

H5N1 Avian Flu in Humans 1997-2022 (25 years/15 Minutes)

Anticipate, Recognize, Act

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Synopsis: 8 Key Points

- WHO 2022: Since 2003 confirmed deaths & cases: 455/863 (53%). How many more not tested?
- Humans infected from avians. No sustained person-to-person spread.
- Recognize infected avians to anticipate infected humans: Asia, Africa...Europe, Americas?
- Most human cases reported in Egypt and Indonesia.
- Typically susceptible to neuraminidase inhibitors.
- Few autopsies, but secondary bacterial pneumonia not commonly reported.
- “Gain of Function” serial passage in ferrets begun in 2010/2011 by Dutch & USA.
- CDC “Influenza Risk Assessment Tool (IRAT)” links to avian flu candidate vaccines.
<https://www.cdc.gov/flu/pandemic-resources/national-strategy/risk-assessment.htm>

H5N1 HPAI Chronology 1996-2014 FAO-OIE-WHO: Events in Animals and in Humans

- FAO-OIE-WHO Chronology of Human and Avian H5N1 HPAI from 1996 (Guangdong, SE China farmed goose) to March 2014:

https://www.who.int/influenza/human_animal_interface/H5N1_avian_influenza_update20140317.pdf



H5N1 highly pathogenic avian influenza: Timeline of major events
17 March 2014

Early Events

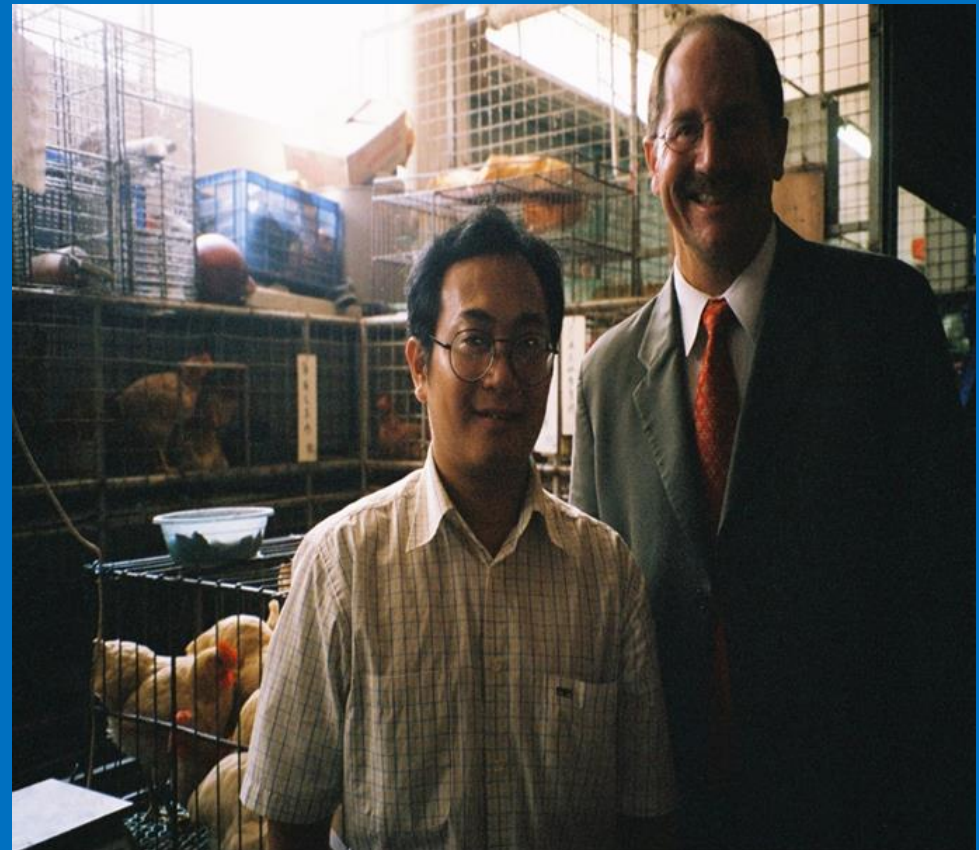
Date	Events in Animals	Events in Humans
1996	Highly pathogenic H5N1 virus is isolated from a farmed goose in Guangdong province, China .	
1997	Outbreaks of highly pathogenic H5N1 are reported in poultry at farms and live animal markets in Hong Kong .	Human infections with avian influenza H5N1 are reported in Hong Kong . Altogether, 18 cases (6 fatal) are reported in the first known instance of human infection with this virus.
Feb 2003		2 human cases of avian influenza H5N1 infection (1 fatal) are confirmed in a China Hong Kong SAR family with a

