HEALTH RISK ASSESSMENT FOR AVIAN INFLUENZA (H7N9 2013) BASED ON PAST AND PRESENT TRENDS

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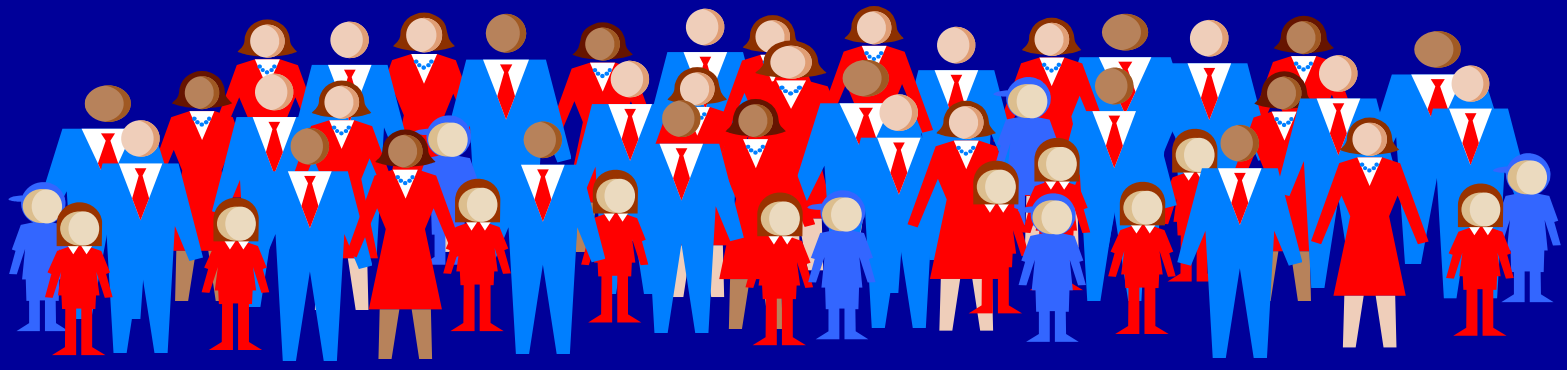


Clinical Definition of Influenza

- Influenza is an Acute respiratory illness with fever affecting nose, throat, bronchial tubes, lungs
- Must be clinically distinguished from other respiratory pathogens
  - Adenovirus, parainfluenza viruses, rhinoviruses, mycoplasmas, SARS, etc.
- Is associated with considerable morbidity and mortality
  - Also anxiety for some

Influenza viruses: basics A,B,C

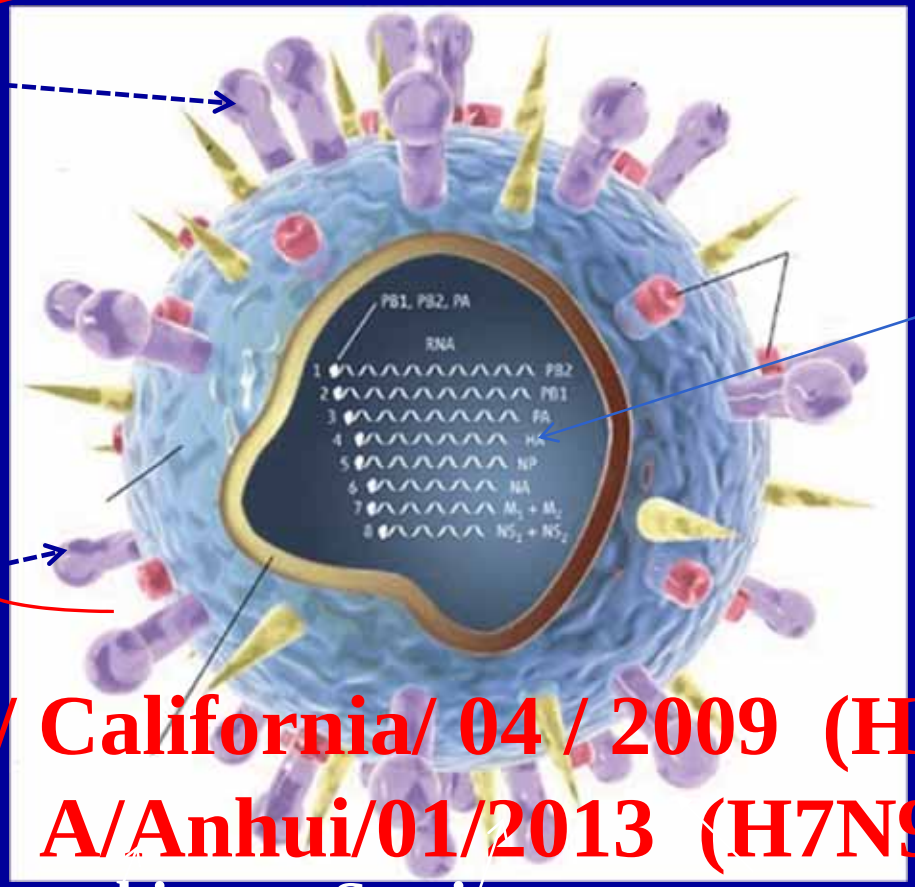
- There are three types of influenza viruses
  - A, B and C
- Influenza A is the major cause of disease
  - Major hosts are: human, pigs and birds
- Wild bird: reservoir of all influenza A subtypes
- Pigs: can be co-infected with pigs, human and avian influenza: vessel for generating novel viruses
- Human: bears the brunt of novel influenza viruses

Nomenclature of Influenza A viruses

NA (neuraminidase)

Envelope (coat)

HA (hemagglutinin)



8 different RNA genes

A / California/ 04 / 2009 (H1N1)

A/Anhui/01/2013 (H7N9)

