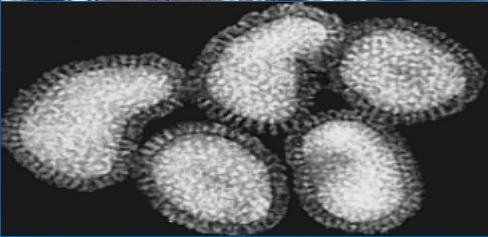


Epidemiology of Influenza – Seasonal, Avian and Pandemic



What is Influenza?

An acute Respiratory Tract Infection (RTI), caused by Influenza virus, characterised by sudden onset of:

- ❑ Fever/chills
- ❑ Headache, myalgia
- ❑ Sore throat
- ❑ Cough
- ❑ Coryza
- ❑ Prostration
- ❑ Range of symptoms differs by age
 - Vomiting & diarrhea in children/elderly
 - Fever alone in infants
 - May be atypical in elderly
- ❑ Serious complications can occur among high risk groups

Influenza Virus – 3 Types

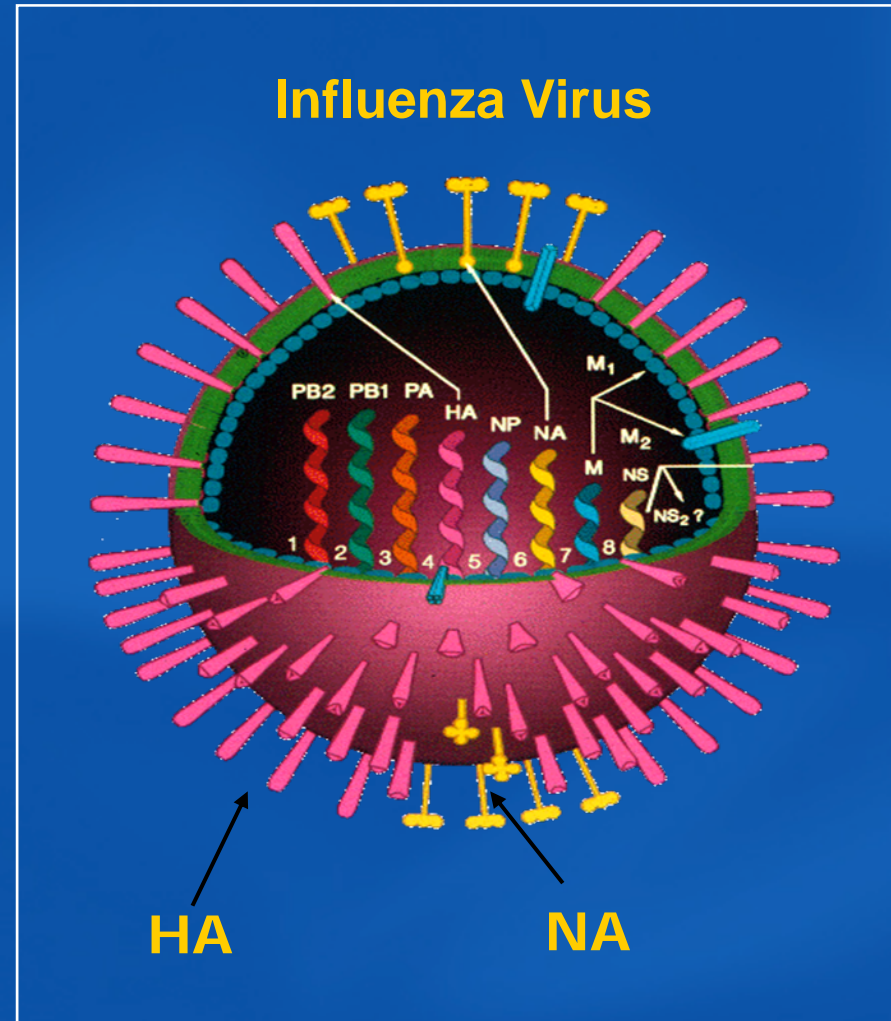
- ❑ RNA virus
- ❑ Antigenically distinct types
- ❑ No cross-immunity between different types

Type A	Type B	Type C
Causes significant disease: epidemics; pandemics	Causes significant disease: milder epidemics	Does not cause significant disease
Infects both humans <i>and</i> other species	Limited to humans	Limited to humans
Frequent antigenic variations	Infrequent antigenic variations!	Antigenically stable

Influenza A – Important Feature

2 surface antigens:

- Haemagglutinin (HA)
 - Initiates infection following attachment of virus to susceptible cells
- Neuraminidase (NA)
 - Release of virus from infected cell
- 16 'H' antigens (1-16)
- 9 'N' antigens (1-9)
- Different combinations of H and N antigens



