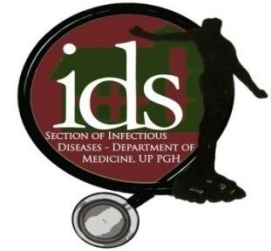


# Highly Pathogenic Avian Influenza (HPAI): Origins and Virology

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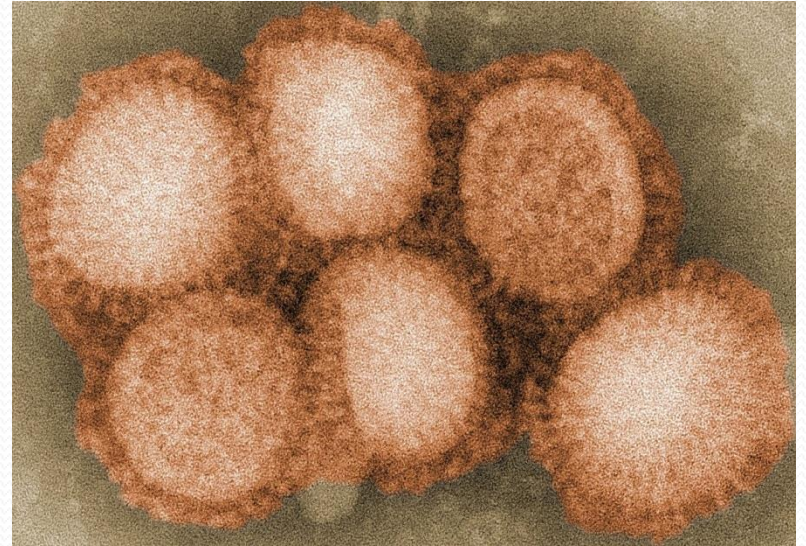


# Objectives

- to examine the virologic mechanisms that underpin the impressive genetic diversity of this virus
- To explore the pathophysiology of changes in pathogenicity in human and avian hosts
- To discuss the molecular epidemiology of recent HPAI outbreaks worldwide.

# Influenza

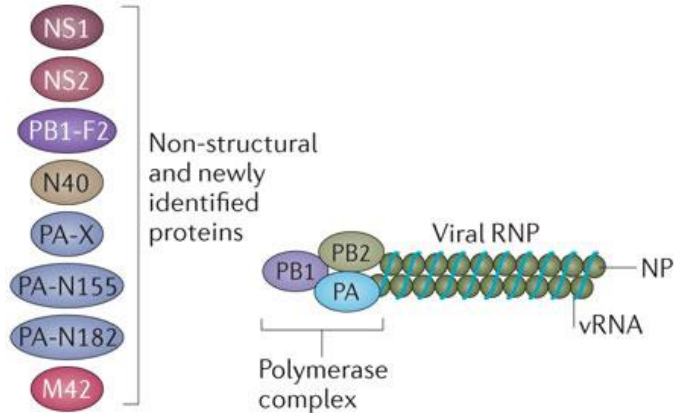
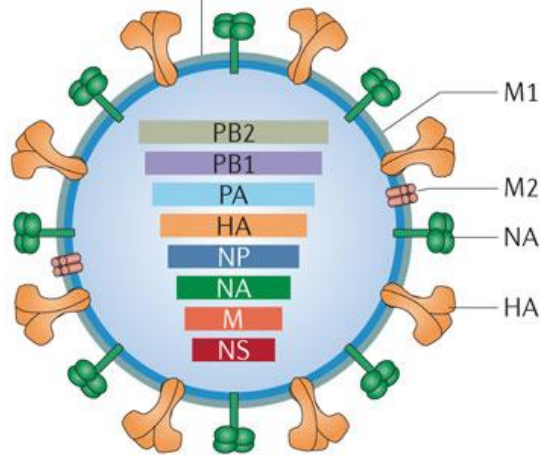
- segmented, negative-sense RNA viruses of the Orthomyxoviridae family
- Three Types: A, B, C
- **Influenza A** with epidemic and pandemic potential
- Most important hosts: humans, pigs, birds



