



Influenza

Transmission and Clinical Features

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Outline

- What is Influenza?
 - The Virus
 - The Disease
 - Transmission and Infection
 - Clinical Course
 - Complications
 - Non-pulmonary considerations
- What about H5N1?



Influenza

- A contagious disease caused by an RNA virus
- A global infectious disease threat
- An annual public health problem
 - Primarily affects the respiratory tract
 - Can cause severe illness and lead to life-threatening complications



Influenza Viruses



- Naturally infect several animal species
 - Birds
 - Mammals including people

- People usually infected only by human viruses

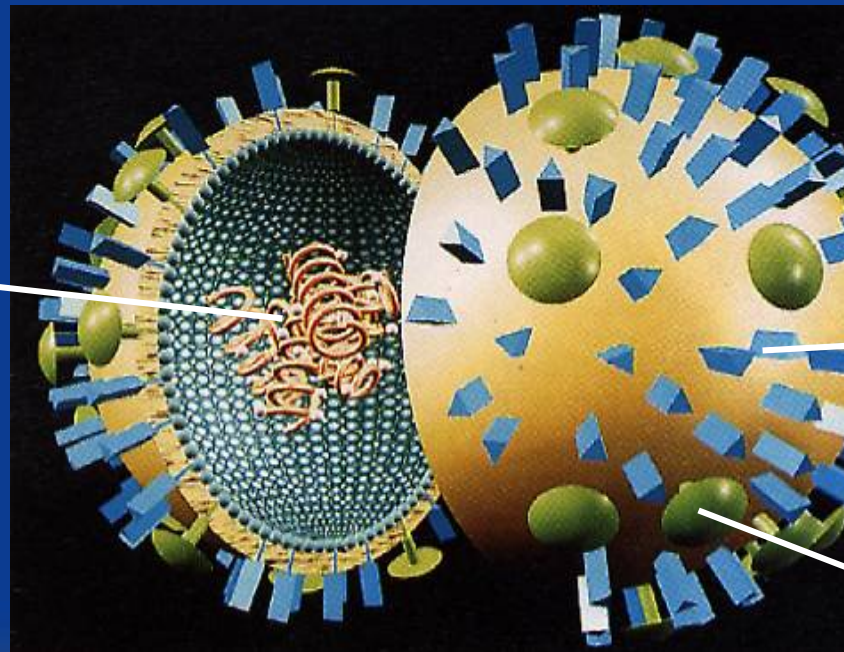
- Wild birds main reservoir for influenza A viruses
 - All known “A” subtypes circulate in wild birds
 - Infect wild and domesticated birds
 - Ultimate source for viruses (and virus genes) infecting other animal species



Influenza Virus Composition



**Genome:
8 segments
of negative
sense,
single-
stranded
RNA**



Hemagglutinin

Neuraminidase

A/Beijing/32/92 (H3N2)