Influenza A – Antigenic Variations

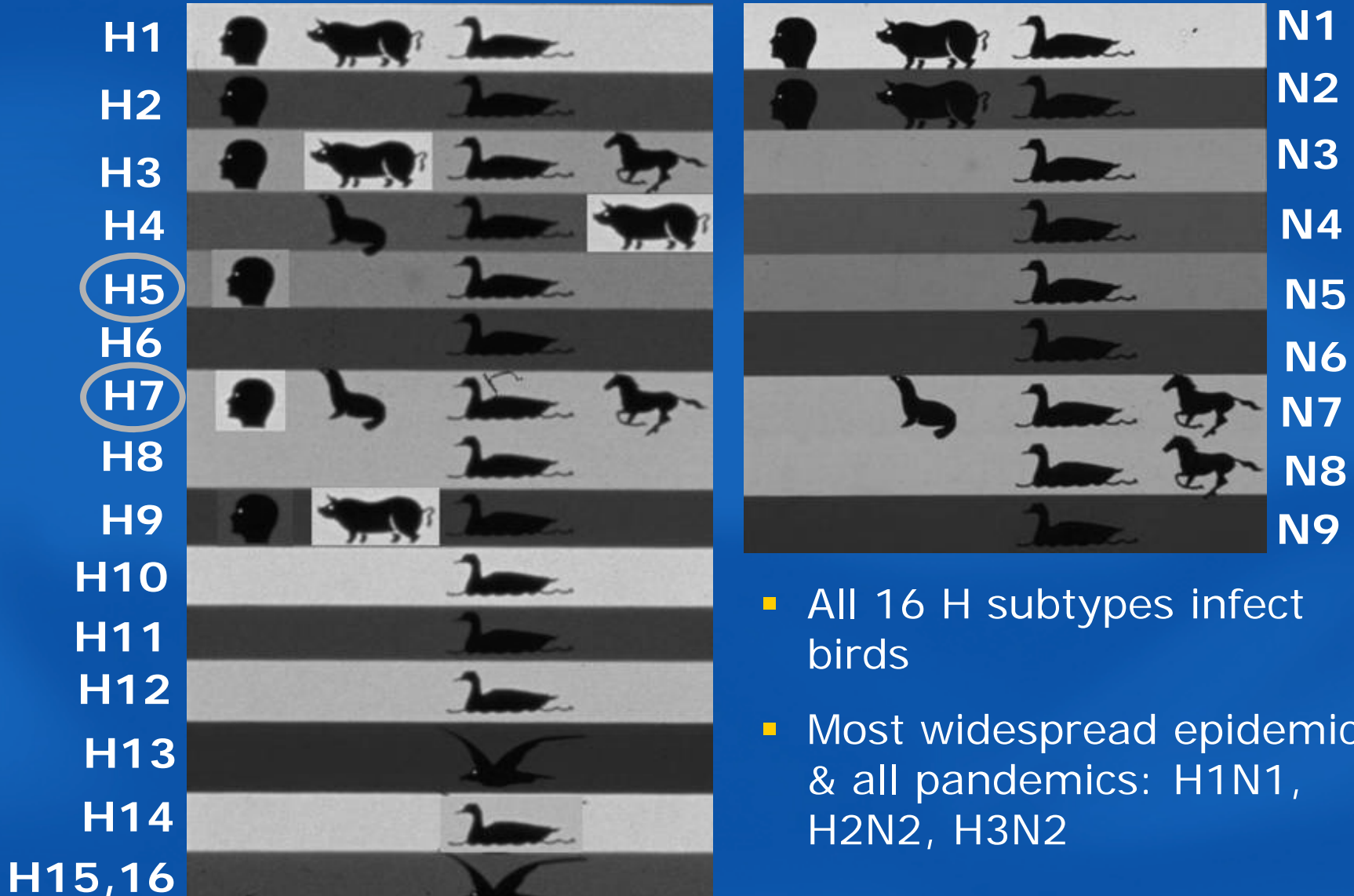
Antigenic drift: gradual antigenic change over a period;

- ❑ Involves 'point mutations' in genes owing to selection pressure by immunity in host population
- ❑ Responsible for frequent influenza epidemics; necessitates reformulations of seasonal influenza vaccines

Antigenic shift: sudden, complete or major change;

- ❑ Results from genetic recombination of human with animal/avian virus
- ❑ Leads to a novel subtype different from both parent viruses
- ❑ If 'novel subtype' has sufficient genes from HI viruses which make it readily transmissible from person to person, it may cause pandemics
- ❑ Evidence suggests that human influenza viruses responsible for last 3 pandemics and current H1N1 pandemic contained gene segments closely related to avian influenza viruses

