Human Infections with Highly Pathogenic Avian Influenza A(H5N1) Viruses - Global Update and Experience in the Americas

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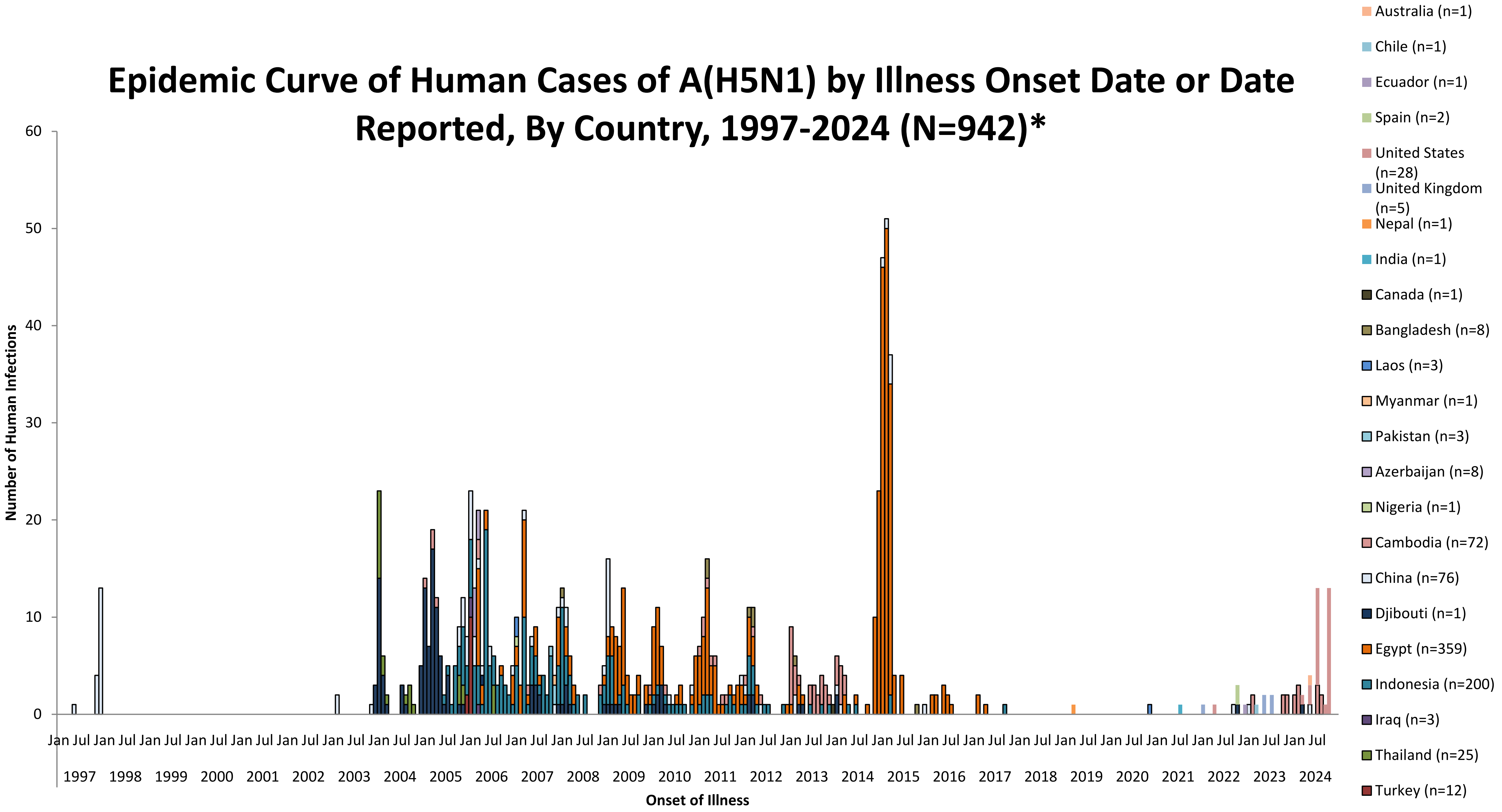
Epidemiology of Human H5N1 Cases

- **First human infections identified: Hong Kong, 1997 (18 cases, 6 deaths)**
  - Median age: 17 years (range 1-60); wide severity: pneumonia: 11; mild illness: 7
- **Re-emergence in humans: 2003-2005 (China, Southeast Asia)**
- **Since 2005: Cases identified in other regions (Middle East, Europe, Africa, Americas)**
- **1997-2024: 942 cases (@50% case fatality; 24 countries)***
  - **Mostly sporadic human cases with pneumonia**
    - Most cases in young adults, some pediatric cases
  - **H5N1 viruses continue to evolve (classified into genetic clades)**
    - **2023-2024: Clade 2.3.2.1c virus infections in rural villagers (Cambodia)**
    - **2022-2023: Clade 2.3.4.4b virus infections with critical illness (Chile, China, Ecuador)**
    - **2022-2024: Clade 2.3.4.4b virus infections (mostly conjunctivitis, U.S.)**
    - **2024: Clade 2.3.2.1a virus infection (critical illness, Australia)**

