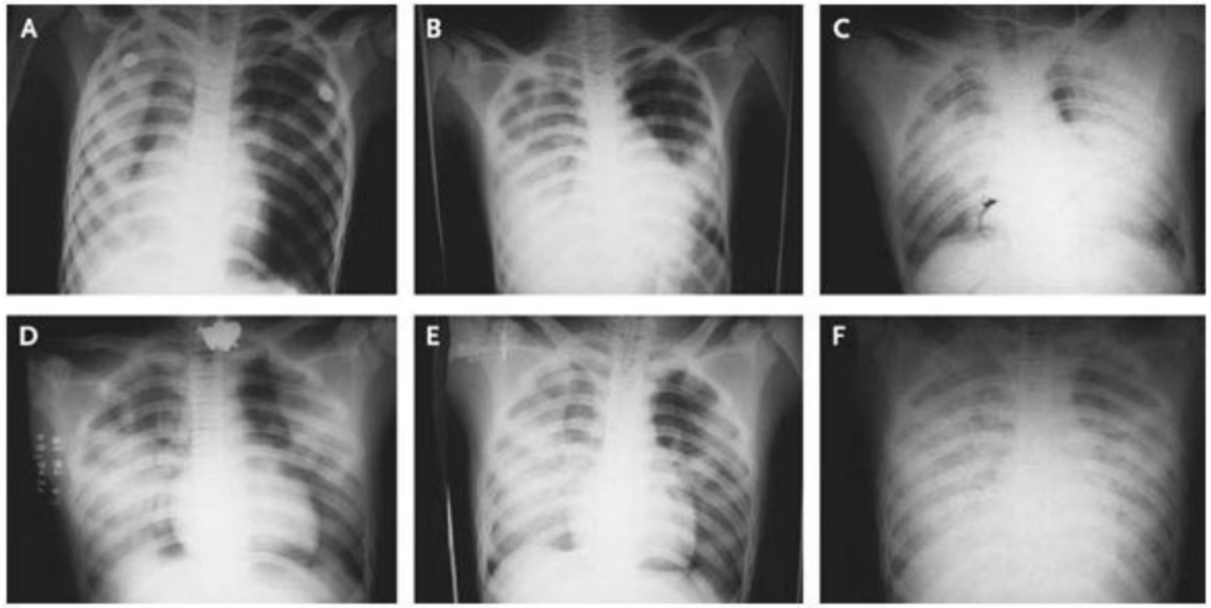
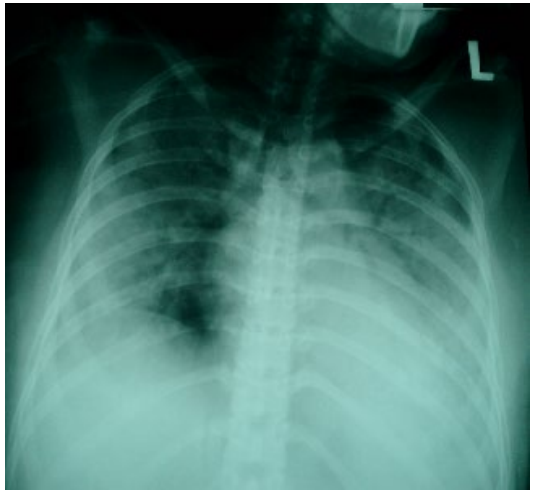
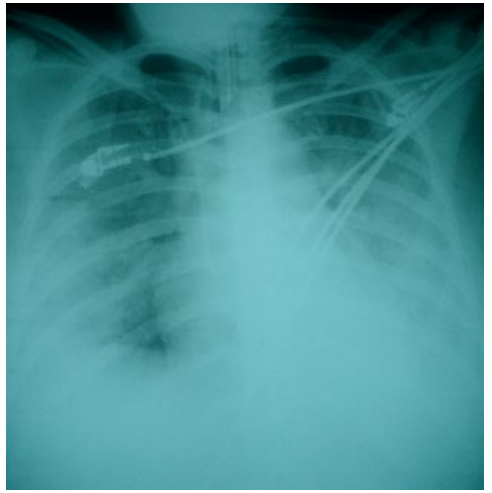
Examples of H5N1-associated severe pneumonia cases



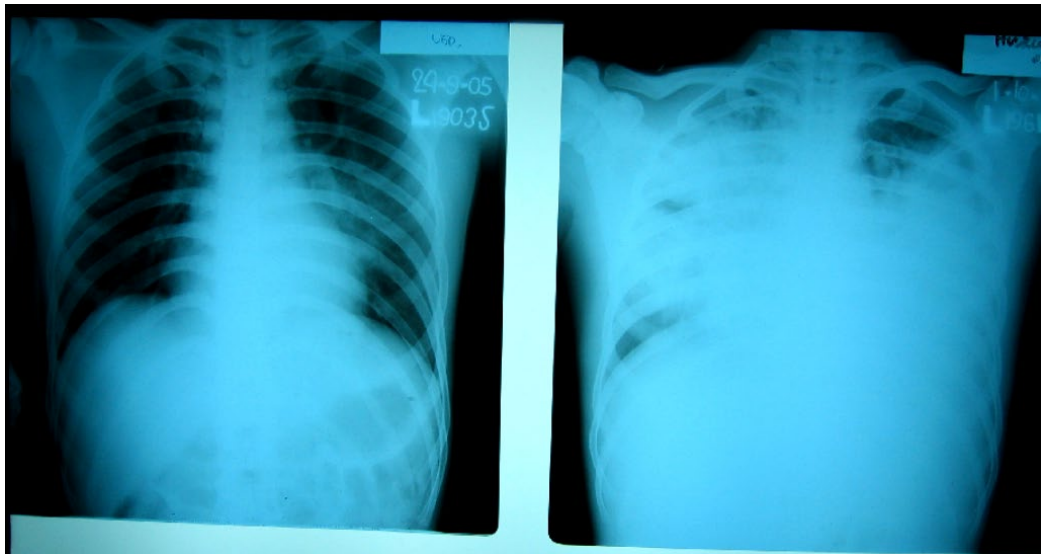
Hien NEJM 2004



37-yo woman, illness day #7
Admission CXR



Illness day #10; died day #11



21-yo male, illness day #5
Admission CXR

Illness day #12; survived
(not ventilated)