Virus type

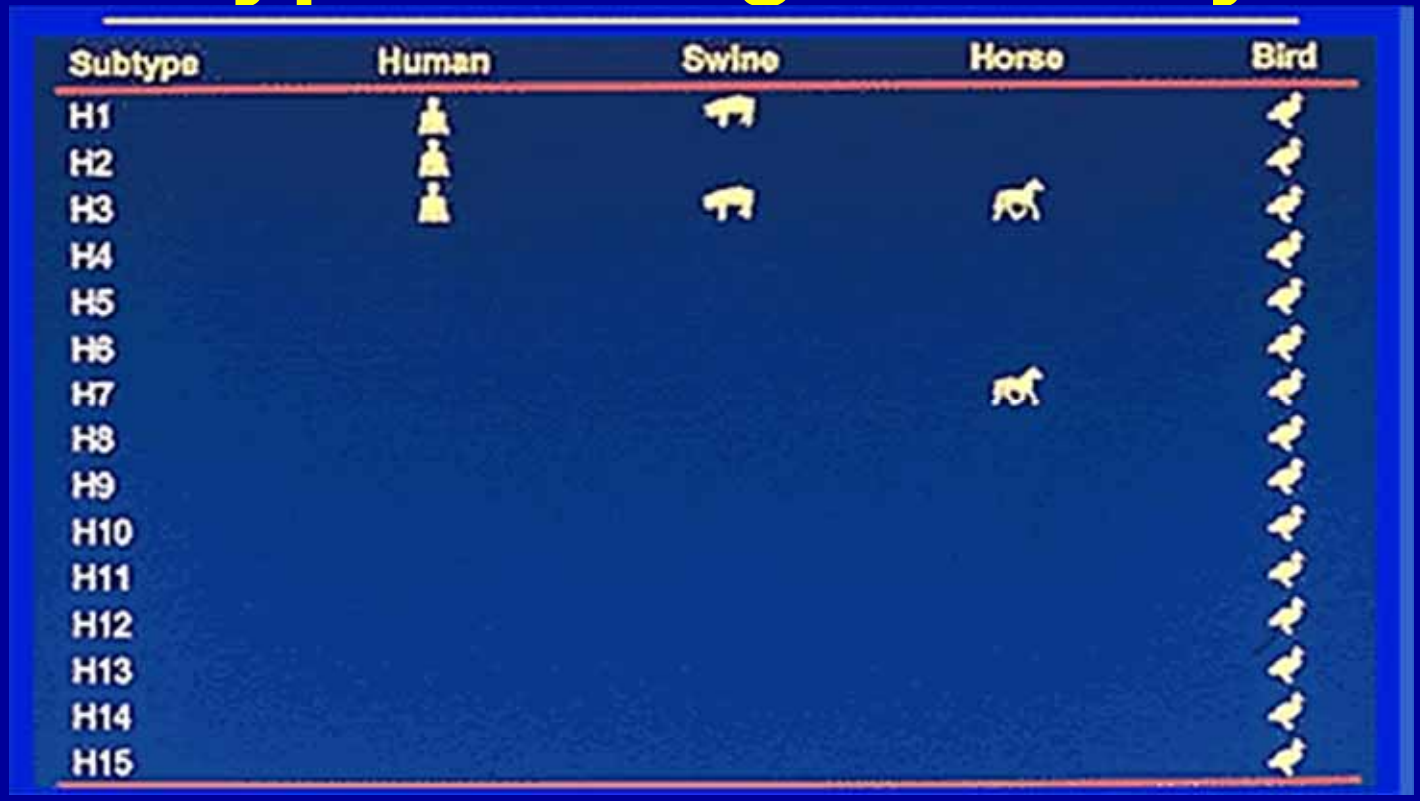
Geographic origin

Strain number

Year of isolation

Virus subtype

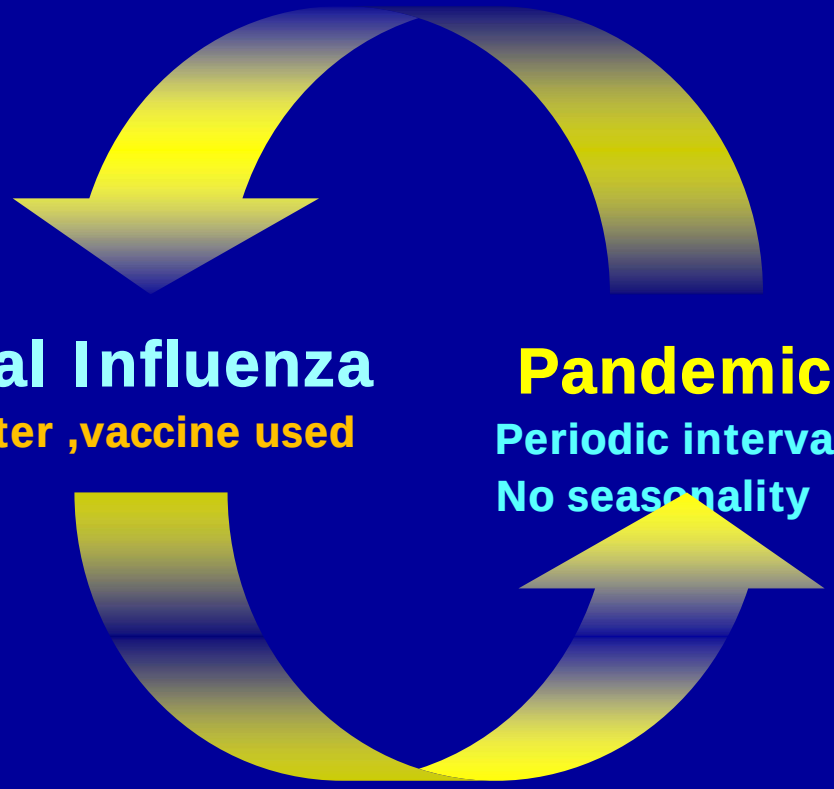
Influenza A Hemagglutinin Subtypes Categorized by Host



H16 +

*Note: Birds have the whole repertoire of 16 Hemagglutinin (H1-H16)
Swine: H1, H3
Human: H1, H2 H3