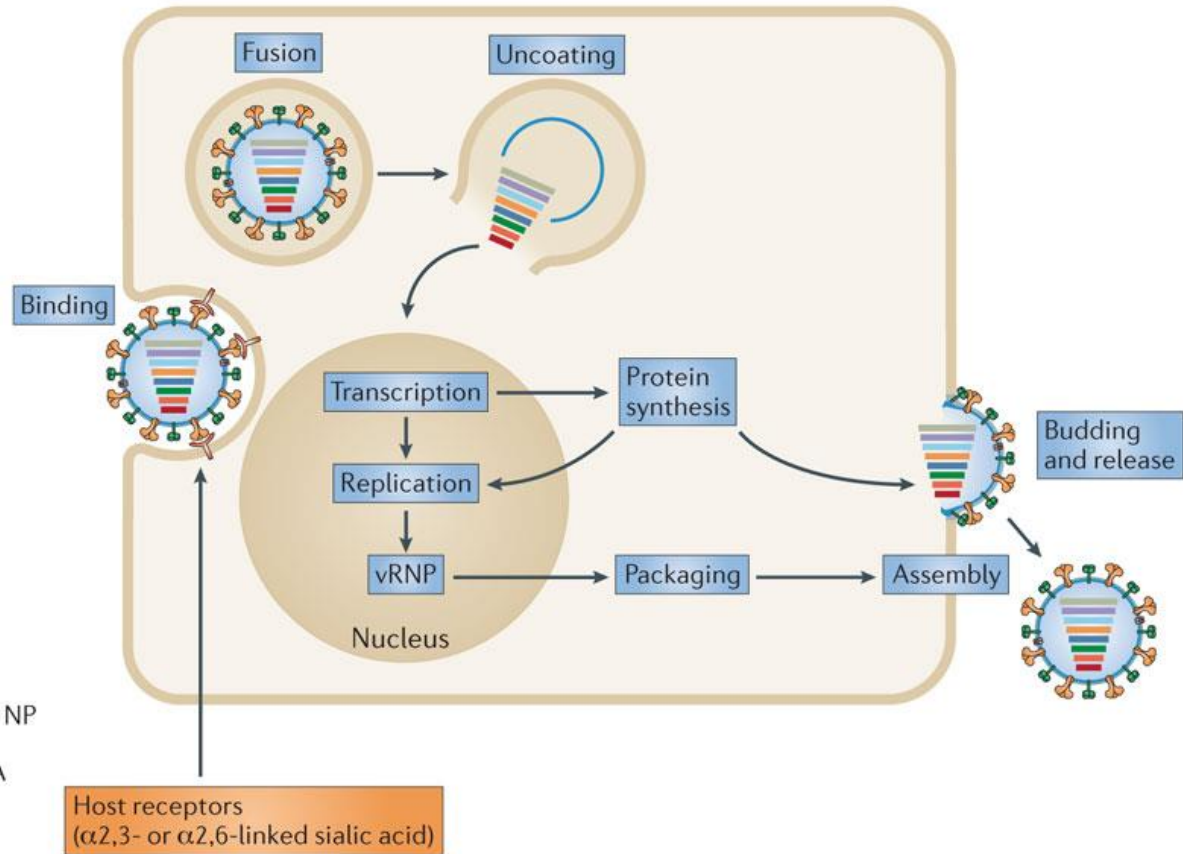
# Pathogenic Determinants

- Hemagglutinin – glycoprotein responsible for binding to sialic acid receptors in hosts, 18 types
- Neuraminidase – glycoprotein responsible for cleaving hemagglutinin from sialic acid to enable new viral particles to infect other cells, 11 types
- Immunity to infection is intimately tied to neutralizing antibodies against these ligands

**a** Lipid envelope derived from host cell



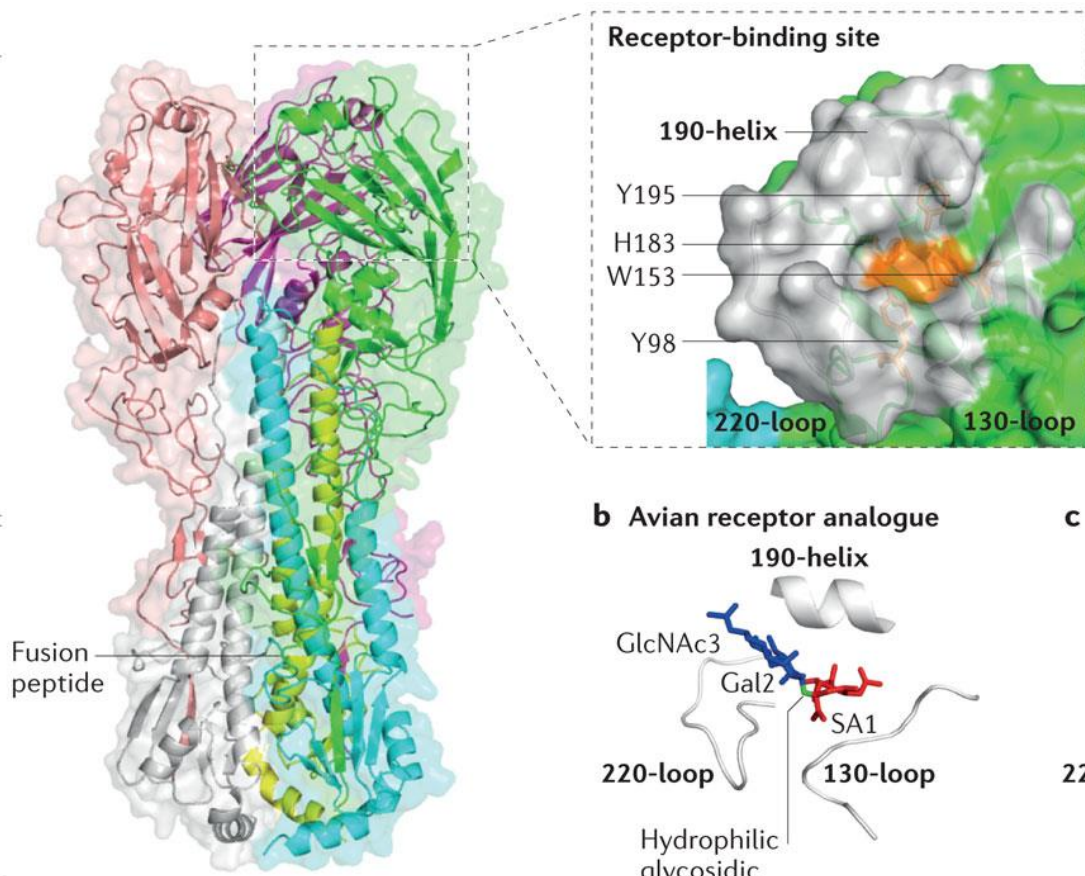
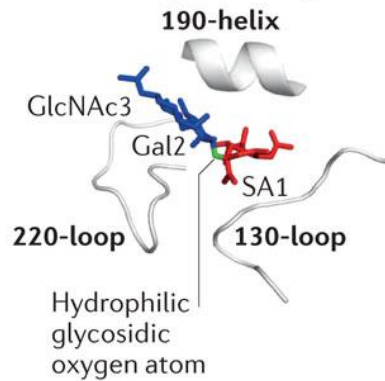
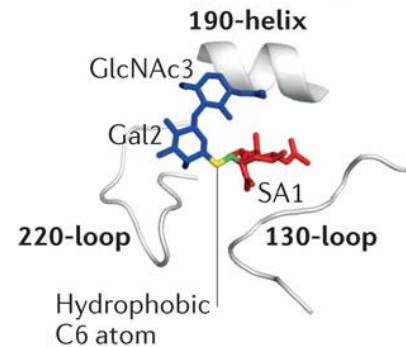
**b**