T Uyeki, CDC September 2005

Complications of H5N1 Virus Infection

- **Pneumonia is the most common complication**
  - **Progression to respiratory failure, ARDS**
    - **Community-acquired bacterial co-infection is rare; ventilator-associated pneumonia can develop in ventilated patients**
- **Other severe complications**
  - **Acute kidney injury**
  - **Cardiac failure**
  - **Sepsis, shock, DIC, multi-organ failure (respiratory and renal failure)**
  - **Atypical complications**
    - **Encephalitis with diarrhea and pneumonia; encephalitis with obstructive hydrocephalus; meningoencephalitis with pneumonia**
    - **Reye syndrome with salicylate exposure**
    - **Spontaneous miscarriage in a pregnant woman**
    - **Vertical transmission (mother-to-fetus)**

Uyeki Clin Infect Dis 2009

Pathogenesis of Severe Illness with H5N1 Virus Infection

- **Patients with severe disease:**
  - **Infection of the respiratory tract (lower respiratory tract) → high viral levels → triggers an abnormal or dysregulated host inflammatory response**
    - **High upper respiratory tract H5N1 viral levels associated with fatal outcome**
    - **Proinflammatory cytokines and chemokines are induced and can cause pulmonary (diffuse alveolar damage) and multi-organ injury**
    - **Extrapulmonary viral dissemination can occur from viremia**
      - **H5N1 virus isolated from respiratory specimens, blood/serum/plasma, rectal swab/feces, CSF**

de Jong Nature Medicine 2006; WHO NEJM 2008

Infection Prevention and Control Recommendations

- **Rationale: Potential for close range large droplet and small particle (aerosol) spread, and H5N1 virus infection with high mortality**
  - **Place patient in airborne infection isolation room (AIIR)**
    - **If not available, isolate in single-patient room, place facemask on patient, keep door closed; arrange transfer to facility with an AIIR (negative-pressure, HEPA filtration)**
  - **Standard, contact, airborne precautions recommended**
  - **PPE: single-use gown, gloves, eye protection (goggles), fit-tested N95 respirator**

CDC. Interim Guidance for Infection Control Within Healthcare Settings When Caring for Confirmed Cases, Probable Cases, and Cases Under Investigation for Infection with Novel Influenza A Viruses Associated with Severe Disease: https://www.cdc.gov/flu/avianflu/novel-flu-infection-control.htm

H5N1 Virus Diagnostic Testing

- **Commercially available influenza assays**
  - **Cannot specifically identify H5N1 virus**
    - **Tests that identify influenza A virus do not distinguish seasonal influenza A viruses from novel influenza A viruses, including H5N1 virus**
- **Patients with mild respiratory disease:**
  - **Collect nasopharyngeal (NP) swab and combined nasal & throat swabs for rRT-PCR testing for influenza A and B viruses at public health laboratories**
    - **Influenza A positives are subtyped for H1 and H3; if A positive, H1 & H3 negative:**
      - **Test for H5 at public health laboratories**

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      - **Test for H5 at public health laboratories**
- **Patients with lower respiratory tract disease (pneumonia):**
  - **Collect upper respiratory specimens and sputum for rRT-PCR testing for influenza A virus subtypes H1, H3, and H5 at public health laboratories**
    - **Intubated patients: Also collect endotracheal aspirate specimens (or BAL fluid) for testing**
    - **Collect multiple specimens different respiratory sites on multiple days to increase detection**
      - **Cambodia, January 2023: severe H5N1 case in a child diagnosed by NP swab and BAL specimens**
      - **Chile, March 2023: severe H5N1 case in an adult diagnosed by BAL specimen (NP swab was negative)**

Clinical Management: Antiviral Treatment for H5N1

- **No evidence of Oseltamivir resistance in H5N1 viruses circulating in birds**
- **Patients with mild disease:**
  - **Start Oseltamivir treatment empirically as soon as possible for patients with suspected H5N1 virus infection (based on history of exposures)**
    - **Oseltamivir standard dosing: twice daily x 5 days (*no data for Baloxavir treatment*)**
    - **No clinical trials - Observational studies reported earlier Oseltamivir treatment is associated with greater survival versus later treatment initiation**

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- **Patients with lower respiratory tract disease:**
  - **Start Oseltamivir treatment empirically as soon as possible for patients with suspected H5N1 virus infection (based on history of exposures)**
    - **Optimal dosing and duration unknown; extend duration for severe disease and prolonged viral shedding; well absorbed when given enterically**
    - **Emergence of oseltamivir resistance has been reported**

➢ **Gap: no data on combination antiviral treatment of H5N1**

Uyeki Clin Infect Dis 2009

Clinical Management: Supportive Care

- **Clinical management of severe disease → supportive care of complications**
  - **Respiratory support: may require invasive mechanical ventilation**
  - **Other advanced organ support:**
    - **Extracorporeal membrane oxygenation (ECMO) has been used for H5N1 patients**
    - **Renal replacement therapy (dialysis) for kidney failure**
  - **Adjunctive therapy**
    - **Avoid moderate to high-dose corticosteroids**
      - **Associated with prolonged viral shedding**
      - **May increase the risk for ventilator-associated pneumonia and death**

➢ **Gap: no data on combination antiviral treatment of H5N1**

Current Situation and Recent H5N1 Cases

- **U.S. 2022 to date: >6500 persons monitored after poultry/bird exposures: >165 persons reported symptoms: H5N1 virus detected in 1 person's respiratory specimens (only fatigue reported)**
  - **Human H5N1 cases: 2022 to date (N = 17, 8 countries)** ***(most had recent poultry exposures)***
    - **Severe illness: 8 cases (4 deaths); Mild illness: 2 cases; Asymptomatic: 7 cases**
      - ***UK (Dec. 2021): Elderly asymptomatic man who raised ducks in England,*** clade 2.3.4.4b
      - ****US (April 2022): Adult involved in poultry culling, reported "fatigue,"*** clade 2.3.4.4b
      - **Vietnam (October 2022): child developed critical illness, survived**
      - **China (September/October 2022): adult developed critical illness, died,** clade 2.3.4.4b
      - ****Spain (September): 2 asymptomatic adult poultry workers,*** clade 2.3.4.4b
      - **Ecuador (Dec 2022/January 2023): child developed critical illness, survived,** clade 2.3.4.4b
      - **China (January 2023): adult developed severe illness,** clade 2.3.4.4b
      - **Cambodia (February 2023): 2 cases, girl (died) and father (mild illness)**, poultry exposures: clade 2.3.2.1c
      - **Chile (March 2023): adult developed critical illness**, clade 2.3.4.4b
      - ****UK (May 2023): 2 asymptomatic adult poultry workers,*** clade 2.3.4.4b
      - ****UK (July 2023): 2 asymptomatic adult poultry workers,*** clade 2.3.4.4b
      - **Cambodia (October 2023): 2 cases, child (died); adult (died),** poultry exposures: clade 2.3.2.1c