Seasonal and Pandemic Influenza



Seasonal Influenza

Yearly / winter ,vaccine used

Pandemic Influenza

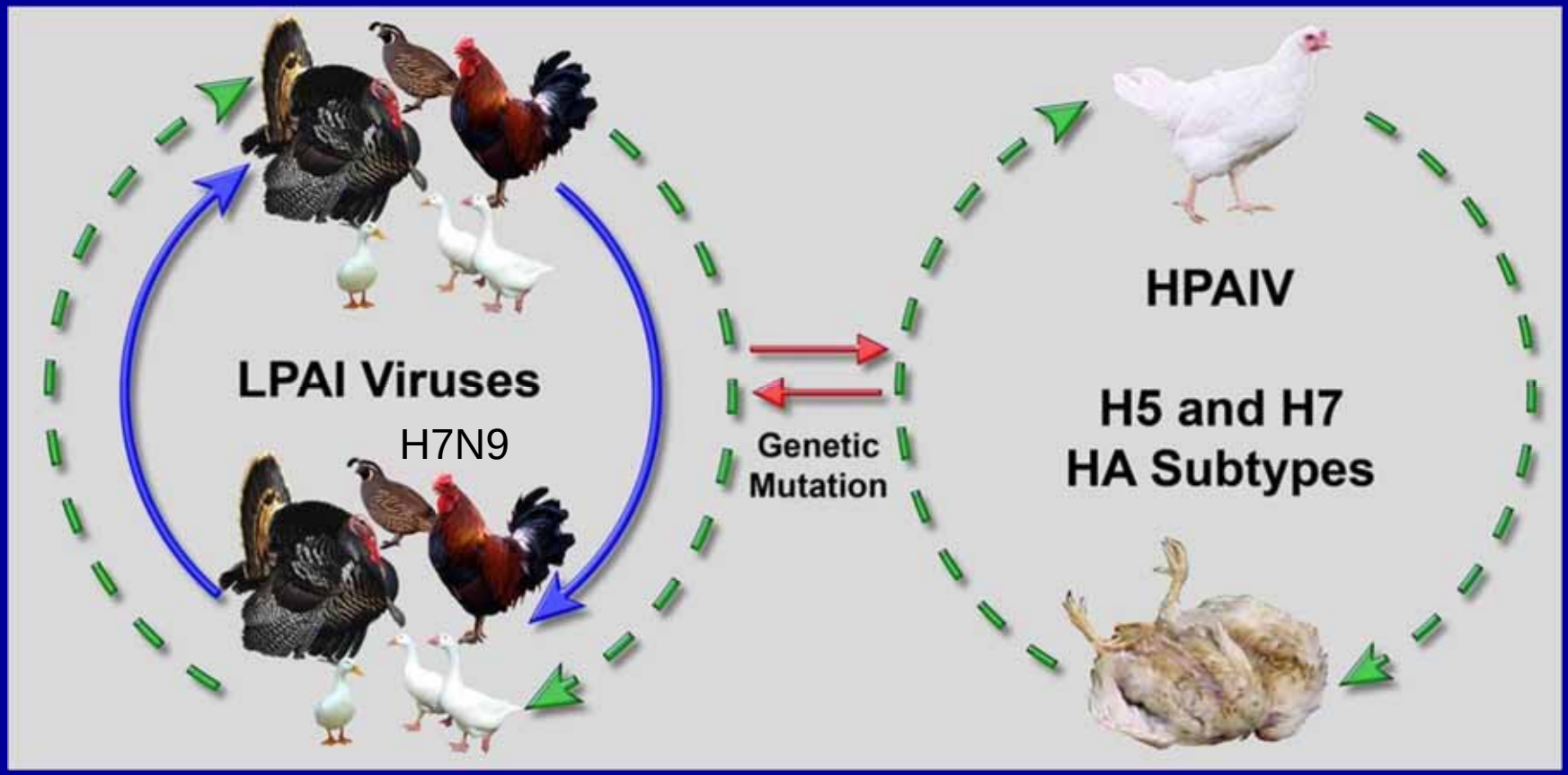
Periodic interval of 10-20 years

No seasonality

Why are we so concerned about avian influenza?

- Avian influenza can have a large impact on poultry
  - Can cause high mortality
  - Significant economic impact
  - Sustained epizootic
- Rarely, avian influenza can cause illness in humans
- Avian influenza viruses can serve as source of next pandemic strain

Evolution of Highly Pathogenic Avian Influenza Viruses (HPAI)



- Low Pathogenicy Avian Influenza Can Evolve into High Pathogenicity
- Usually associated with mutation of the hemagglutinin precursor protein,
- Infected stock are culled to prevent evolution into pathogenic type