Virus
type

Geographic
origin

Strain
number

Year of
Isolation

Virus subtype



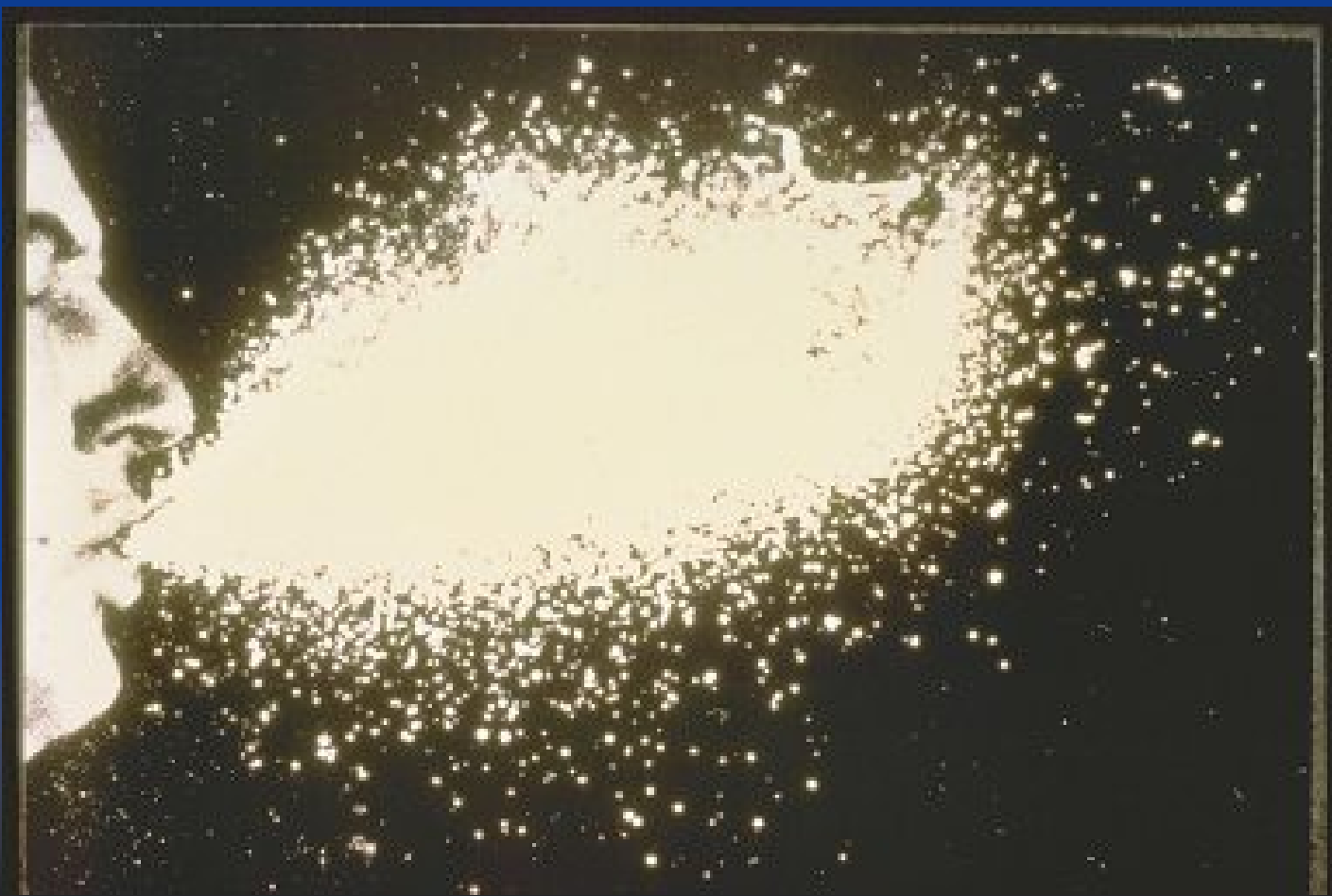
Influenza Types

- **Type A**
 - Epidemics and pandemics
 - Animals and humans
 - All ages

- **Type B**
 - Milder epidemics
 - Humans only
 - Primarily affects children



TRANSMISSION





Influenza is a Respiratory Illness

- Transfer mechanisms
 - Coughing, sneezing, talking
 - Hand contact
- Influenza A appears relatively stable in dry cool environments
 - Transferred from solid surfaces by touching respiratory droplets on self, another person, or an object, then touching mucus membranes (e.g., mouth, nose, eyes) without washing hands



Infection

- Virus attaches to respiratory tract epithelium
- Replication cycle: 4-6 hours
- Respiratory epithelial cells die as they release virus at apical surface (toward the airway lumen)
- Released virus then initiate infection in adjacent cells