****Unclear whether cases represent true infection***

Aznar et al. Euro Surveill. Feb. 23, 2023; UKHSA Technical Briefing 5 July 14, 2023

Public Health Assessment

- **Clade 2.3.4.4b H5N1 viruses are circulating in wild birds and poultry in many regions of the world, with sporadic spillover to mammals, and rare sporadic human infections**
  - **H5N1 viruses are well-adapted to infect and spread among wild birds and poultry**
  - **Sporadic spillover to mammals is not surprising; no evidence of sustained transmission among mammals, no instances of mammal-to-human transmission**
  - **Nearly all sporadic human cases reported since 2022 had exposure to poultry**
    - **No indication of human-to-human transmission since 2007**
  - **H5N1 viruses currently lack ability to bind well to receptors in the human upper respiratory tract and lack ability to spread efficiently among people**
  - **The public health risk is low, but because H5N1 viruses continue to evolve, vigilance and on-going monitoring is needed in animals and people**
    - **Expect sporadic human infections with H5N1 viruses to occur**

https://www.cdc.gov/flu/avianflu/spotlights/2022-2023/h5n1-technical-report_september.htm

Resources

- Case definitions: https://www.cdc.gov/flu/avianflu/case-definitions.html
- Monitoring & post-exposure antiviral prophylaxis: https://www.cdc.gov/flu/avianflu/guidance-exposed-persons.htm
- Follow-up of close contacts: https://www.cdc.gov/flu/avianflu/novel-av-chemoprophylaxis-guidance.htm
- Summary for clinicians: https://www.cdc.gov/flu/avianflu/clinicians-evaluating-patients.htm
- Specimen collection & testing: https://www.cdc.gov/flu/avianflu/severe-potential.htm
- Infection prevention and control: https://www.cdc.gov/flu/avianflu/novel-flu-infection-control.htm
- Antiviral guidance: https://www.cdc.gov/flu/avianflu/novel-av-treatment-guidance.htm
- Current situation: https://www.cdc.gov/flu/avianflu/avian-flu-summary.htm
- de Jong et al. Fatal outcome of H5N1 associated with high viral load and hypercytokinemia. *Nat Med 2006;12:1203-7*
- Gambotto et al. Human infection with highly pathogenic H5N1 influenza virus. *Lancet 2007;371:1464-75*
- WHO Writing Committee Update on H5N1 virus infection in humans. *N Engl J Med 2008;358:261-273*
- Uyeki. Human infection with H5N1 virus: review of clinical issues. *Clin Infect Dis 2009;49:279-90*
- White et al. What is the optimal therapy for patients with H5N1 influenza? *PLoS Med 2009;6:e1000091.*
- CDC H5N1 Technical Report: https://www.cdc.gov/flu/avianflu/spotlights/2022-2023/h5n1-technical-report_september.htm

The Evaluation of a Patient with Suspected Avian Influenza

David Banach, MD MPH
Associate Professor of Medicine
Hospital Epidemiologist
Division of Infectious Diseases
UConn Health
October 23, 2023

Case Presentation

October 2023

- 34-year-old male with no significant past medical history presents to the Emergency Department with 4 days of fevers, chills and muscle aches
- Symptoms began abruptly and over the last 3 days have generally worsened
  - Onset of symptoms he began taking acetaminophen every 6 hours
    - near the end of the 6-hour periods fevers returned
  - Intense myalgias of the upper and lower extremities
  - Hydration and symptom management –
    - Day of presentation began to develop cough and shortness of breath

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Case Presentation

- Emergency Department vitals at triage
  - Temperature 38.9^0 C (102^0 F)
  - Blood pressure 114/72
  - Heart rate 96 beats/minute
  - Respiratory rate 18/minute
  - Oxygen saturation 92% on room air
- Provided a procedure mask
  - Instructed to wear it while in the waiting area
- Escorted to a private room in the ED

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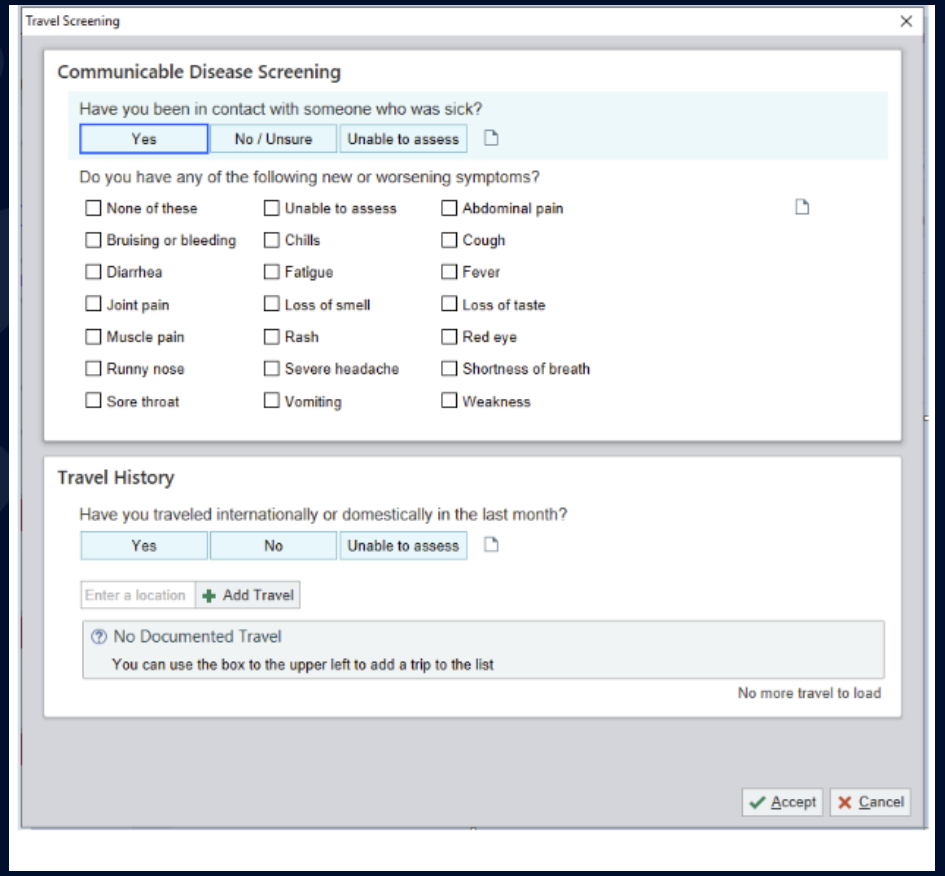
Travel Screen