Summary of Human Cases of Avian Influenza infections

H7N7 — 1996 — 2003

H5N1 — 1997

H7N2 — 2002 — 2003 — 2005 — 2007

H10N7 — 2007

H7N3 — 2005

H5N2 — 2004

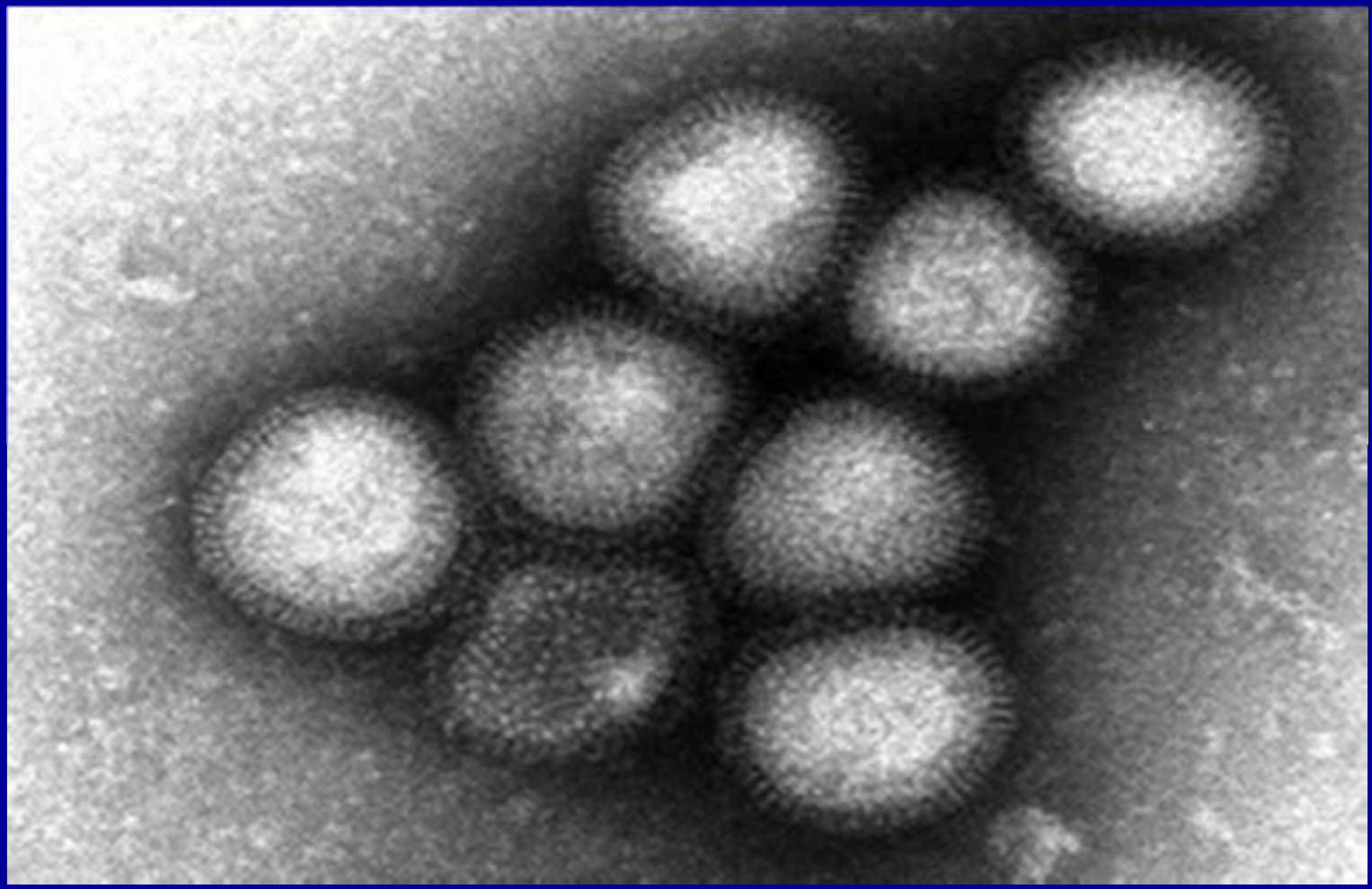
H7N9 — 2013

Cause conjunctivitis and mild respiratory complications, sometimes death e.g. H5N1 and H7N9

1996 1997 2002 2003 2004 2005 2006 2007 2013

Main risk factors are Environmental and occupational exposure

The Star of the show: H7N9



A closer look at H7N9 outbreak

Outbreak: Alerted by WHO and OEI

Infections in Shanghai reported by WHO on 31st March

As of 29th April 126 cases reported with 24 deaths

Disease: fulminant pneumonia, ARD, multi-organ failure

Determinants of H7N9 infection in 82 Humans (

source: New Eng J Med 26 April 2013)

Determinants	% with characteristics
age	27-85 years
Sex	Male 73%
Contact with chicken or wet market	77%
Residence	84% urban

Source of infection is contested: This is a prevalence study. A case-control study urgently warranted to determine exposure risk factors,

Epidemic Curve of H7N9

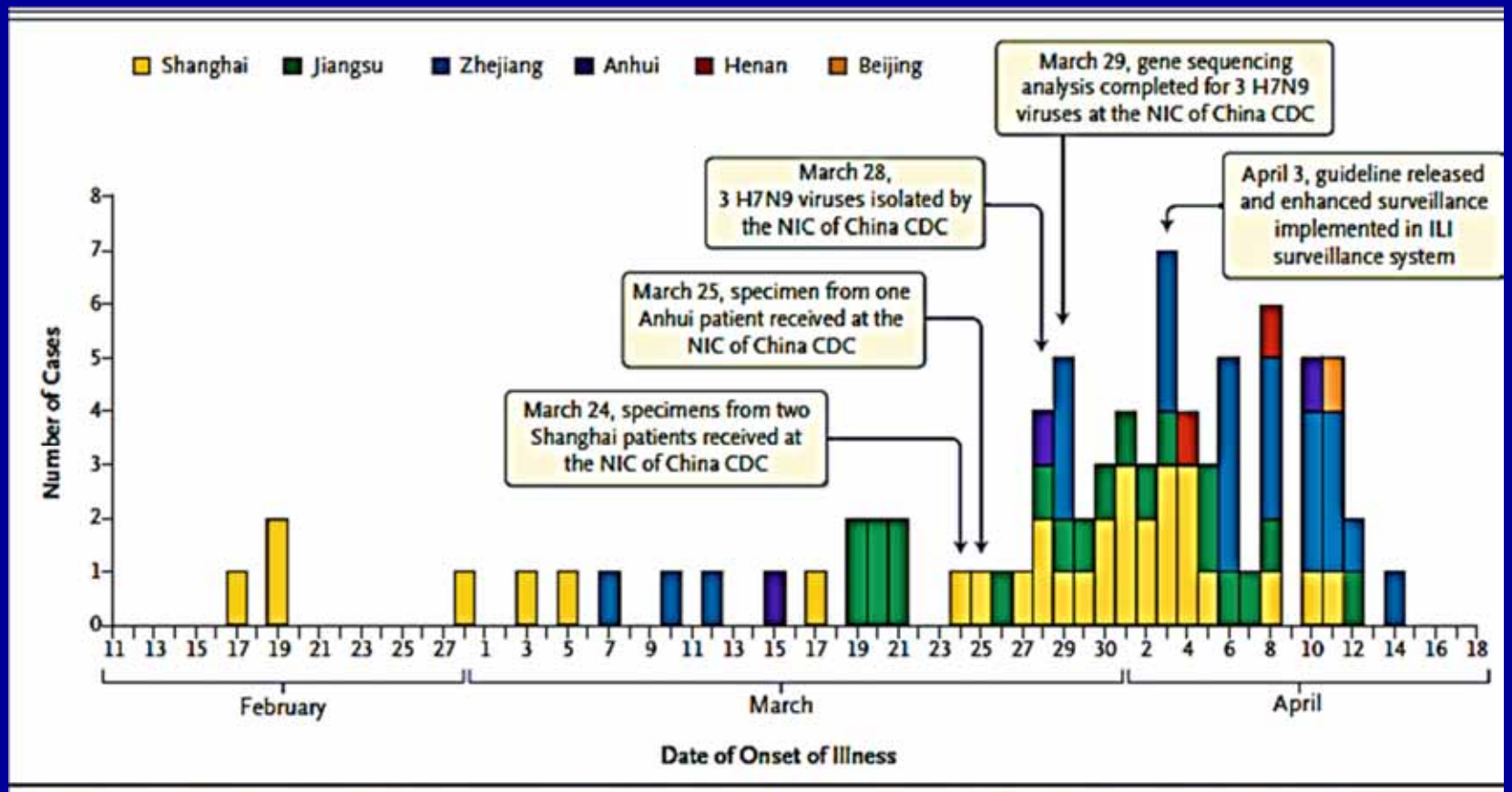
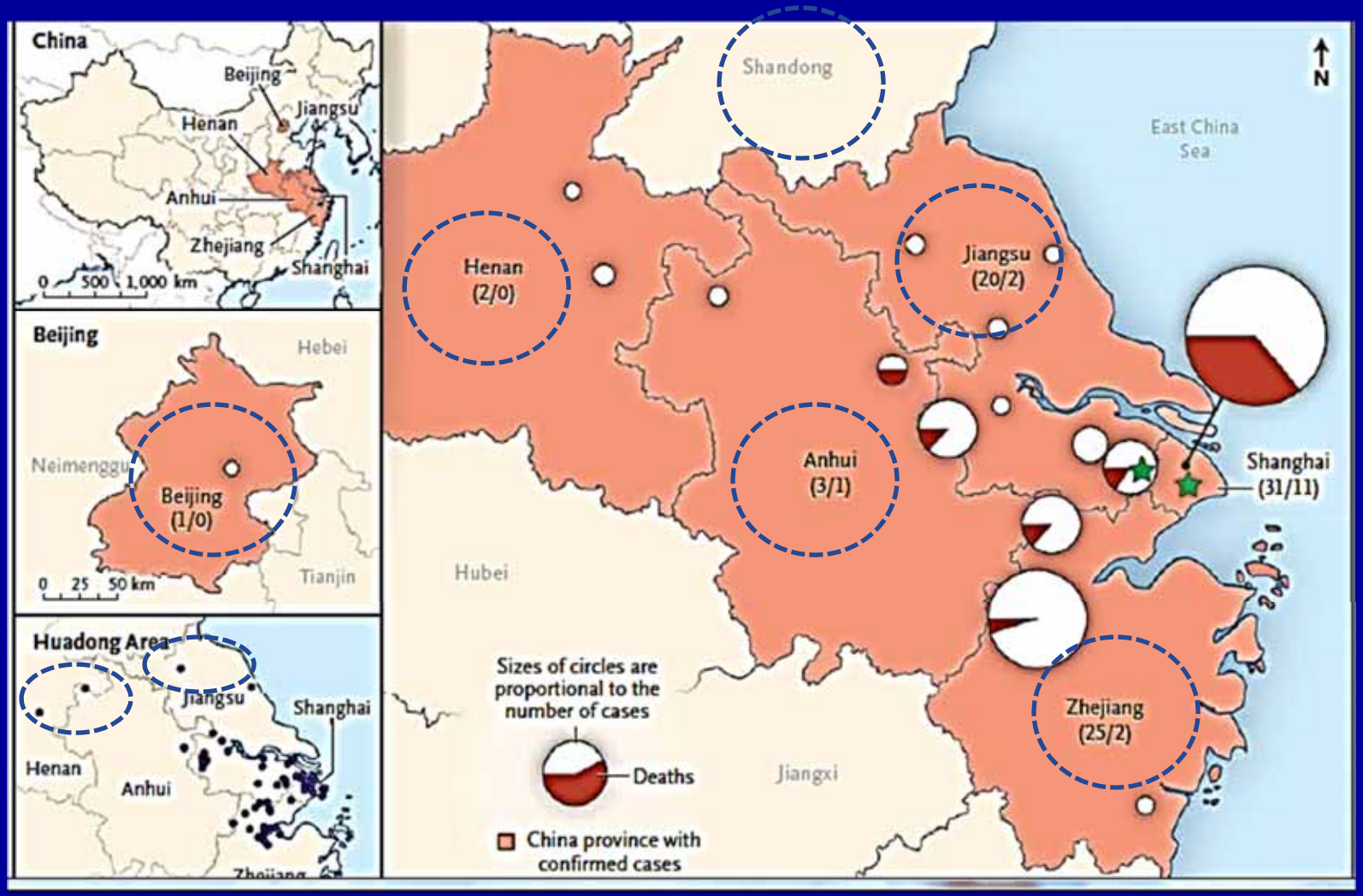