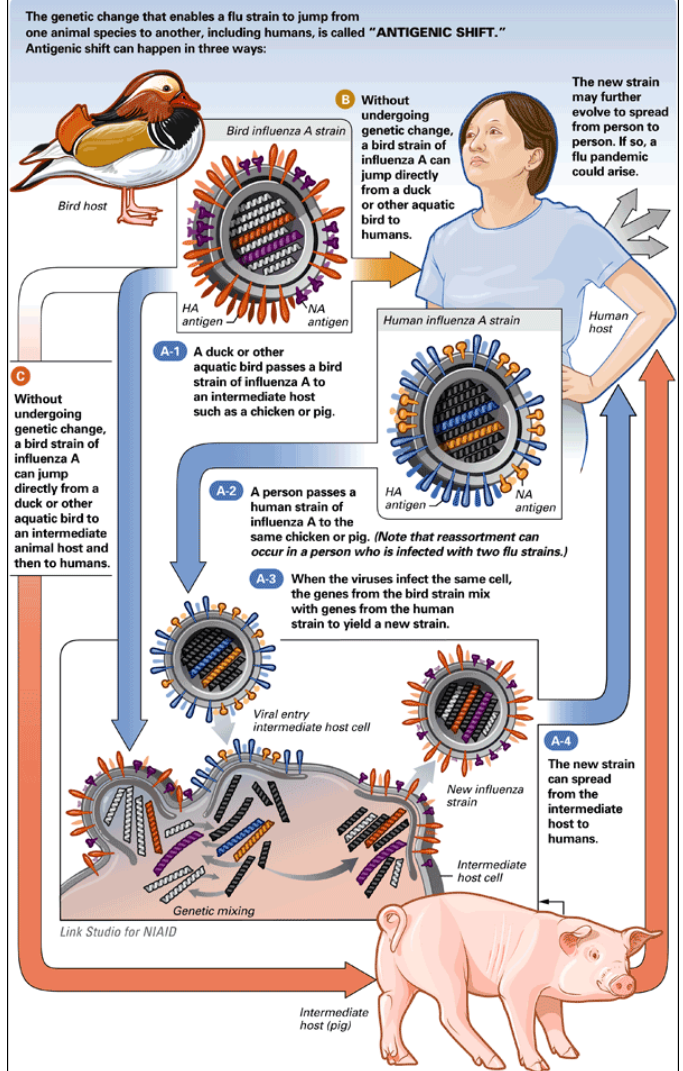
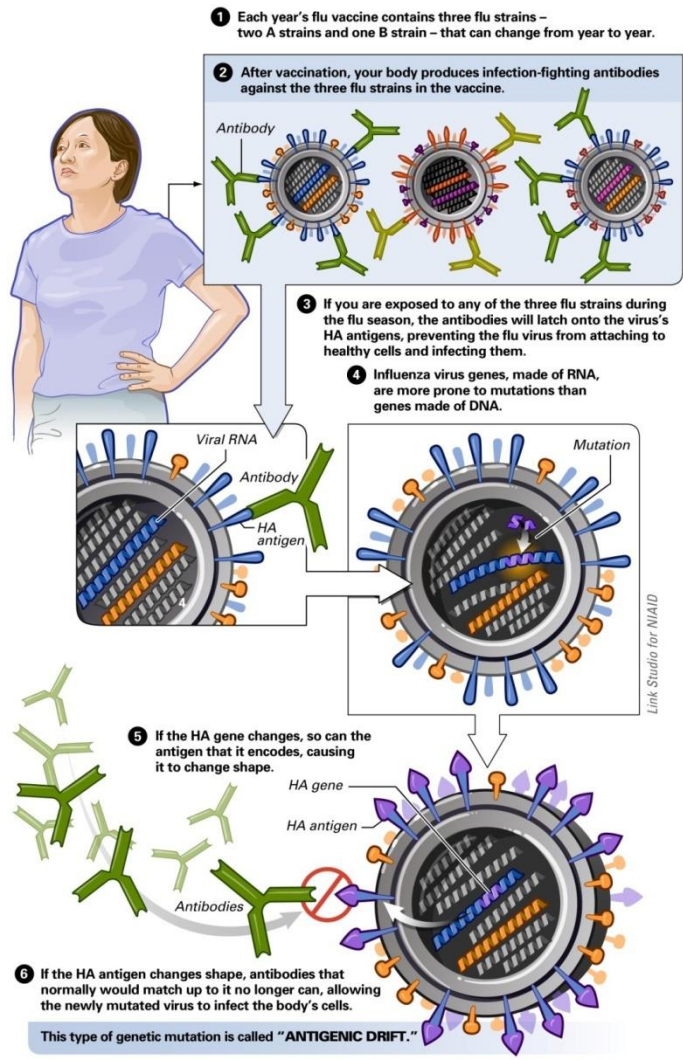


**a**

Globular domain

Stem domain

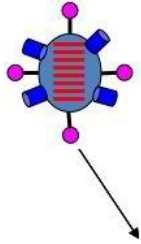
**b Avian receptor analogue****c Human receptor analogue**