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Initial Evaluation

- History components
  - Associated symptoms – ENT, gastrointestinal, skin rashes/lesions, urinary, neurological
  - Medical history – medical comorbidities, (immunosuppression), medications, medical procedures/surgeries
  - Epidemiological exposures – travel history, home/workplace exposures, exposures to animals/vector-borne diseases

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Case

- Additional history
  - Associated symptoms
    - + fatigue, diarrhea, nausea, headache, arthralgias
    - - sore throat, abdominal pain, rash, dysuria, hematuria
  - No significant past medical history and no medications
  - Resides in Central NY with wife and daughter (age 7)
    - Both have been healthy, asymptomatic
  - No recent travel outside the Northeastern U.S. in the last 6 months
  - Works as an accountant. Enjoys hiking outdoors with family in New England

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Animal Exposure

- Live with domesticated dog – Golden retriever who is up to date with vaccines and has been good health
- Has been feeding and providing care for neighbor's pet bird for the past 5 days
  - Recently acquired from a bird market in Brooklyn about a week ago
  - Bird has been lethargic – "found down", unarousable in cage yesterday

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Differential Diagnosis

- Infections
  - Viral – COVID-19, influenza, RSV, acute Epstein-Barr virus, acute cytomegalovirus, gastrointestinal viruses (ex. norovirus)
  - Bacterial – community-acquired pneumonia (*S. pneumoniae*, *H. influenzae*), Legionella, bloodstream infection, gastrointestinal bacterial infection (ETEC/EHEC, salmonella/shigella)
  - Vector-borne diseases – anaplasmosis, babesiosis, Powassan, WNV/EEE
  - Zoonotic infections – Pasteurella, capnocytophaga

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Differential Diagnosis

- Non-infectious etiologies
  - Connective tissue diseases
    - Vasculitis, lupus, rheumatoid arthritis, polymyalgia rheumatica
  - Malignancy
    - Leukemia/lymphoma, solid tumor neoplasms
  - Drugs/Medications

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Avian flu - Epidemiologic Criteria (CDC)

- **Recent (< 10 days) exposure to infected birds**:
  - Close exposure (< 2 meters) to birds, with confirmed avian influenza A virus infection by A(H5), A(H7), A(H9) viruses
    - Handling, slaughtering, defeathering, butchering, culling, or preparation of birds for consumption; **OR**
  - Direct contact with surfaces contaminated with feces/bird parts (carcasses, organs) from infected birds; **OR**
  - Visiting a live poultry market with confirmed bird infections or associated with a case of human infection with avian flu A virus

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Avian Influenza - Epidemiologic Criteria (CDC)

- **Exposure to an infected person**
  - Close (< 2 meters) unprotected (without use of respiratory and eye protection) exposure to a person who is a confirmed, probable, or symptomatic suspected case of human infection with avian influenza A virus (household or healthcare facility).
- **Laboratory exposure**
  - Unprotected (without use of respiratory and eye protection) exposure to avian influenza A virus in a laboratory.

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Avian Influenza – Clinical Criteria (CDC)

- Signs and symptoms consistent with acute or lower respiratory tract infection or conjunctivitis, or complications of acute respiratory illness without an identified cause.
  - **Mild flu-like illness** (cough, sore throat, fever or feeling feverish, rhinorrhea, fatigue, myalgia, arthralgia, headache) or conjunctivitis
  - **Moderate - severe illness**: shortness of breath or difficulty breathing, altered mental status, seizures
  - **Complications**: pneumonia, respiratory failure, acute respiratory distress syndrome, multi-organ failure, meningoencephalitis

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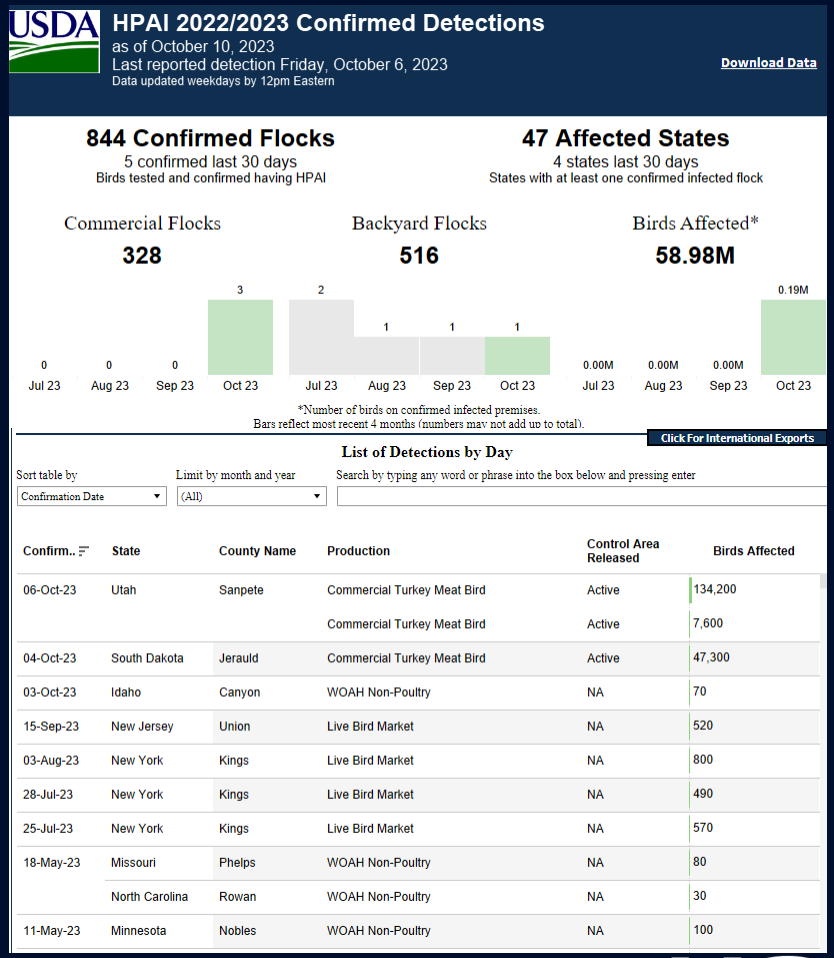
Avian Influenza Reporting