Figure 1. Date of Onset of Illness in First 82 Patients with Confirmed H7N9 Virus Infection, According to Province in China.
CDC denotes Chinese Center for Disease Control and Prevention, ILI influenza-like illness, and NIC National Influenza Center.

The curve shows: infection propagating, Shanghai may be the point of origin or simply detection

Geographic distribution of H7N9



The spot-map shows the virus has spread Shanghai, Anhui, Beijing, Fujian, Zhejiang, Jiangsu, Shandong, Hunan, Henan,

Human Behavior: illustration of H5N1 from Myanmar

The epidemic kept propagating from one area to another by the movement of infected poultry to avoid culling
Culminating in a human case

Can similar factors be responsible for new cases in China now?

Other ways of Avian Influenza spread

- Legal poultry business
- Illegal bird trade
- Untreated fertilizer
- Migrating birds
- Humans (contaminated objects, intentional spread)

Human-to-human transmission of H7N9

- In 3 family clusters, unambiguous transmission could not be established
- ~1689 close contacts of confirmed H7N9 have tested negative for the virus
- The basic reproductive rate, rho is zero thus far

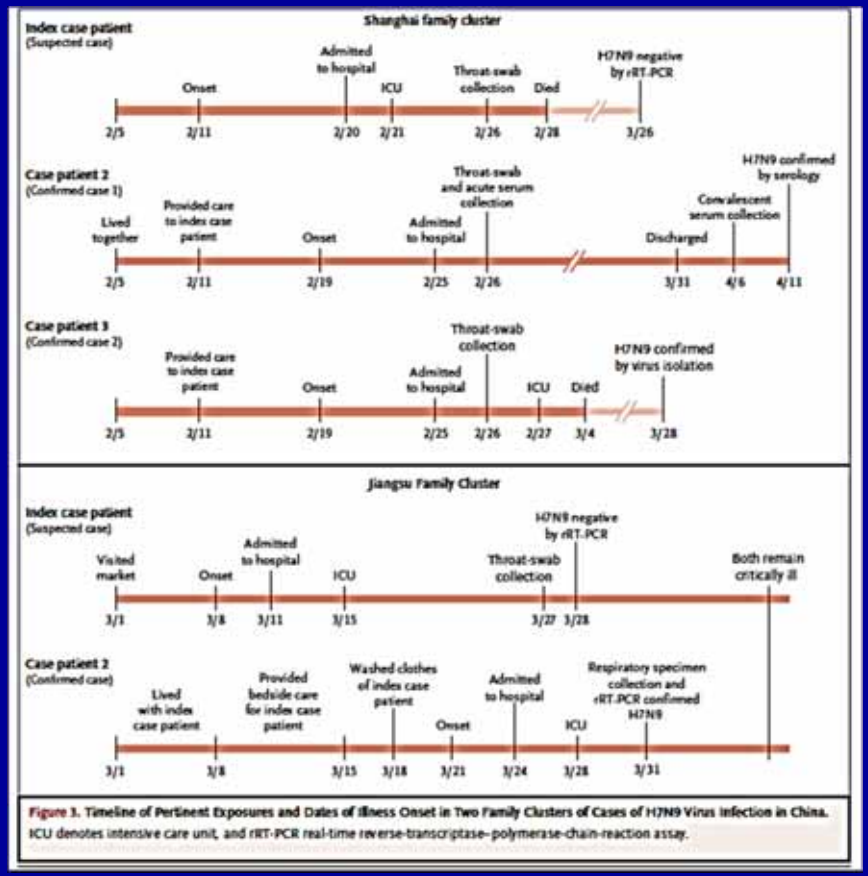


Figure 3. Timeline of Pertinent Exposures and Dates of Illness Onset in Two Family Clusters of Cases of H7N9 Virus Infection in China.
ICU denotes intensive care unit, and rRT-PCR real-time reverse-transcriptase–polymerase-chain-reaction assay.