H5N1 HPAI Recognized 1996 in a Farmed Goose in SE China Guangdong province, then:
First Human Cases in Hong Kong 1997. In 2003 rare case(s) in China during SARS.

Hong Kong 1997:

- Hong Kong: 18 patients (6 deaths)
- One child had Reye's syndrome (aspirin-link).
- Outbreak stopped with culling of chickens and more in live bird markets
- New hygiene measures & surveillance in markets: no more human cases.
- Feb. 2003 HK: 2 cases after travel to mainland

w/Chinese physician 2003 Guangdong market



Vietnam: Early Cases, Controversies, Control

Early Cases Dec. 2003-Jan. 2004

- Possible Link to Social Behaviors e.g., at a Wedding and Lunar New Year.
- 2004 H5N1 isolate (“Clade 1”) used to make the initial US H5N1 vaccine in Strategic National Stockpile (SNS). Of questionable effectiveness now as many other clades circulating.

2005 at Hanoi Hospitals & with an MoH team

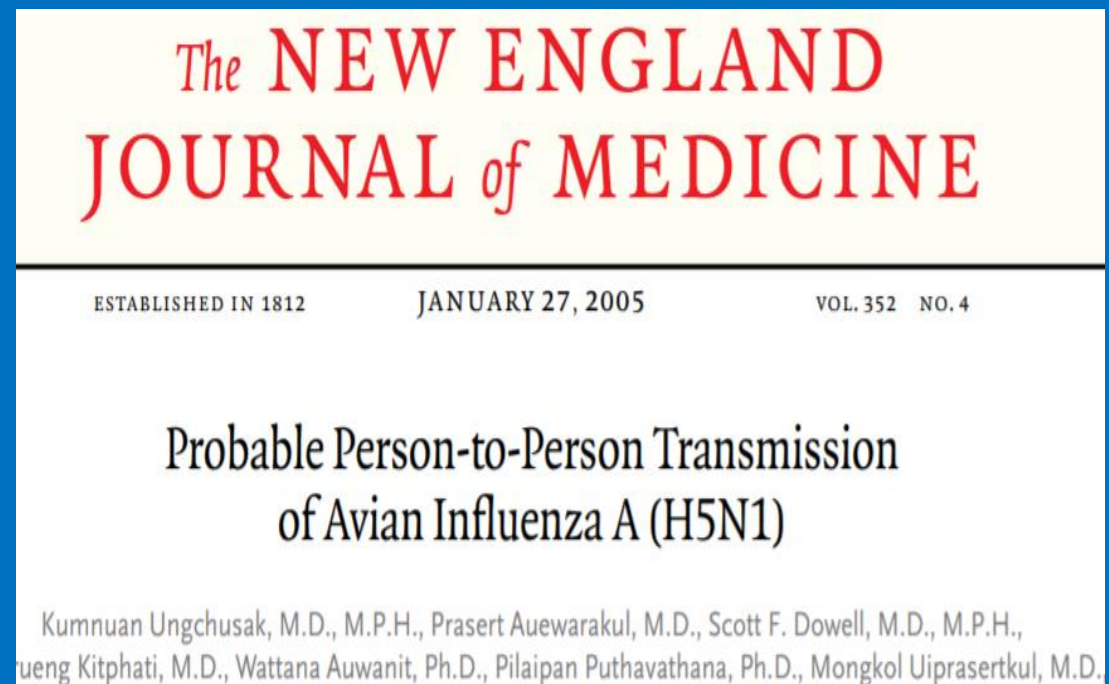


Thailand Sept. 2004: Initial Person-to-Person Transmission In a 3-member Family (2 deaths)