Confirm..	State	County Name	Production	Control Area Released	Birds Affected
06-Oct-23	Utah	Sanpete	Commercial Turkey Meat Bird	Active	134,200
			Commercial Turkey Meat Bird	Active	7,600
04-Oct-23	South Dakota	Jerauld	Commercial Turkey Meat Bird	Active	47,300
03-Oct-23	Idaho	Canyon	WOAH Non-Poultry	NA	70
15-Sep-23	New Jersey	Union	Live Bird Market	NA	520
03-Aug-23	New York	Kings	Live Bird Market	NA	800
28-Jul-23	New York	Kings	Live Bird Market	NA	490
25-Jul-23	New York	Kings	Live Bird Market	NA	570
18-May-23	Missouri	Phelps	WOAH Non-Poultry	NA	80
	North Carolina	Rowan	WOAH Non-Poultry	NA	30
11-May-23	Minnesota	Nobles	WOAH Non-Poultry	NA	100

https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/animal-disease-information/avian/avian-influenza/hpai-2022/2022-hpai-commercial-backyard-flocks

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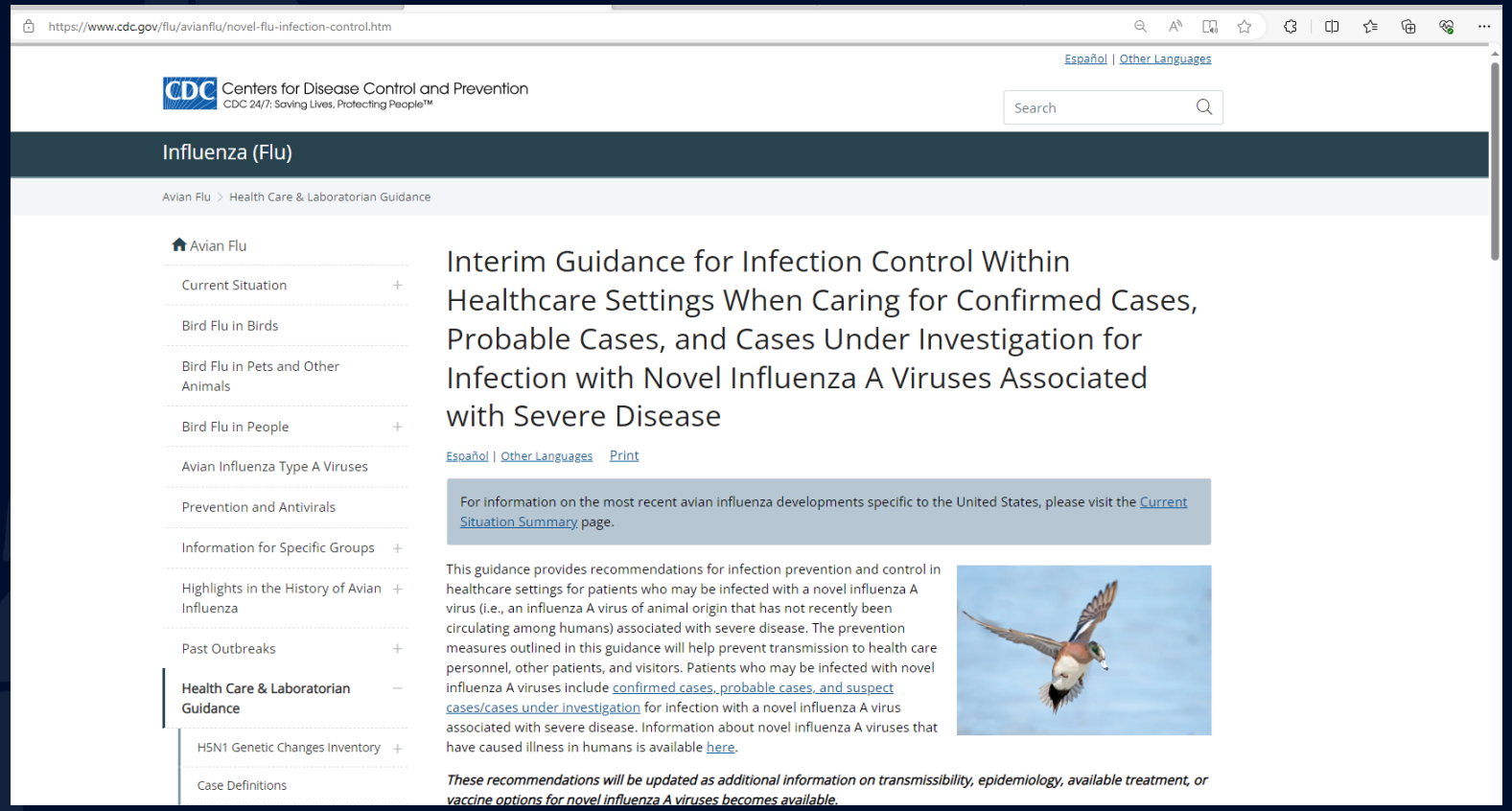
Infection Prevention and Control Measures



https://www.cdc.gov/flu/avianflu/novel-flu-infection-control.htm

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CDC Guidance

- Based on limited data on transmission and other factors
  - Lack of an available safe and effective vaccine against novel influenza A viruses associated with severe disease in infected humans
    - Avian influenza A(H5) or A(H7) viruses
  - Concern for increased morbidity and mortality among infected patients
  - Few or no confirmed cases in the United States
- Different from that recommended for patients with seasonal influenza
  - Among important differences from seasonal influenza guidance are recommendations for *Contact and Airborne Precautions*

https://www.cdc.gov/flu/avianflu/novel-flu-infection-control.htm

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Infection Control in Healthcare Settings – Suspected Novel Influenza A