**As of October 20, 2024; Chan Clin Infect Dis 2002; Katz J Infect Dis 1999*

Epidemic Curve of Human Cases of A(H5N1) by Illness Onset Date or Date Reported, By Country, 1997-2024 (N=942)*



**As of October 20, 2024*

Risk Factors for Human Infection with H5N1 Virus

- **Exposure to infected poultry**
  - **Direct/close unprotected exposure to sick/dead backyard poultry (rural areas)**
  - **Visiting a live poultry market**
- **Exposure to infected wild birds**
  - **Defeathering wild swans that died** (2 case clusters, Azerbaijan, 2006)
- **Some cases with no known source of infection**
  - (e.g., returned traveler to Canada Dec. 2013; one case in August 2024, U.S.)
- **2024: Sporadic mammal-to-human H5N1 virus transmission**
  - **First cases of dairy cattle-to-human transmission (U.S.)**
- **Limited, non-sustained human-to-human transmission (rare)**
  - **Not reported since 2007**

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

U.S. Cases, 2022-2024)* (H5N1 clade 2.3.4.4b viruses)

- **28 Human cases (27 in 2024) (no secondary transmission identified)**
  - **Associated with poultry exposures: 10**
    - **April 2022: 1 case reported "fatigue" while depopulating poultry**
    - **July 2024: 9 cases of conjunctivitis in poultry workers depopulating poultry** (one state)
    - ***Oseltamivir treatment given/offered; post-exposure prophylaxis used***
  - **Associated with dairy cattle exposures: 17** (contact transmission)
    - **>320 H5N1+ dairy cattle farms in 14 states (March-October 2024)**
    - **March - October 2024: 17 cases in dairy farm workers** (4 states)
    - **Mild illness (16 with conjunctivitis, 1 with respiratory illness)**
    - ***Oseltamivir treatment given/offered; post-exposure prophylaxis used***
  - **Unknown source: 1**
    - **August 2024: 1 case in a person with no exposures to animals or sick persons**
    - **Moderate non-respiratory illness in a person with chronic medical conditions (hospitalized)**
    - **Hospitalized for 3 days, received Oseltamivir treatment; recovered**

Figure 1. Conjunctivitis with Subconjunctival Hemorrhage in Both Eyes.

Uyeki NEJM 2024

**As of October 20, 2024; Morse NEJM 2024; Uyeki NEJM 2024; Drehoff MMWR 2024*

South America Cases (2022-2023) (H5N1 clade 2.3.4.4b viruses)

- **Ecuador, December 2022**
  - 9-year-old girl with upper respiratory symptoms, conjunctivitis, nausea, vomiting, progressed to pneumonia, respiratory failure, septic shock. History: exposure to backyard poultry that died (rural area)
    - Hospitalized illness day #4; transferred illness day #8 to pediatric hospital in critical condition
    - Day #10: NP swab collected per SARI surveillance: influenza A(H5)+
    - Received Oseltamivir treatment during hospitalization, survived; no secondary transmission
- **Chile, March 2023**
  - 53-year-old man with cough and sore throat, progressed to pneumonia, respiratory failure (lived in coastal area with die-offs of seabirds and marine mammals)
    - Hospitalized illness day #10 with pneumonia; NP swab negative for SARS-CoV-2
    - Admitted to ICU on illness day #11; illness day #12: antibiotics, Oseltamivir treatment started
    - Illness day #15: BAL fluid specimen: influenza A+; A(H5) confirmed on illness day #17.
    - Survived and discharged after prolonged hospitalization; no secondary transmission

Bruno J Travel Med 2023; Castillo J Travel Med 2023

Cambodia Cases (2023-2024) (H5N1 clade 2.3.2.1c viruses)

- **16 cases in rural villagers exposed to sick/dead backyard poultry**
  - **Some clinically mild cases (children, adults)**
  - **H5N1 not suspected in most patients with severe/critical illness until hospital admission (missed opportunities for earlier initiation of oseltamivir treatment)**
  - **Some patients diagnosed through routine SARI surveillance at hospital admission**
  - **10 severe/critical illness cases, 6 deaths**
    - **Oseltamivir post-exposure prophylaxis given to close contacts (household members)**

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