Epidemiologic Interpretation of A (H7N9) infections

- Cases keep increasing
  - Surveillance has been enhanced and focussed also
  - Case definition has been formulated
  - Diagnostic reagents have been developed

- The virus is very lethal ~20% case-fatality: biased towards severely ill cases
  - Case fatality is the ratio of deaths: infected (24:126~20% (caution)
  - We cannot accurately estimate all the infected cases because
    - They may not come to the peripheral health facilities
    - All infected cases cannot be confirmed by laboratory means
    - We are only seeing tip of the ice-berg, there may be many sub-clinical cases
    - Human H7 infections are usually mild causing conjunctivitis with moderate respiratory complications
- The virus is spreading
  - Can be equally explained by movement of infected poultry
  - Compare the experience of Myanmar

What is the pandemic potential of H7N9?

Localized in China → The world

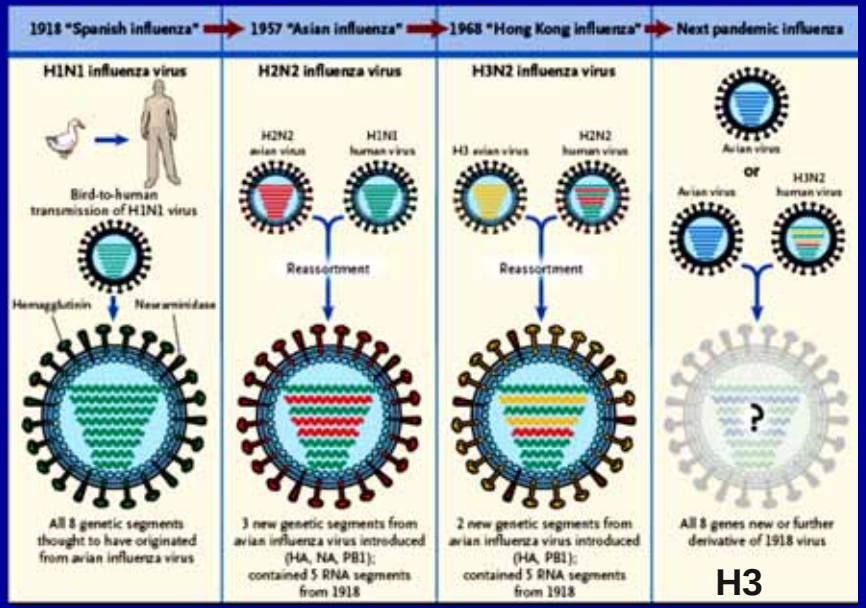
Pandemic Potential of A (H7N9) for humans

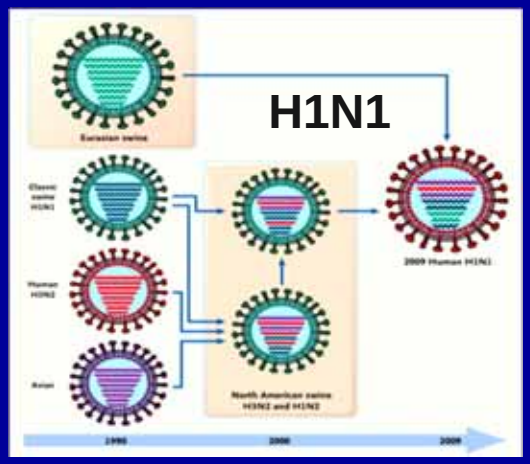
- Re-assuring news for humans
  - No sustained human-to-human transmission
    - The basic reproductive rate is currently zero compared to 1.5 for H1N1
  - Sensitive to Oseltamivir, commonly used anti-viral
- Moderate concerns
  - Most human populations have no immunity to H7 avian gene
  - Sequence of H7N9 H gene shows a mutation in the motif Q226L
  - Compared with H5N1 H gene observation in ferrets, it appears that the virus maybe:
  - adapted to binding to mammalian receptor
  - Transmission by droplet
- But we know H5N1 did not cause a pandemic

Pandemic Potential of A (H7N9) for poultry

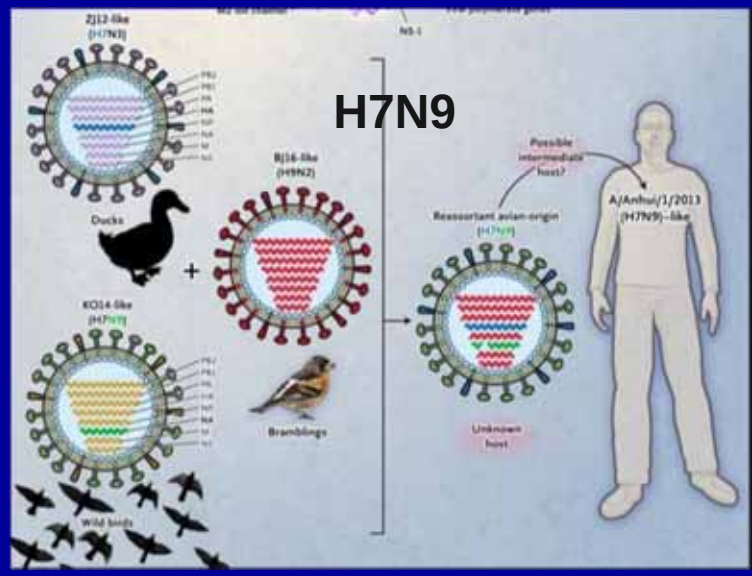
- High risk for being epizootic (endemic) in poultry
  - Because it has low pathogenicity in birds, it will not kill the poultry
  - silent spread elsewhere
- Economic consequences
  - Poultry trade in China and Asia
  - Loss already estimated to be 1 billion $
  - Shares in KFC in China fallen by 20% already
- Could serve as pandemic gene pool for human
  - Increase human contacts because infected birds are not sick
  - Could serve as genetic pool for human reassortants virus to emerge with pandemic potential
    - But then all novel avian viruses have these potential

Not easy to Predict the next pandemic !!