- Airborne Infection Isolation Room
- Minimize number of people entering the room to essential healthcare personnel
- Recommended personal protective equipment for HCP
  - Gown
  - Gloves
  - Respirator (N-95 level of higher)
  - Eye protection (face shield or goggles)

https://www.cdc.gov/flu/avianflu/novel-flu-infection-control.htm

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Case

- Physical examination
  - General Appearance – Uncomfortable appearing, diaphoretic
  - HEENT: Anicteric, no conjunctival suffusion, oropharynx with pink mucosa, no exudates
  - Neck: Supple, no abnormal adenopathy of the head and neck
  - Lungs: Tachypneic, scattered crackles bilaterally
  - Cardiovascular: Tachycardia. Normal S1, S2, no murmur
  - Skin: No rash
  - Extremities: No joint swelling, erythema, or limited range of motion of the upper and lower extremities
  - Neurological: Normal mentation. Cranial nerves examined and all normal. No weakness of the upper and lower extremities

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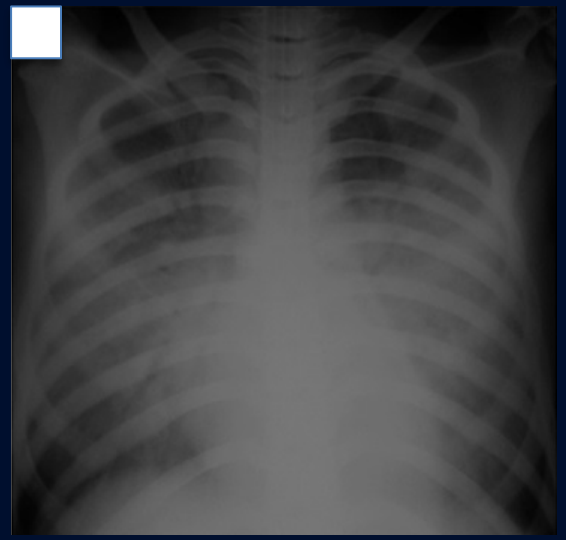
Case - Laboratory Studies/Imaging

- White blood cell count 2,100 /mL
  - Lymphocytes 19%
- Hemoglobin 13.1 g/dL
- Platelet count 213,000 /mL
- Blood urea nitrogen 10 mg/dL
- Creatinine 1.2 mg/dL
- AST 91 U/L
- ALT 82 U/L



CXR: Bilateral multifocal consolidations

Quereshi N et al. *Journal of Thoracic Imaging* 2006: 21(4):p 259-264.

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Laboratory/Imaging in Influenza H5N1

- Leukopenia
  - Lymphopenia
- Thrombocytopenia
- Abnormal liver enzymes (AST/ALT)
- Elevated creatinine kinase (CK)
- Elevated lactate dehydrogenase (LDH)

- Bilateral perihilar consolidations
  - Lobar or interstitial
- Pleural effusions uncommon
- Acute respiratory distress syndrome (ARDS)

Kandun IN et al. *N Engl J Med*. 2006;355(21):2186
Oner AF et al. *N Engl J Med*. 2006;355(21):2179
Quereshi N et al. *J of Thoracic Imaging.* 2006: 21(4): 259-264

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Case – Respiratory Virus Testing

- Multiplex PCR testing (Xpert Xpress CoV-2/Flu/RSV *plus*®, *Cepheid)*
  - Nasal swab
  - SARS-CoV-2 PCR - negative
  - RSV PCR – negative
  - Influenza B PCR – negative
  - Influenza A PCR - **positive**

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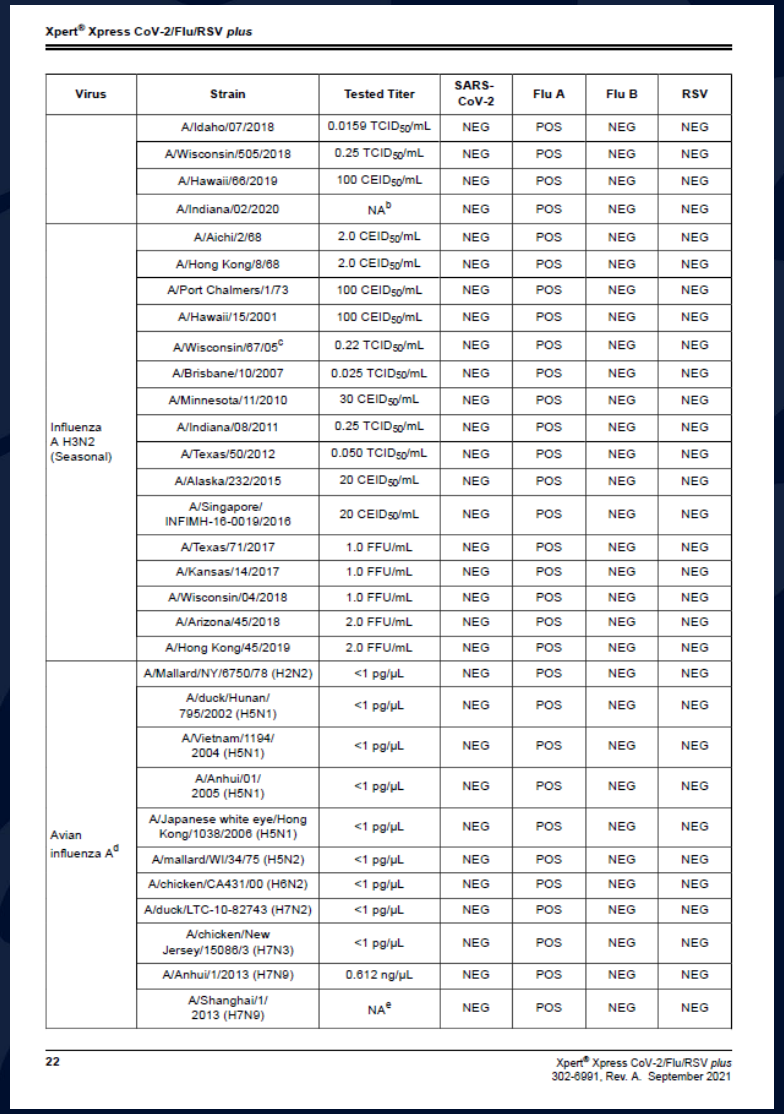
Laboratory Testing for Influenza H5N1 (and Other Avian Influenza)