Influenza Clinical Course

- **Respiratory infection**
 - Onset of symptoms 1- 5 days after exposure
- **Symptoms**
 - Fever, headache, cough, sore throat, myalgia, nasal congestion, weakness and loss of appetite
- **Full Recovery in 2-3 weeks**
 - Fever: 3 days
 - Nasal congestion/discharge persist 3-4 more days
 - Cough may persist for 1-2 more weeks



Complications

- Pulmonary
 - Primary Influenza Viral Pneumonia
 - Secondary Bacterial Pneumonia

- Non-Pulmonary
 - Myositis
 - Myo/Pericarditis
 - Encephalopathy/Encephalitis



Influenza Dogma

- There is no viremia with Influenza infections



Extra-Pulmonary Influenza in Humans

- **No viremia found:**
 - Minuse *et al*, J Lab & Clin Med, 1962
- **Virus present in blood**
 - Naficy, 1963, NEJM
- **Virus present in non-pulmonary organs**
 - Kaji *et al*, 1959, PNAS
 - Yawn *et al*, 1971, JAMA
 - McGregor *et al*, 1984, Am J Obstet Gynecol



Extra-Pulmonary Influenza in Humans



- Khakpour et al, 1969, BMJ
 - 12/21 ILI throat washes positive
 - All 21 had negative blood specimens for influenza virus
 - 1/29 asymptomatic contacts had virus in blood 12 hours before onset of symptoms



Influenza is a serious illness

- Annual deaths: 36,000*
- Hospitalizations: >200,000*

* Average annual estimates during the 1990's

- Who is at greatest risk for serious complications?
 - persons 65 and older
 - persons with chronic diseases
 - infants
 - pregnant women
 - nursing home residents



Variations Occur

- H7N7 in Netherlands, 2003
 - An Avian influenza strain
 - 86 human cases, 1 death
 - Predominately conjunctivitis with few respiratory symptoms
 - Human cases detected because of increased reports of conjunctivitis in areas with avian flu outbreak