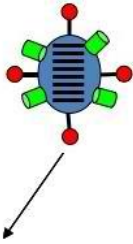


SA- $\alpha$ 2,3-Gal

Avian Virus



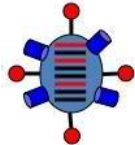
Human Virus



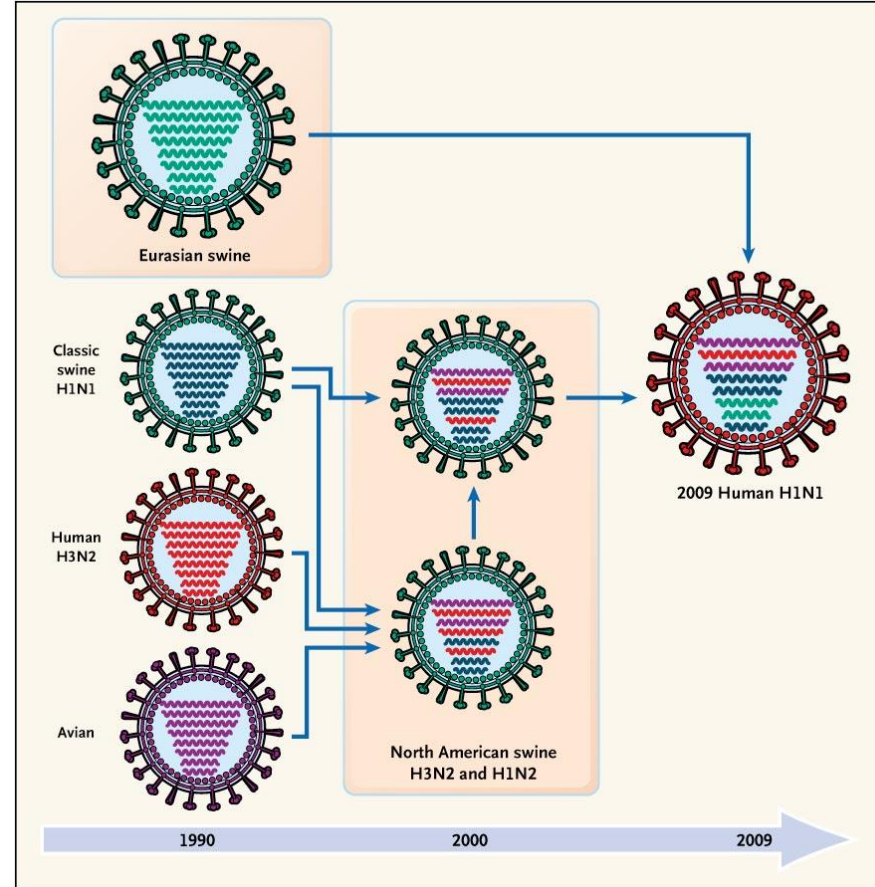
SA- $\alpha$ 2,6-Gal



SA- $\alpha$ 2,3-Gal SA- $\alpha$ 2,6-Gal



Avian/Human Reassortment Virus

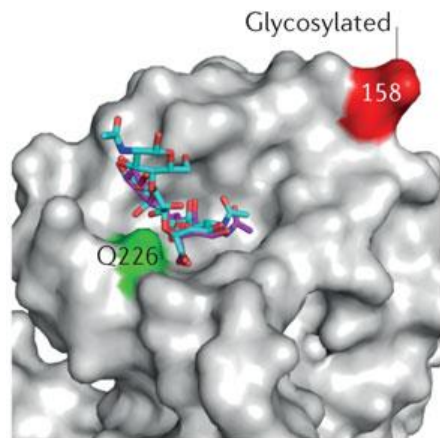




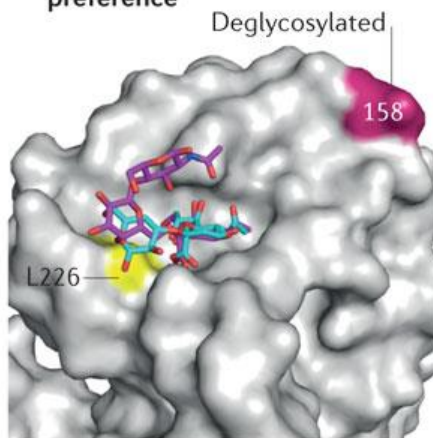
# Avian influenza

- Typically circulate as low pathogenicity variants
- Occasionally mutate and become highly pathogenic strains which cause massive death (“avian ebola”)
- H5 (1<sup>st</sup> in 1997) and H7 strains have show ability to jump from bird to human host with high mortality, but human to human transmission potential remains low; other H types have been sporadically implicated