Xpert® Xpress CoV-2/Flu/RSV *plus*

Virus	Strain	Tested Titer	SARS-CoV-2	Flu A	Flu B	RSV
	A/Idaho/07/2018	0.0159 $TCID_{50}$/mL	NEG	POS	NEG	NEG
	A/Wisconsin/505/2018	0.25 $TCID_{50}$/mL	NEG	POS	NEG	NEG
	A/Hawaii/66/2019	100 $CEID_{50}$/mL	NEG	POS	NEG	NEG
	A/Indiana/02/2020	NA[b]	NEG	POS	NEG	NEG
Influenza A H3N2 (Seasonal)	A/Aichi/2/68	2.0 $CEID_{50}$/mL	NEG	POS	NEG	NEG
	A/Hong Kong/8/68	2.0 $CEID_{50}$/mL	NEG	POS	NEG	NEG
	A/Port Chalmers/1/73	100 $CEID_{50}$/mL	NEG	POS	NEG	NEG
	A/Hawaii/15/2001	100 $CEID_{50}$/mL	NEG	POS	NEG	NEG
	A/Wisconsin/67/05[c]	0.22 $TCID_{50}$/mL	NEG	POS	NEG	NEG
	A/Brisbane/10/2007	0.025 $TCID_{50}$/mL	NEG	POS	NEG	NEG
	A/Minnesota/11/2010	30 $CEID_{50}$/mL	NEG	POS	NEG	NEG
	A/Indiana/08/2011	0.25 $TCID_{50}$/mL	NEG	POS	NEG	NEG
	A/Texas/50/2012	0.050 $TCID_{50}$/mL	NEG	POS	NEG	NEG
	A/Alaska/232/2015	20 $CEID_{50}$/mL	NEG	POS	NEG	NEG
	A/Singapore/INFIMH-16-0019/2016	20 $CEID_{50}$/mL	NEG	POS	NEG	NEG
	A/Texas/71/2017	1.0 FFU/mL	NEG	POS	NEG	NEG
	A/Kansas/14/2017	1.0 FFU/mL	NEG	POS	NEG	NEG
	A/Wisconsin/04/2018	1.0 FFU/mL	NEG	POS	NEG	NEG
	A/Arizona/45/2018	2.0 FFU/mL	NEG	POS	NEG	NEG
	A/Hong Kong/45/2019	2.0 FFU/mL	NEG	POS	NEG	NEG
Avian influenza A[d]	A/Mallard/NY/6750/78 (H2N2)	<1 pg/µL	NEG	POS	NEG	NEG
	A/duck/Hunan/795/2002 (H5N1)	<1 pg/µL	NEG	POS	NEG	NEG
	A/Vietnam/1194/2004 (H5N1)	<1 pg/µL	NEG	POS	NEG	NEG
	A/Anhui/01/2005 (H5N1)	<1 pg/µL	NEG	POS	NEG	NEG
	A/Japanese white eye/Hong Kong/1038/2006 (H5N1)	<1 pg/µL	NEG	POS	NEG	NEG
	A/mallard/WI/34/75 (H5N2)	<1 pg/µL	NEG	POS	NEG	NEG
	A/chicken/CA431/00 (H6N2)	<1 pg/µL	NEG	POS	NEG	NEG
	A/duck/LTC-10-82743 (H7N2)	<1 pg/µL	NEG	POS	NEG	NEG
	A/chicken/New Jersey/15086/3 (H7N3)	<1 pg/µL	NEG	POS	NEG	NEG
	A/Anhui/1/2013 (H7N9)	0.612 ng/µL	NEG	POS	NEG	NEG
	A/Shanghai/1/2013 (H7N9)	NA[e]	NEG	POS	NEG	NEG

22

Xpert® Xpress CoV-2/Flu/RSV *plus*
302-6991, Rev. A. September 2021

- Specimen source
  - URTI – NP swab and combined nasal/throat swab
  - LRTI – Endotracheal aspirate or BAL
  - Following IP&C recommendations
- FDA cleared diagnostics cannot distinguish between seasonal and novel influenza viruses
  - Some may detect novel H1N1 but cannot reliably rule out novel influenza viruses
    - Commercial RT-PCR testing may result influenza A positive, subtype “un-subtypeable”

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Treatment

- Oseltamivir 75 mg PO twice daily for at least 5 days
- Supportive care including supplemental oxygenation/ventilation, when needed, until recovery

https://www.cdc.gov/flu/avianflu/novel-av-treatment-guidance.htm

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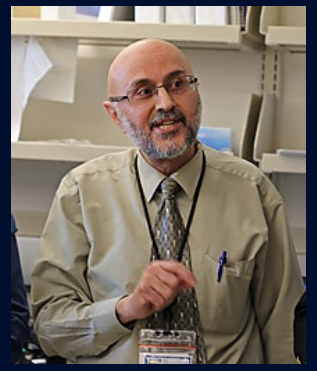
Help!