Different Species Infected by Influenza A Subtypes



- All 16 H subtypes infect birds
- Most widespread epidemics & all pandemics: H1N1, H2N2, H3N2

Influenza Terminology - 1

- ❑ Human seasonal influenza
- ❑ Avian influenza
- ❑ Pandemic influenza

Influenza Terminology - 2

Seasonal influenza:

- ❑ Occurs every year with gradual variations in previous year's virus surface proteins (*antigenic drift*)
- ❑ Spreads around the world in seasonal epidemics, affecting 10 - 20% of total population
- ❑ Annual epidemics thought to result in 3-5 million cases of severe illness and 2.5-5 lakh deaths

Influenza Terminology - 3

Avian Influenza:

- ❑ Primarily a disease of birds due to large group of different influenza A viruses
- ❑ Rarely jumps species and infects humans
- ❑ An influenza pandemic happens when a new subtype emerges that has not previously circulated in humans and is adapted to human to human transmission
- ❑ Viruses in wild water fowl is the ultimate source of new viruses in humans causing pandemics

Influenza Terminology - 4

Pandemic Influenza:

- ❑ A worldwide surge in cases caused by the introduction of a new influenza type A surface protein (antigenic shift).

Seasonal Epidemics vs. Pandemics

Seasonal Influenza	Influenza Pandemics
A public health problem each year	Appears in the human population rarely and unpredictably
Usually some immunity built up from previous exposures to the same subtype	Human population lacks any immunity. Virulence and mortality not entirely linked to immunity
Infants and elderly most at risk	All age groups, including healthy young adults, may be at increased risk for serious complications
Result of Antigenic Drift	Result of Antigenic Shift

Magnitude of Disease Burden (Seasonal Influenza)

World-wide in distribution:

- ❑ Sporadic cases every season/year round
- ❑ Outbreaks (primarily Influenza A): occur every year
- ❑ Major epidemics: at interval of 2-3 years
- ❑ Pandemics: rare; 10-15 years or more
- ❑ Attack rates during epidemics: 10-20% in general community; > 50% in closed populations
- ❑ Epidemics generally last 3-6 weeks



Influenza Pandemics



1918: "Spanish
Flu"
50 million
deaths
A(H1N1)

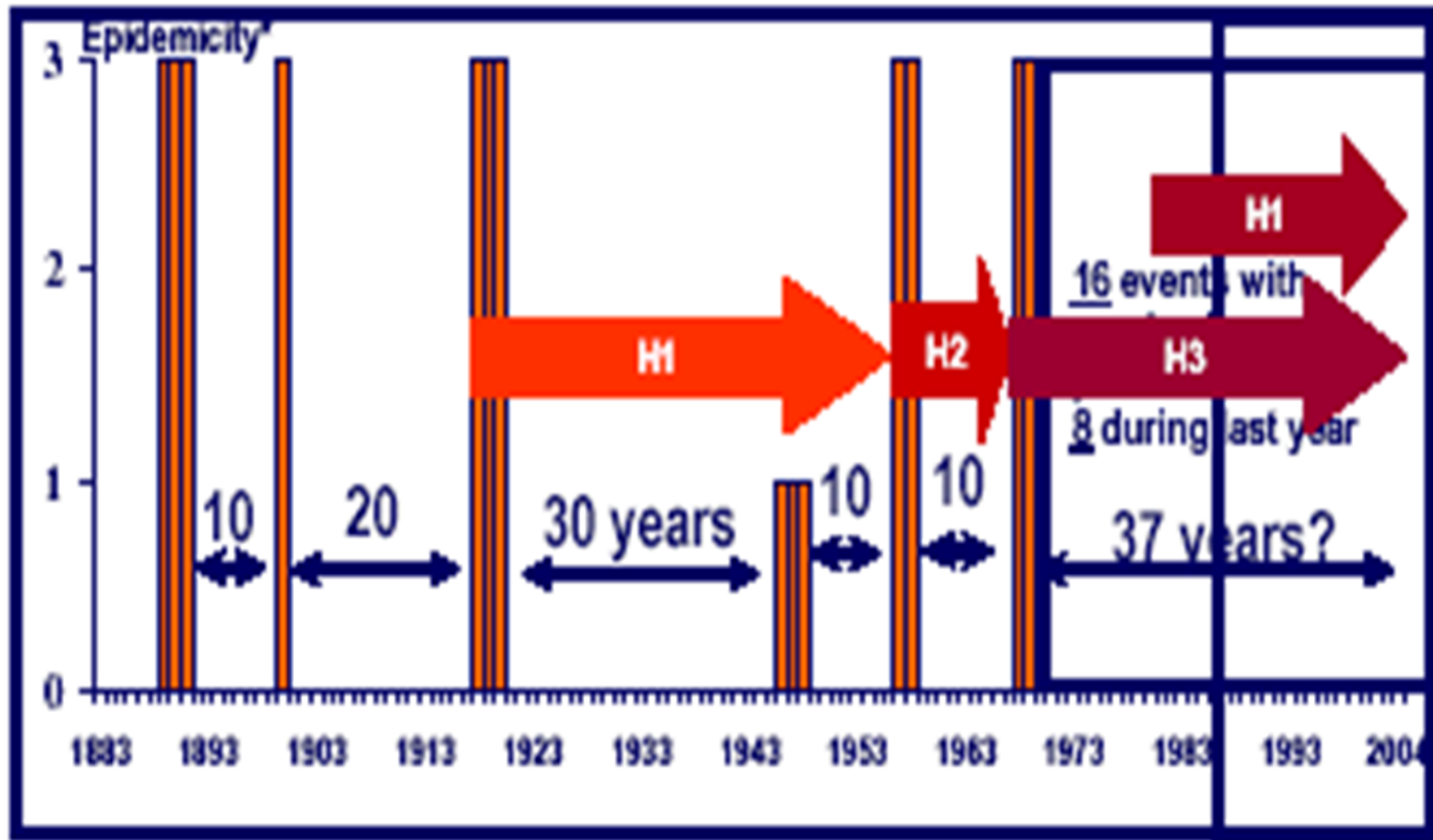
1957: "Asian
Flu"
1 - 4 million
deaths
A(H2N2)