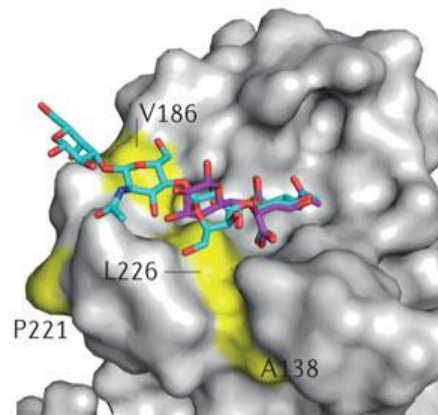
**a** H5 avian receptor preference



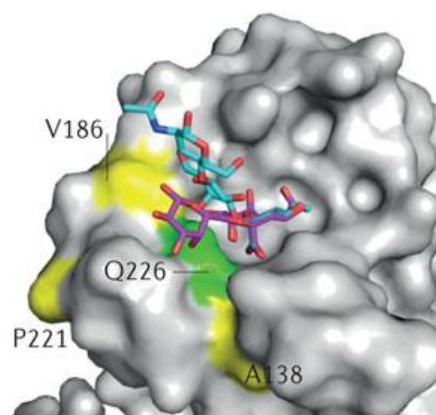
**b** H5mut human receptor preference



**c** AHH7 dual receptor