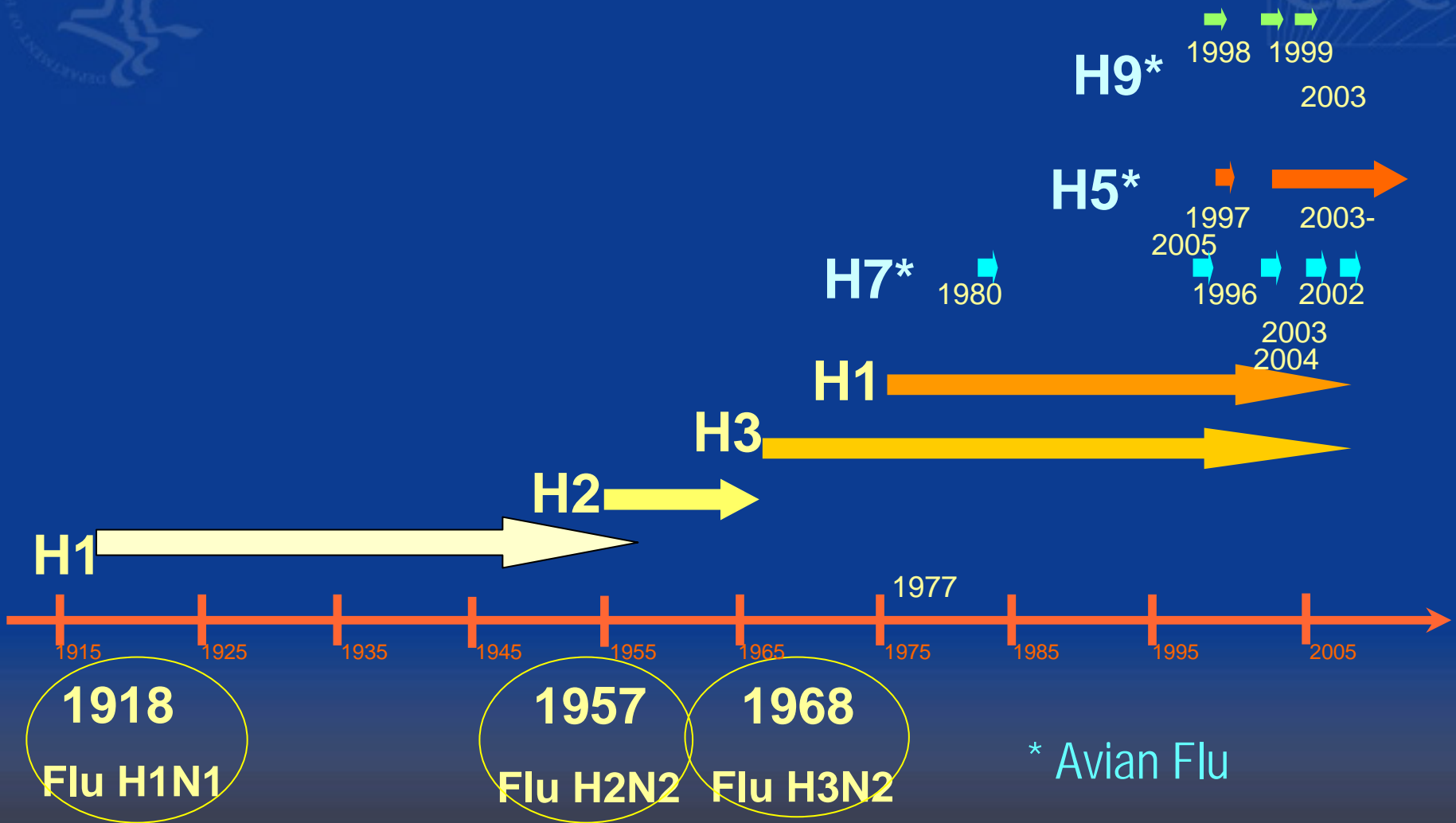


Antigenic Change

A Key Feature of Influenza Viruses

- Change more than other respiratory viruses
- Minor changes occur constantly (“drift”)
 - Cumulative
 - Reason why vaccine is updated each year
- Radical change occurs infrequently (“shift”)
 - New surface protein (no immunity among people)
 - Essential (but insufficient) event for pandemics

Emergence of Influenza A Viruses in Humans



* Avian Flu



So What About H5N1?

Transmission of H5N1



Currently requires close or direct contact with chickens potentially infected with H5N1



Replication of H5N1

- Does not appear to replicate as well in the nasopharynx as other strains
- Replication site may be lower in the respiratory tract
- Incubation may be longer (up to 8 days)




H5N1 Illness

- Fever and cough or dyspnea
- More frequent diarrhea
- Lower respiratory tract symptoms develop early
 - Clinically suggestive of pneumonia
 - Abnormal X-Rays (multi-focal consolidations) which rapidly worsen
 - Primary viral pneumonia
 - Mechanical ventilation required
- Multi-organ failure
 - Renal and cardiac dysfunction



Extra-pulmonary H5N1 Symptomatic Cases



- 6 yr Thai male
 - Viral RNA detected post-mortem in lung, intestine and spleen tissues
 - No mRNA in spleen (no viral replication)
 - mRNA found in intestine and lung
- 9 yr Vietnamese female
 - Virus isolated from CSF, serum, throat, rectum specimens collected ante-mortem

Significant Events in Influenza Virology and Blood Banking



1900: ABO Described

1915-16: Citrated Anticoagulants

2006: Can Influenza be transmitted by transfusion?

1932: 1st Blood Bank (Leningrad)

1933: Influenza A virus first isolated

1941: Hemagglutination described

1945: First Inactivated Vaccine Licensed in US

1947: AABB formed

80's & 90's: PCR and Internet

2000: Rapid Flu Tests

1918

1957 1968

2000

Spanish Flu

Hong Kong Flu
Asian Flu



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