Effective “One Health” Response

- Thailand Prime Minister orders two Cabinet Ministers responsible for Human and Animal Health to work jointly and comprehensively to stop H5N1 in Avians and in Humans.
- They do. No further human cases reported.
- (2005 Visited Bangkok with Thai MoH, CDC)

1st Human-to-Human Cases (3 total) Sept 2004



President Bush at NIH Nov. 1, 2005 announces Pandemic Influenza Preparedness
And Global H5N1 Actions <https://georgewbush-whitehouse.archives.gov/infocus/pandemicflu/>

“The United States Has Made Pivotal Contributions To Control The International Spread Of H5N1:

- The United States Is Working On Avian Influenza Issues In More Than 100 Countries To Combat The Spread Of Avian Influenza And Prepare For A Possible Pandemic.
- Over the past year, the U.S. Government has supported the training of more than 129,000 animal health workers and 17,000 human health workers in H5N1 surveillance and outbreak response.
- We have deployed more than 300,000 personal protective equipment kits to more than 70 countries for use by surveillance workers and outbreak-response teams”.

Indonesian Archipelago: Outbreaks (>80% CFR), Virus Sharing Stopped, US Navy Medical Research Unit (NAMRU) closed, WHO PIP Framework proposed, more.

Controversy and Outcomes.

- Minister of Health Dr. Supari: US created H5N1 virus. US NAMRU in Jakarta is closed.
- MoH stops sharing H5N1 viruses with WHO. Claims “viral sovereignty”. Later sharing restored. WHO Pandemic Influenza Preparedness (PIP) Framework is created.
- Publishes a book & reports being called by an Australian company offering to sell vaccine that used Indonesian H5N1 isolate.

**w/Indonesian Physicians @H5N1 hospital
Indonesia 2008. Later in 2008 USAID team visits.**



Egypt (Along the Nile): Virus in Avians and Humans Recognized in early 2006

Separate Treatment Areas for H5N1 patients during 2009-10 Flu Pandemic pH1N1

Egypt Live Bird Market 2012



Egypt 2012 w/Colleagues



US and Dutch Labs “Gain of Function” Ferret-to-Ferret H5N1 via Air Droplets Published 2012 after Controversy in Nature and in Science

2-Step Gain-of-Function H5N1 research

- (1) Site-directed mutations *in vitro*,
- (2) Serial passage in Ferrets x 10

- (Later requests for other GoF work)

Nat'l Science Advisory Board Biosecurity (NSABB)

- 2 papers in 2012: Dutch & Americans

- Herfst...Fouchier.
<https://www.science.org/doi/10.1126/science.1213362>

- Imai et al...Kawaoka. Nature
<https://www.nature.com/articles/nature10831>

Lesson: “What’s Next?” Is Already Here, We Just Haven’t Recognized It Yet
Exhibit on Viral Epidemics @Smithsonian Museum Natural History 2018-Oct., 2022



1st UK Case in England: ~24 December 2021

79 year-old man lived with 20 Muscovy Ducks in house

WHO report: January 2022

- [https://www.who.int/emergencies/disease-outbreak-news/item/influenza-a-\(h5\)---united-kingdom-of-great-britain-and-northern-ireland#:~:text=Since%202003%2C%20a%20total%20of,case%20in%20the%20United%20Kingdom](https://www.who.int/emergencies/disease-outbreak-news/item/influenza-a-(h5)---united-kingdom-of-great-britain-and-northern-ireland#:~:text=Since%202003%2C%20a%20total%20of,case%20in%20the%20United%20Kingdom)

GLOBALLY 2003-2022: 455 deaths/863 cases

- WHO risk assessment
- Since 2003, a total of 863 cases and 455 deaths of influenza A(H5N1) human infection have been reported worldwide, including this case in the United Kingdom.