1968: "Hong
Kong Flu"
1 - 4 million
deaths
A(H3N2)

2009: "Swine Flue" A
(H1N1)
77201 human cases
332 deaths in 120
countries*

*Data as on 1st July 2009

Recorded Influenza Pandemics



1: epidemic, 2: probable pandemic, 3: pandemic

Potter, C.W: Textbook of Influenza by Nichols, Webster, Hay, Blackwell Science 1998

Influenza: Key Characteristics— Agent Factors

Reservoir of Infection:

- Humans primary reservoir for human infections
- Major reservoir – animals & birds (swine, horses, dogs, cats, domestic poultry, water birds, wild birds etc.)

Source of Infection:

- Usually a case or sub-clinical case

Communicability:

- 3-5 days from clinical onset in adults;
- Up to 7 days in young children
- Peak viral shedding occurs on day 1 of symptoms

Influenza: Key Characteristics—

Host Factors

Age & Sex:

- All ages, both sexes
- Attack rates lower among adults
- High Case Fatality Ratio (CFR) during epidemic in high risk cases: (old people; children; persons with diabetes, ch. heart disease, renal & resp. diseases)

Human Immunity

- Antibodies to 'H': neutralises the virus
- Antibodies to 'N': modifies the infection
- Antibodies appear in 7 days after an attack; reach maximum. Level in 2 weeks; drops to pre-infection level in 8-12 months

Influenza: Key Characteristics— Environmental Factors

Seasonality:

- Temperate zones: epidemics occur in winter
- Tropics: epidemics occur in rainy season
- Sporadic cases: any month

Overcrowding:

- Enhances transmission
- Higher attack rates in closed popn. groups
(schools, institutions, ships etc.)

Influenza: Key Characteristics— Disease Transmission

Mainly airborne:

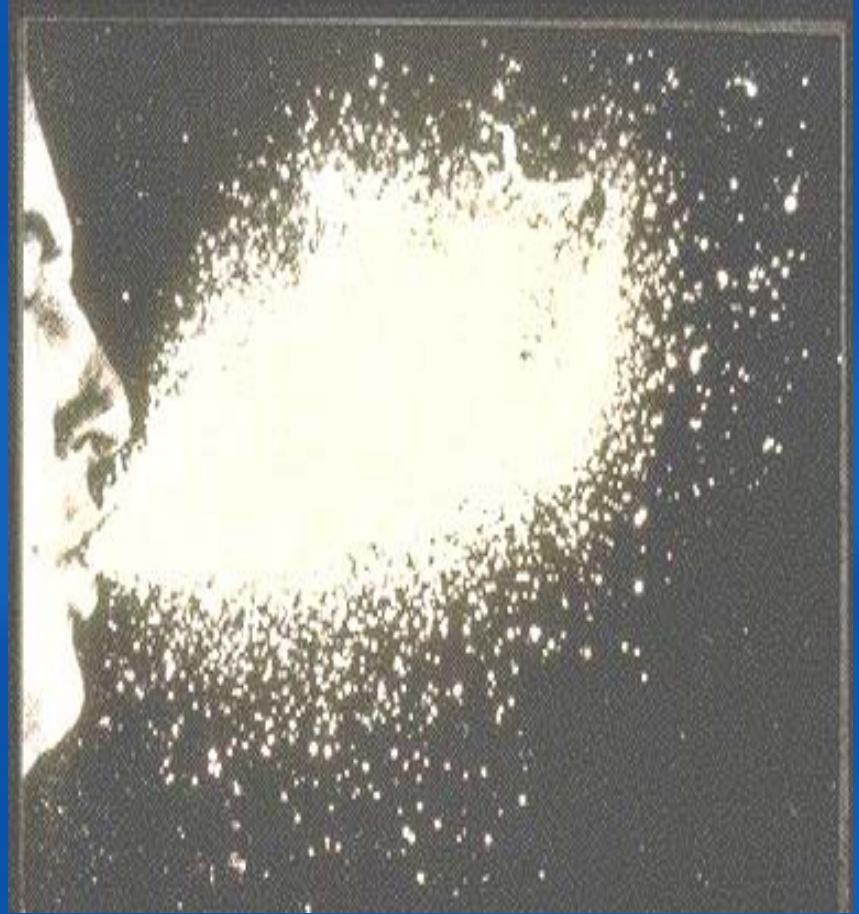
- Droplet infection
- Droplet nuclei

Through direct contact

Transmission from objects possible

Incubation period:

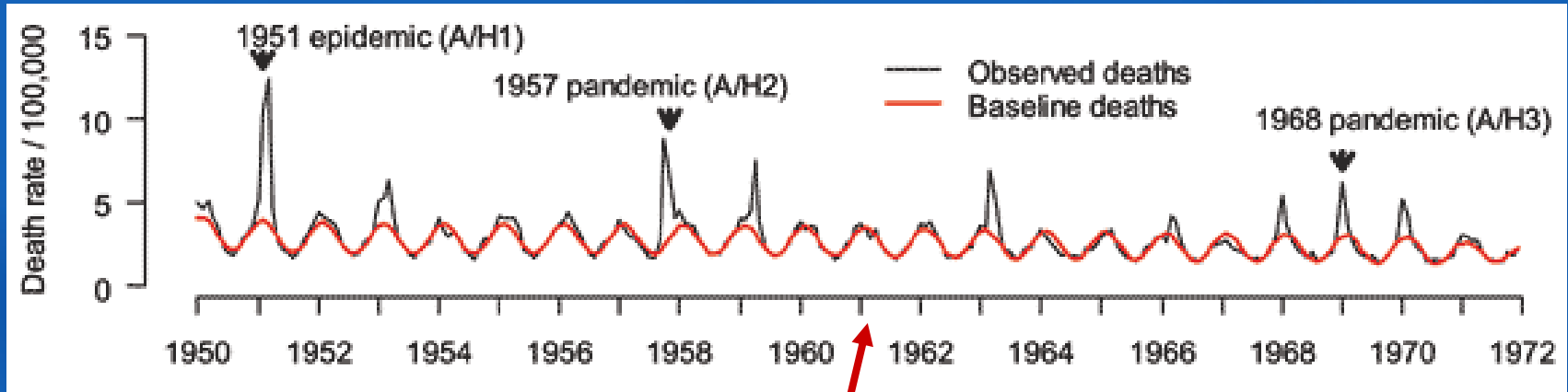
- 18 to 72 hours



Epidemiology Terms

□ Endemic

- A disease that occurs at an expected constant level in a population
- “Background” level



Red line: Expected deaths each year

Cécile Viboud, et al. Emerg Infect Dis [serial on the Internet]. 2006 Apr. Available from <http://www.cdc.gov/ncidod/EID/vol12no04/05-0695-G2.htm>