binding

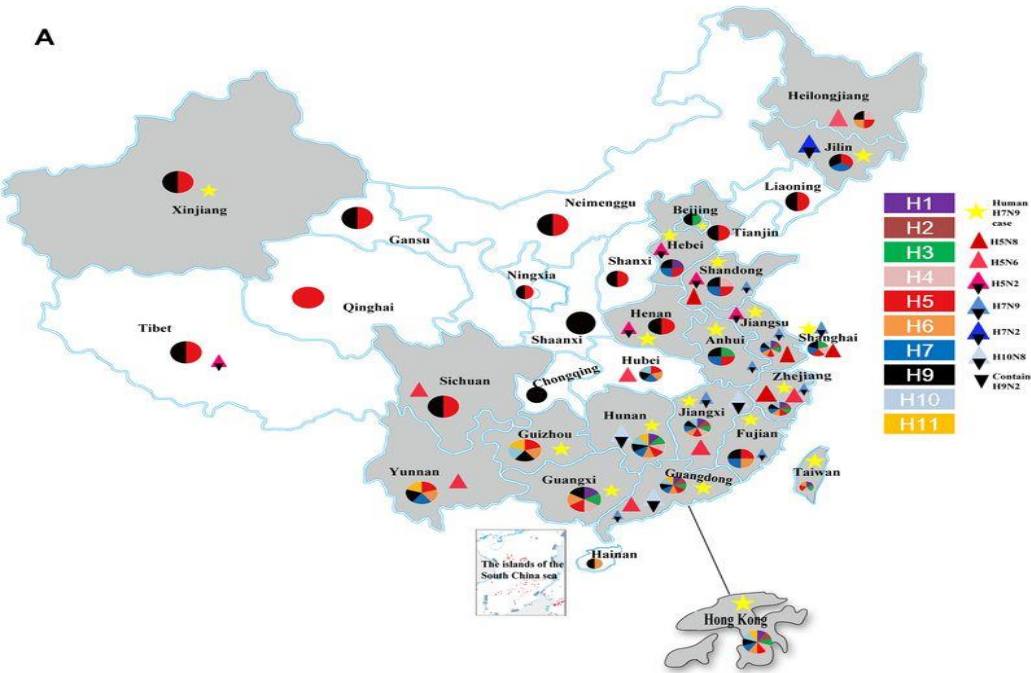


**d** AHH7mut dual receptor binding

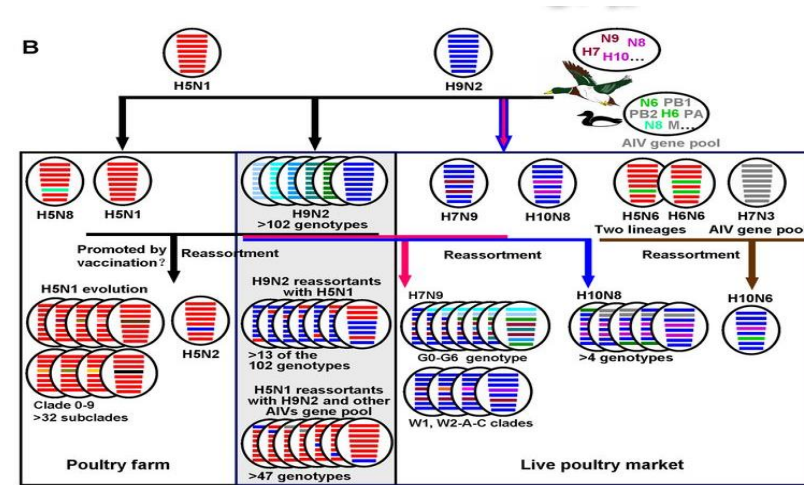


# Emergence and distribution of avian influenza viruses in China.

A