Expected H3 but got H1 in 2009



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Will H7N9 or derivative be pandemic

Signature of past influenza pandemics

1918: “Spanish Flu”

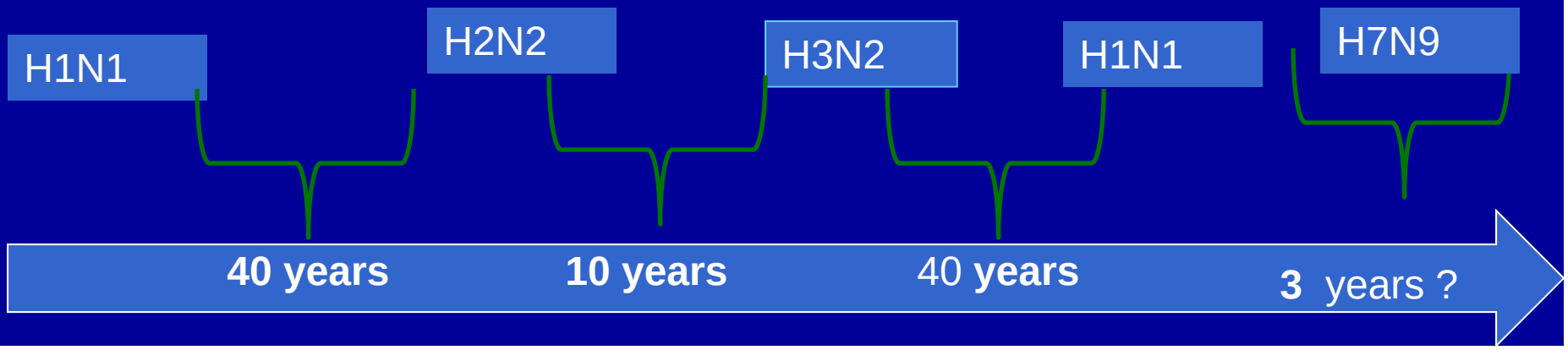
1957: “Asian Flu”

1968: “Hong Kong Flu”

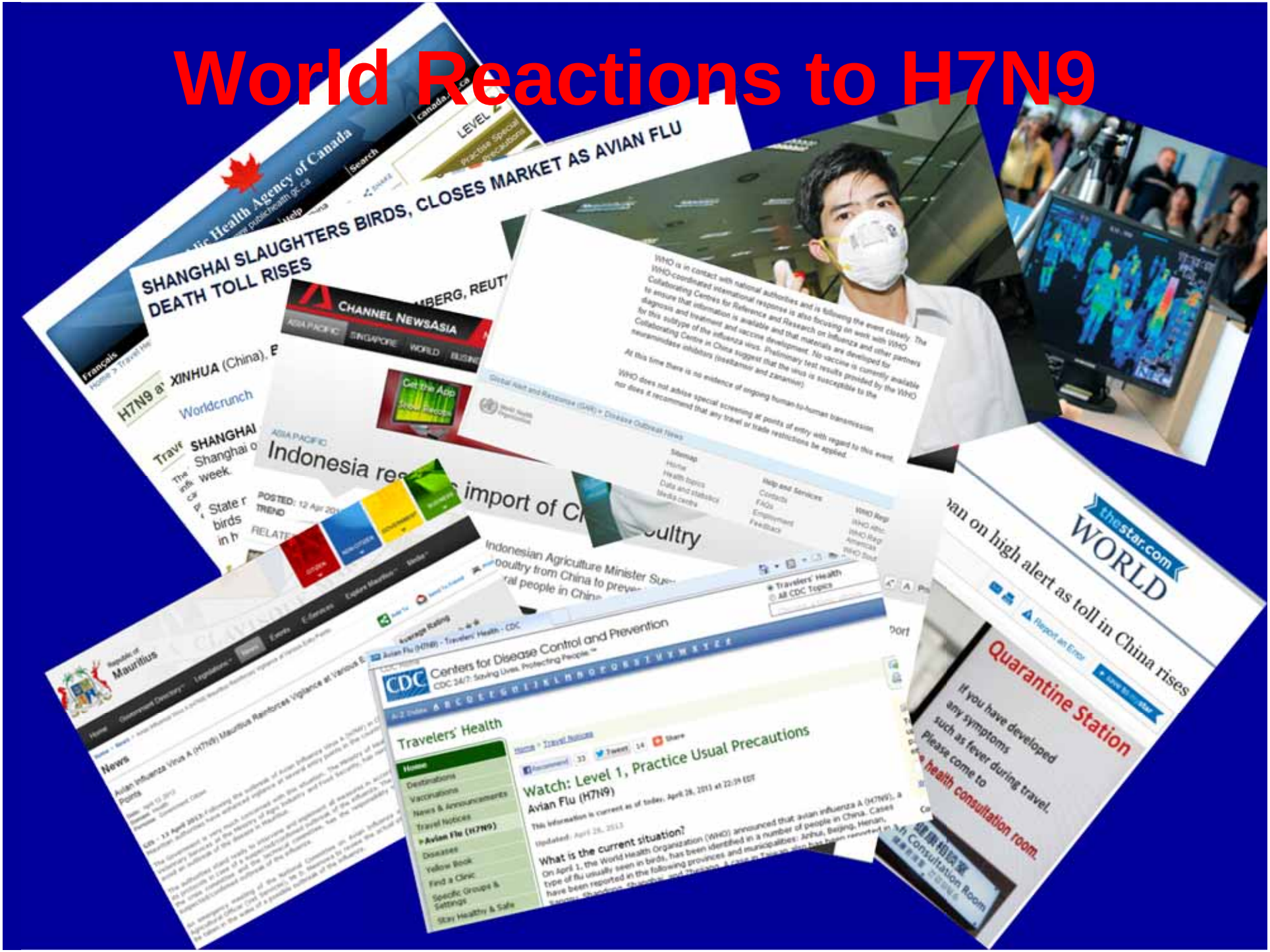
2009: “swine Flu”

Next pandemic ?