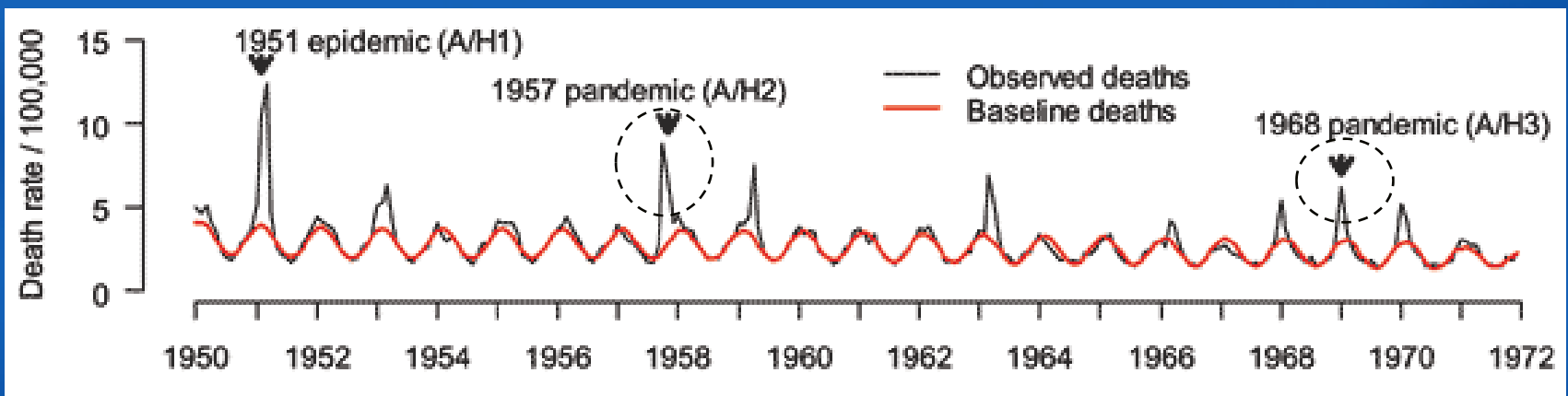
Epidemiology Terms

□ Epidemic

- When the cases of a disease exceed what is normally expected

□ Pandemic

- An epidemic that occurs over a large geographic area, or across the whole world



When does the pandemic start?

- ❑ Usually not known
- ❑ H5N1 is not the only avian influenza A virus to worry about
- ❑ Circulation of H5N1 viruses among poultry must be controlled
- ❑ WHO Pandemic alert period:
 - Phase 3 (Avian H5N1 influenza)
 - Phase 6 (Novel H1N1 influenza)

Recent Human Infections:

Avian Influenza

Year	Place	Subtype	Cases	Deaths
1997	Hong Kong	H5N1	18	6
1999	Hong Kong	H9N2	2	0
2003	Hong Kong	H5N1	2	1
2003	Netherlands	H7N7	83	1
2003	Hong Kong	H9N2	1	0
2004 - Feb . 2009 *	Azerbaijan, China, Cambodia, Djibouti, Egypt, Indonesia, Iraq, Lao's PD R, Myanmar, Nigeria, Pakistan, Thailand, Turkey, Vietnam Bangladesh	H5N1	436	2 62