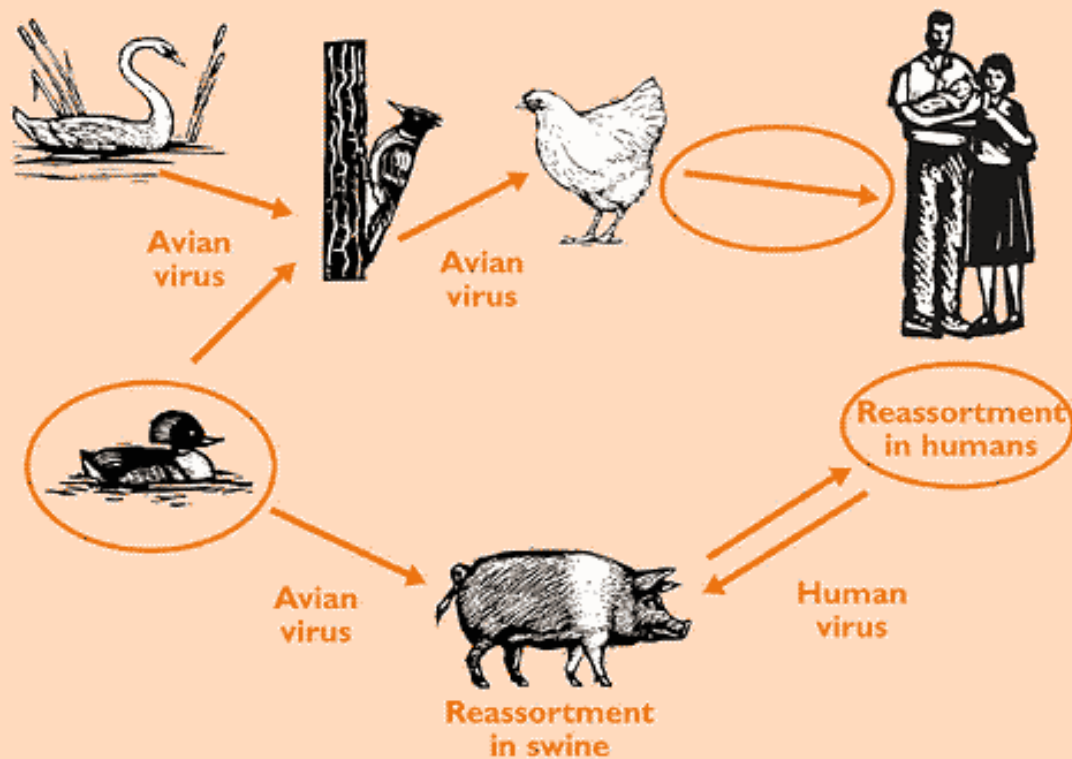
B

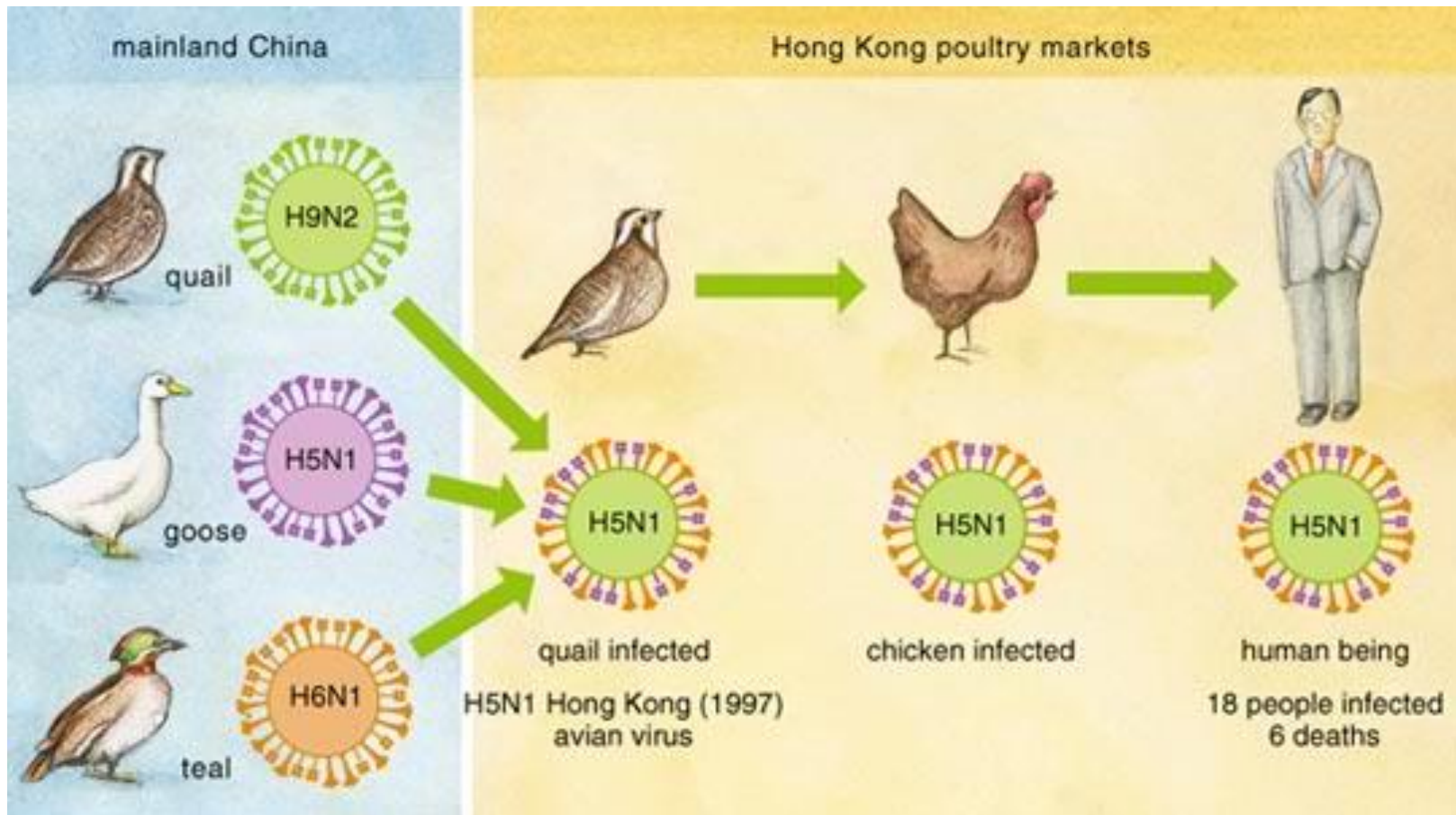


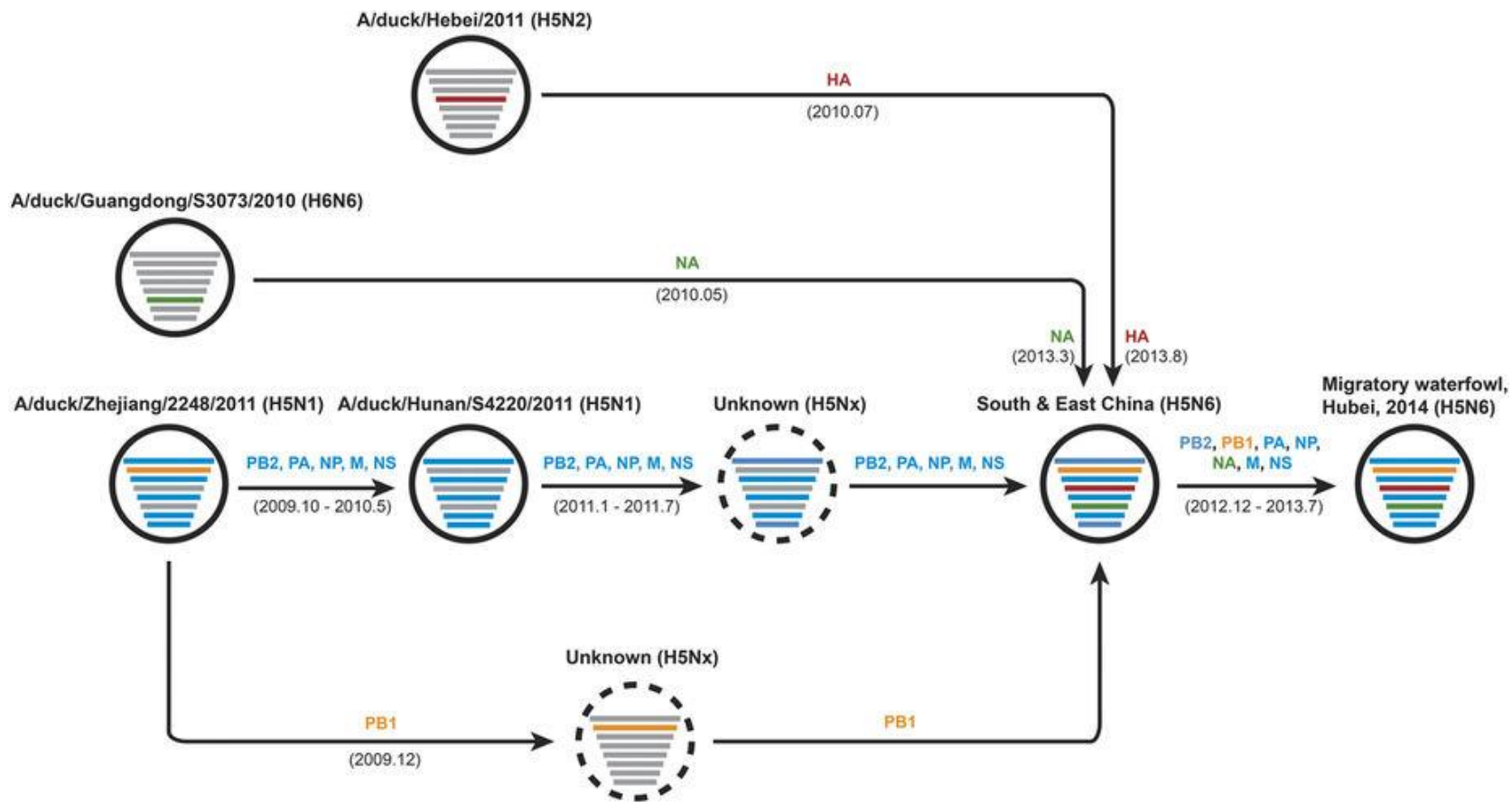
Shuo Su et al. J. Virol. 2015;89:8671-8676