Lynn Sosa, MD
CT DPH State
Epidemiologist



Jafar Razeq, PhD
CT DPH
Director of Public Health
Laboratory

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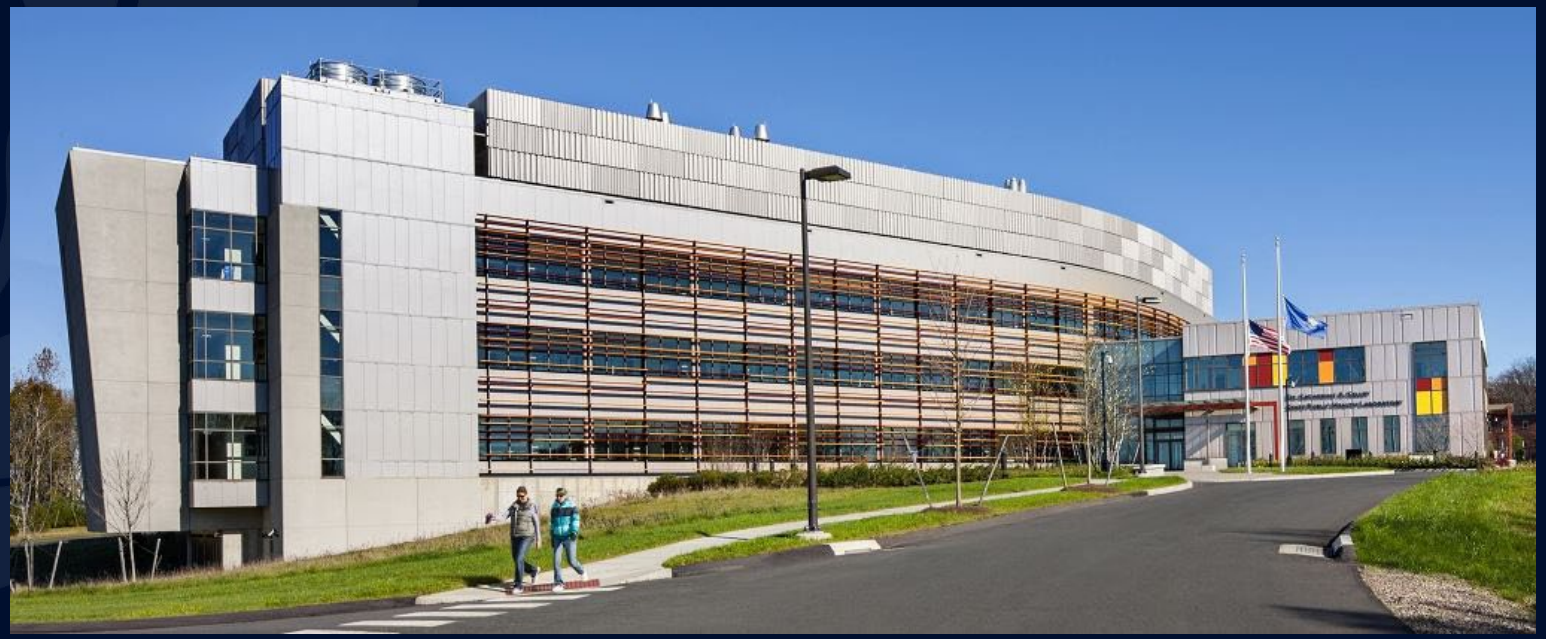
Additional Laboratory Testing

CT Department of Public Health Public Health Laboratory
(Rocky Hill, CT)



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Additional Testing – CT SPHL

- ABI7500 multiplex
- CDC Protocol
  - InfA-positive specimens with the CDC Influenza A subtyping kit using all primer/probe sets: H3, pdmInfA and pdmH1
  - Detect subtypes (H5, H7)
- **Specimen positive for Influenza A (H5N1)**
- CDC notified
  - Specimen sent to CDC for further testing

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https://www.cdc.gov/flu/pdf/swineflu/data-interpretation-update.pdf

Treatment

Table 4. Effects of Treatment and Time to Treatment with Oseltamivir on Survival among Patients with Influenza A (H5N1) Infection.*

Type of Infection and Location of Patients	Year	Survival		Days from Onset of Illness to Initiation of Antiviral Therapy		Comment	Reference
				Nonfatal Illness	Fatal Illness		
		no. of survivors/ no. treated (%)	*no. of survivors/ no. not treated (%)*	*median (range)*			
Presumed clade 1 virus infections		45/82 (55)	6/26 (23)			Significant survival benefit with oseltamivir treatment as compared with no treatment (P=0.006, Fisher's exact test)	
Thailand	2004–2005	3/10 (30)	2/7 (29)	5 (4–7)	9 (5–22)		Chotpitayasunondh T (unpublished data)
Vietnam (southern)	2004–2005	5/17 (29)	0/1 (0)	6 (4–12)	5.5 (2–7)		de Jong M (unpublished data)
Vietnam (northern)	2004–2005	37/55 (67)	4/12 (33)	NR	NR	Significant survival benefit with oseltamivir treatment as compared with no treatment (P=0.048); most patients (73%) began to receive oseltamivir after 4 days of illness	Cao T, Thanh Liem N, and Duc Hien N (personal communication)
Cambodia	2005–2006	NA	0/6 (0)			Median time to hospitalization, 6 days (range, 2–7)	Buchy et al.[37]
Presumed clade 2 virus infections		43/106 (41)	1/30 (3)			Significant survival benefit with oseltamivir treatment as compared with no treatment (P<0.001)	
Turkey, clade 2.2 virus infections	2005	4/7 (57)	0/1 (0)	4 (1–10)	8 (8–10)		Oner et al.[21]
Egypt, clade 2.2 virus infections	2006–2007	20/34 (59)	NA	1 (0–3)	4 (1–14)	Significantly shorter time from onset of illness to oseltamivir treatment among patients who survived than among those who did not survive (P=0.001, Kruskal–Wallis test)	Abdel-Ghafar A (unpublished data)
Indonesia, clade 2.1 virus infections	2005–2007	19/65 (29)	1/29 (3)	NR	NR	Significant survival benefit with oseltamivir treatment as compared with no treatment (P=0.005)	Sedyaningsih et al.[63]
Total		88/188 (47)	7/56 (12)			Significant overall survival benefit with oseltamivir treatment as compared with no treatment (P<0.001)	

* NA denotes not applicable, and NR not reported.

Early antiviral therapy improves outcomes

N Engl J Med 2008; 358:261-273

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Case

- The patient is treated with oseltamivir and over the next 4 days and recovers and is discharged home
- The neighbor's bird succumbed to illness and was disposed of per EPA guidelines
  - Tested positive for influenza A (H5N1)
- CDC investigated close human and avian contacts of the infected human and bird and no other cases were identified

https://www.epa.gov/homeland-security-waste/carcass-management-during-avian-influenza-outbreaks

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Question and Answer Session

Thank you!

REGION 1
Regional Disaster Health Response System

RESPTC
REGION 1 EMERGING SPECIAL PATHOGENS TREATMENT CENTER

Region1RDHRS@mgh.harvard.edu
www.rdhrs.org
@Region1RDHRS

MGHBRT@partners.org
www.massgeneral.org/disaster-medicine
@MGHDisasterMed