Unlikely for another pandemic within 3 years



World Reactions to H7N9



Universal Precautions

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Poultry Hygiene wet market Properly cooked

Environmental hygiene

N94 mask

Hand-washing

Cough etiquette

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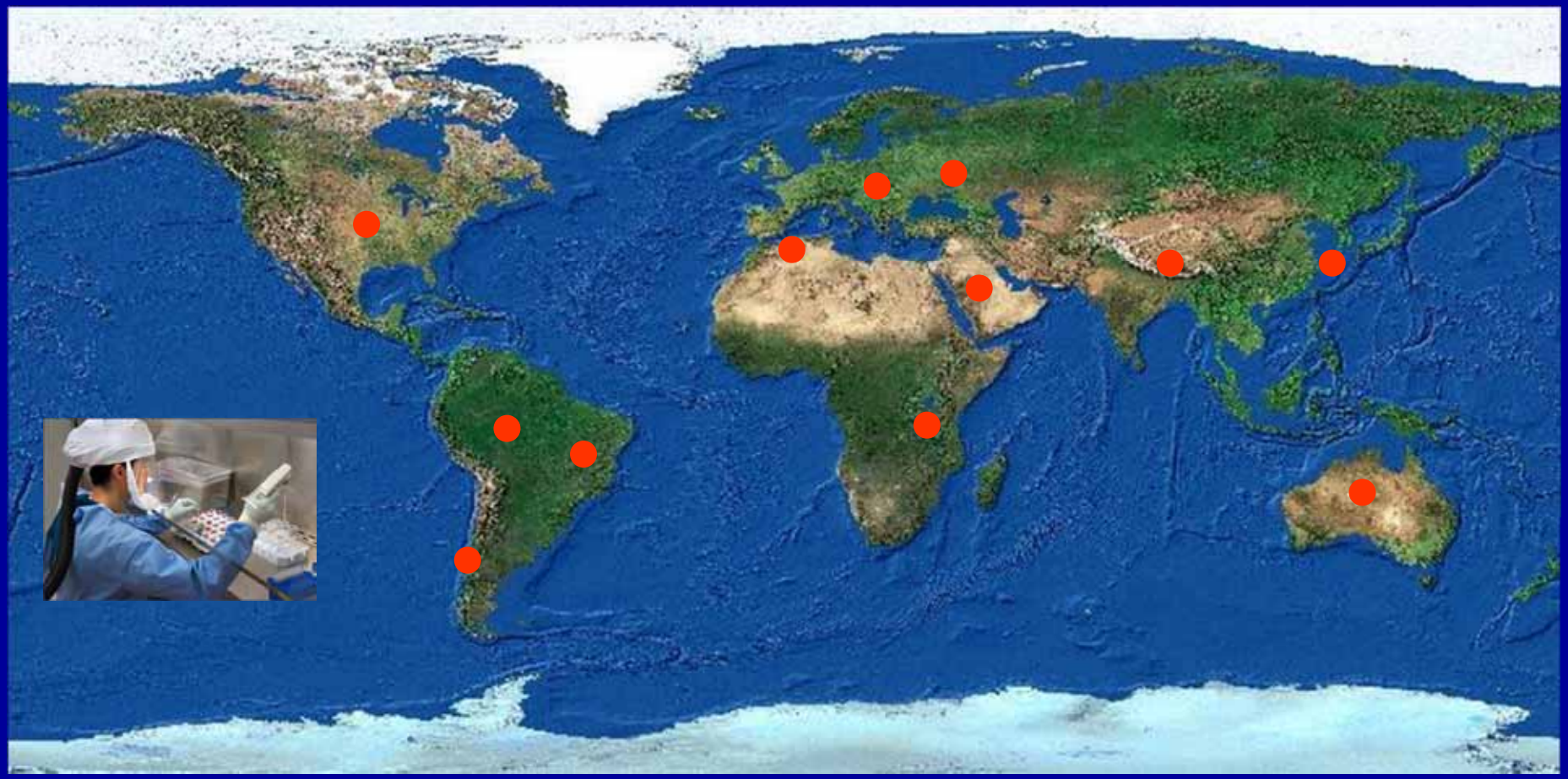
Works for both direct and indirect mode of transmission

Conclusions

- Avian influenza is common among poultry and wild birds
- Avian influenzas invariably serve as genetic pool for human influenza to undergo genetic reassortants
- Novel human-avian influenza poses a theoretical threat to human health
- A novel strain of A H7N9 Avian influenza virus has been detected.
- At this point there is no sustained human-to-human transmission
- Some countries adjoining to China have stepped up surveillance at airport
- On-going surveillance is critical both in humans and animals to detect any virulence and genetic changes

Continue Surveillance for Influenza variant viruses!



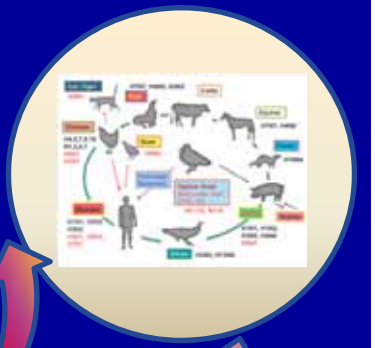
Origin of seasonal and pandemic influenza virus

3. Undergoes mutation called "antigenic drift" Produces new seasonal flu

Antigenic Drift

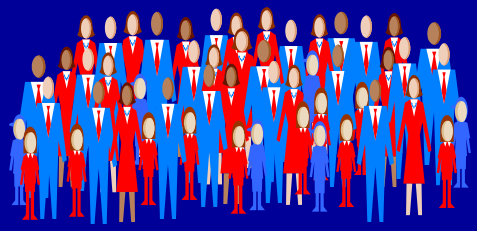
1. Seasonal influenza

Animal Influenza reservoir

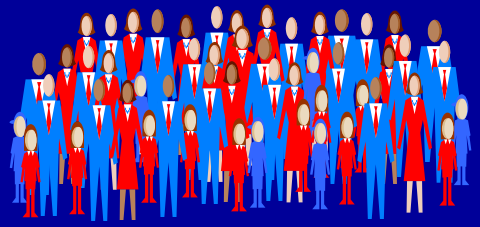


Antigenic shift

4. Process is called "antigenic shift" or genetic reassortment



2. Pandemic influenza



Responding to the expected but unpredictable

Uncertain art to predict next pandemic
Alternative Approach Use
Precautionary Principle to implement the zero- risk policy
Implication of not stock-pile options:
Patients progress to complications
Implications of stock piling for all
Not all cases develop complications
Waste scare resources in public-funded system

Generation of novel influenza by co-infection of birds and pigs