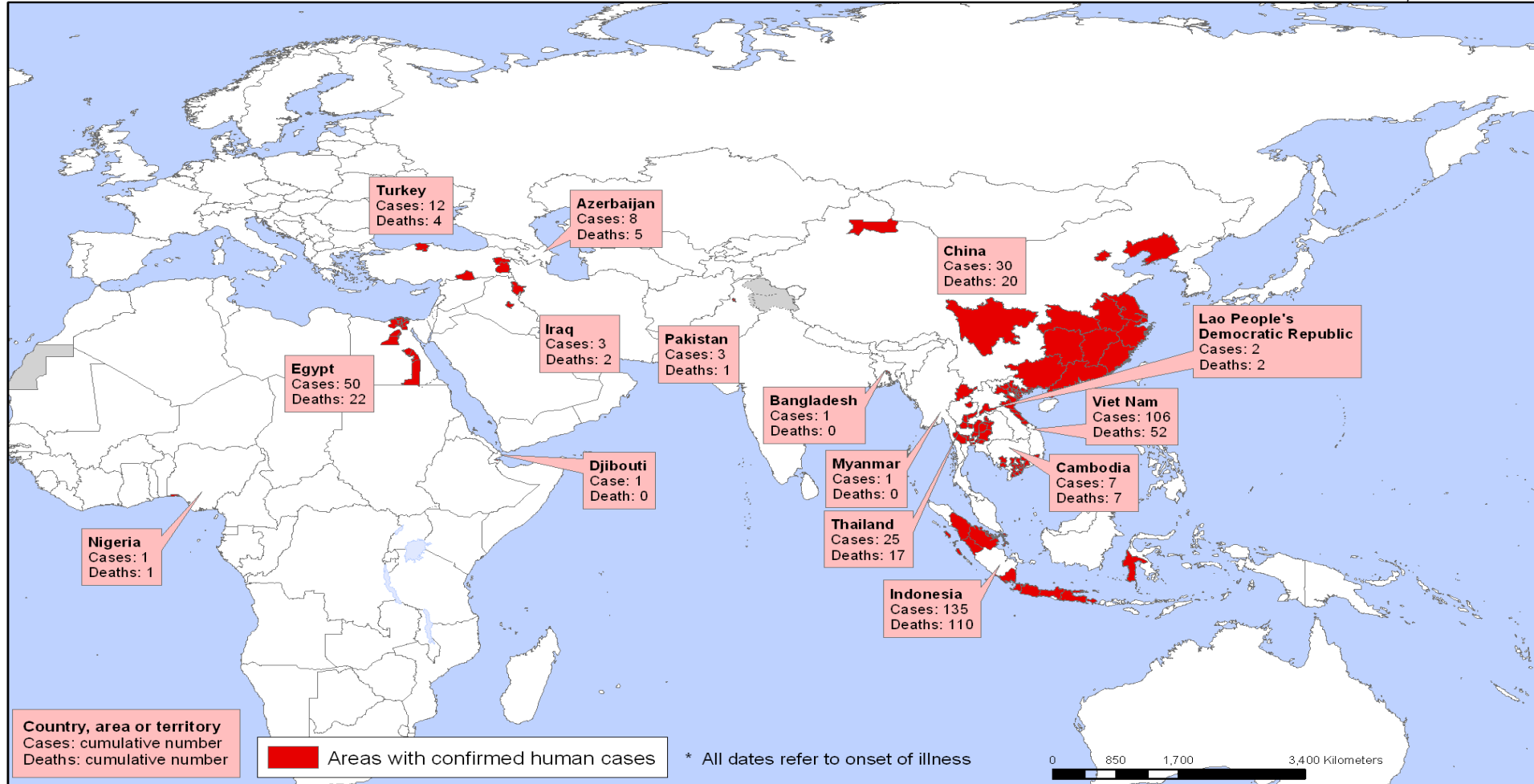
* As of 1st July 2009

Emergence of Avian Influenza (H5N1)

2003 - Feb' 09: 436 human cases, 262 deaths, CRR > 60%

Areas with confirmed human cases of H5N1 avian influenza since 2003 *

Status as of 19 June 2008
Latest available update



Epidemiology of Avian Influenza in Humans (H5N1)

Demographic characteristics

- ❑ Despite widespread exposures to avian influenza (H5N1) infected poultry, disease in humans remains rare
- ❑ Since May 2005, number of both affected countries and confirmed cases of H5N1 infection (408 cases) have increased, in part because of the spread of clade 2.2 viruses across Eurasia and Africa
- ❑ Median age of patients with H5N1 infection is approximately 18 yrs; 90% patients 40 years or younger

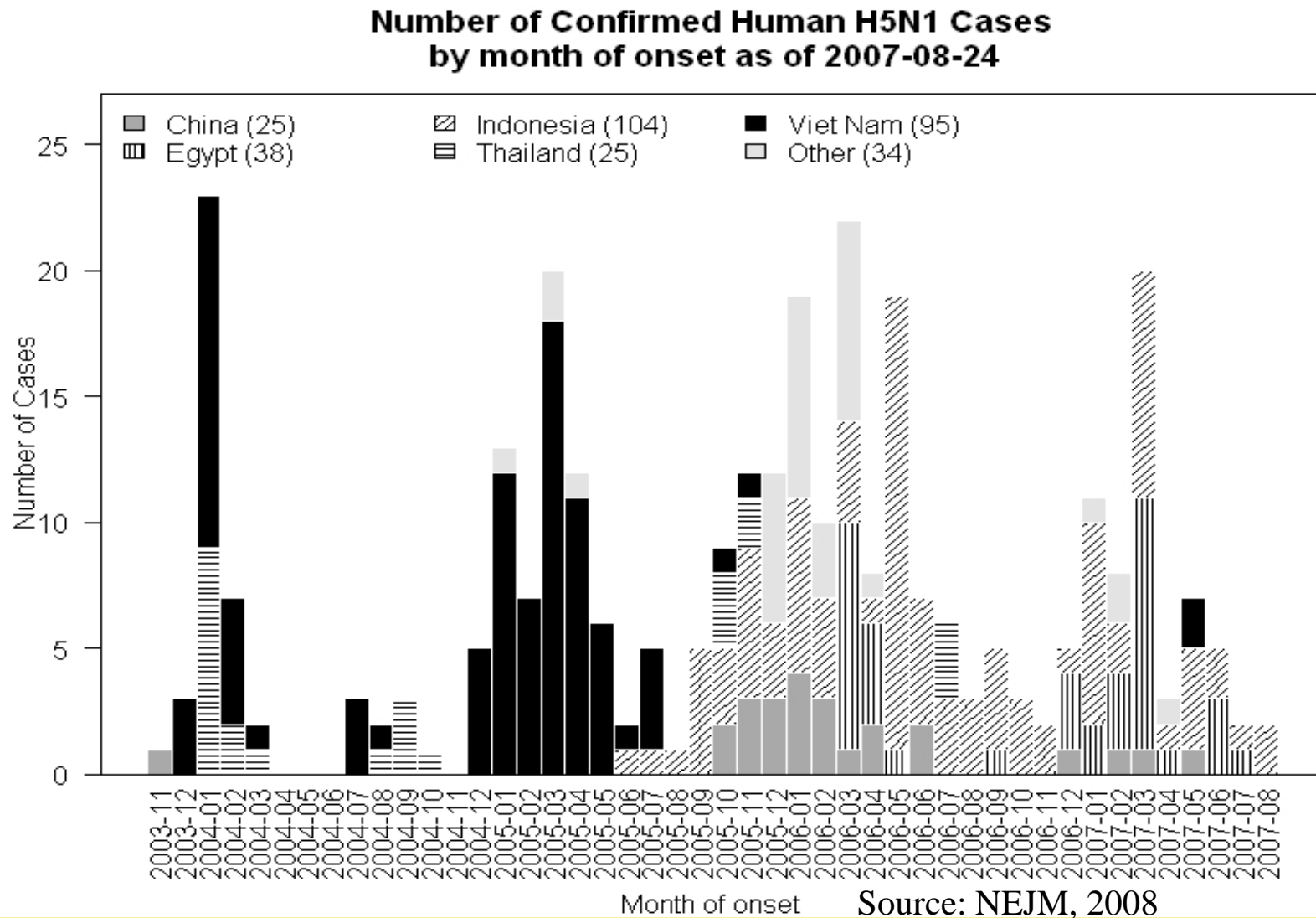
Epidemiology of Avian Influenza in Humans (H5N1)

Demographic characteristics

- ❑ **Overall Case Fatality Ratio (CFR):** 63%; highest among 10-19 yrs; lowest among persons 50 years or older:
 - pre-existing immunity
 - differences in exposure or
 - other factors
- ❑ **Increased H5N1 human cases during cooler months:** associated with increased poultry outbreaks
- ❑ **Cases occur year-round:** clinicians must be alert at any time, especially in countries with H5N1 poultry outbreaks

Epidemiology of Avian Influenza in Humans (H5N1)

Seasonality



Epidemiology of Avian Influenza in Humans (H5N1)

Transmission

Direct avian-to-human transmission: predominant route

Most common risk factor: Handling of sick/dead poultry
(week before the onset of illness)

Potential risk factors:

- ❑ Slaughtering, defeathering, or preparing sick poultry for cooking
- ❑ Playing with or holding diseased/dead poultry
- ❑ Handling fighting cocks/ducks that appear healthy
- ❑ Consuming raw or undercooked poultry (products)

Epidemiology of Avian Influenza in Humans (H5N1)

Transmission

- ❑ **Human clusters:** at least 2 epidemiologically linked cases of H5N1 illness; identified in 10 countries - approximately 25% of reported cases.
- ❑ **Cluster size:** mostly 2-3; largest 8 persons
- ❑ **Possible genetic susceptibility:** more than 90% of clusters among blood-related family members; might be chance alone

Epidemiology of Avian Influenza in Humans (H5N1)

Transmission

- ❑ **Transmission in clusters:** Mostly common-source exposure to poultry, but limited, non-sustained H-to-H transmission probably occurred during very close, unprotected contact with a severely ill patient
- ❑ **Largest cluster:** probable transmission from index case to 6 blood-related family members; subsequently to another family member
- ❑ Respiratory secretions, all body fluids, incl. feces considered potentially infectious

Epidemiology of Avian Influenza in Humans (H5N1)

Transmission

- ❑ In 25% patients, source of exposure is unclear; environment-to-human transmission possible
- ❑ For some patients, only identified risk factor was visiting a live-poultry market contact with virus-contaminated fomites or fertiliser containing poultry feces
- ❑ Drinking potable water and eating properly cooked food not considered to be risk factors, but ingestion of virus-contaminated products or swimming or bathing in virus-contaminated water might be risky

Epidemiology of Avian Influenza in Humans (H5N1)

Incubation period

- ❑ **After exposure to infected poultry:**
 - Generally 7 days or less
 - 2-5 days in many cases
- ❑ **Clusters with limited H-to-H transmission:**
 - Approximately 3-5 days
 - Estimated 8-9 days in one cluster

Thank You