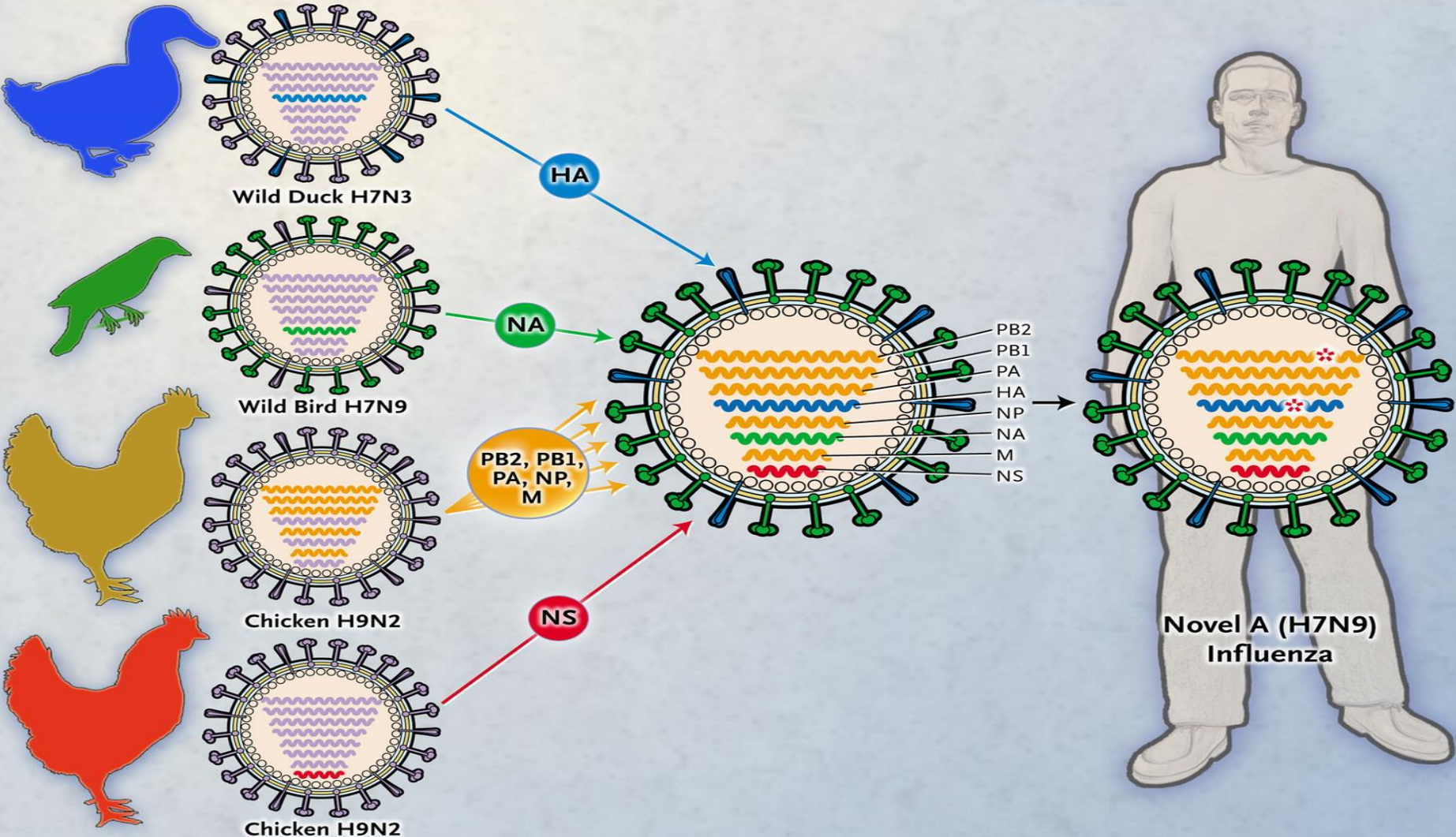
Journal of Virology

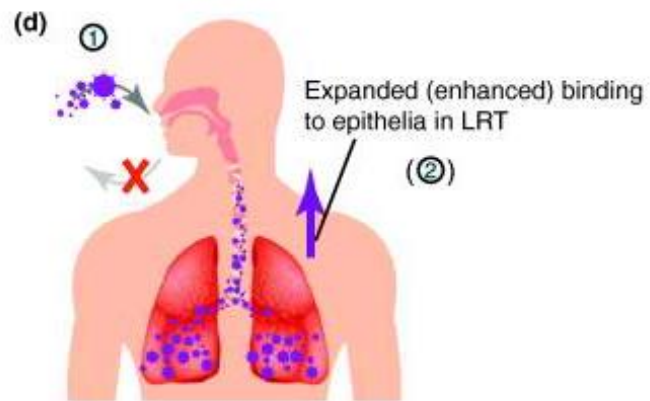
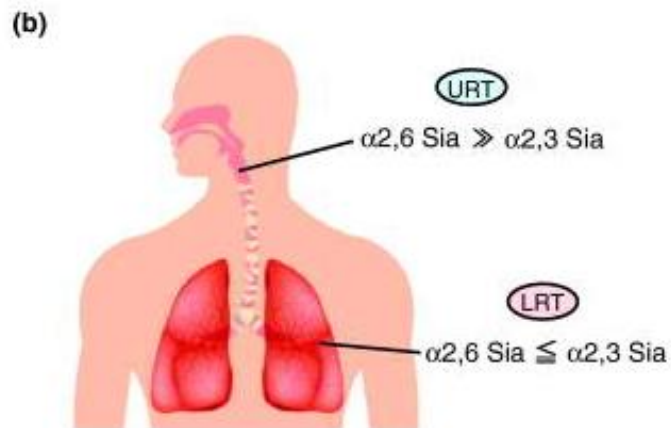
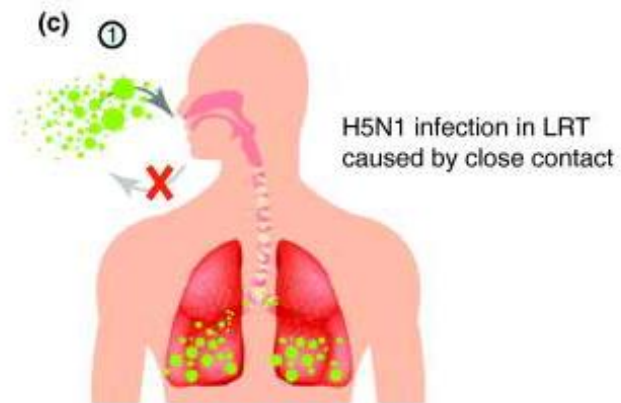
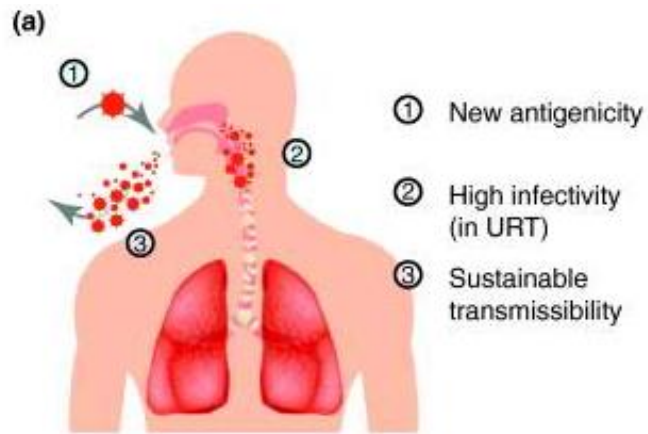
## Transmission to Humans





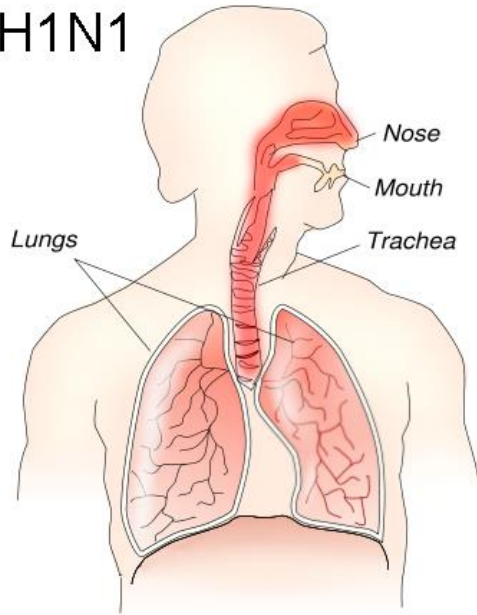








H1N1

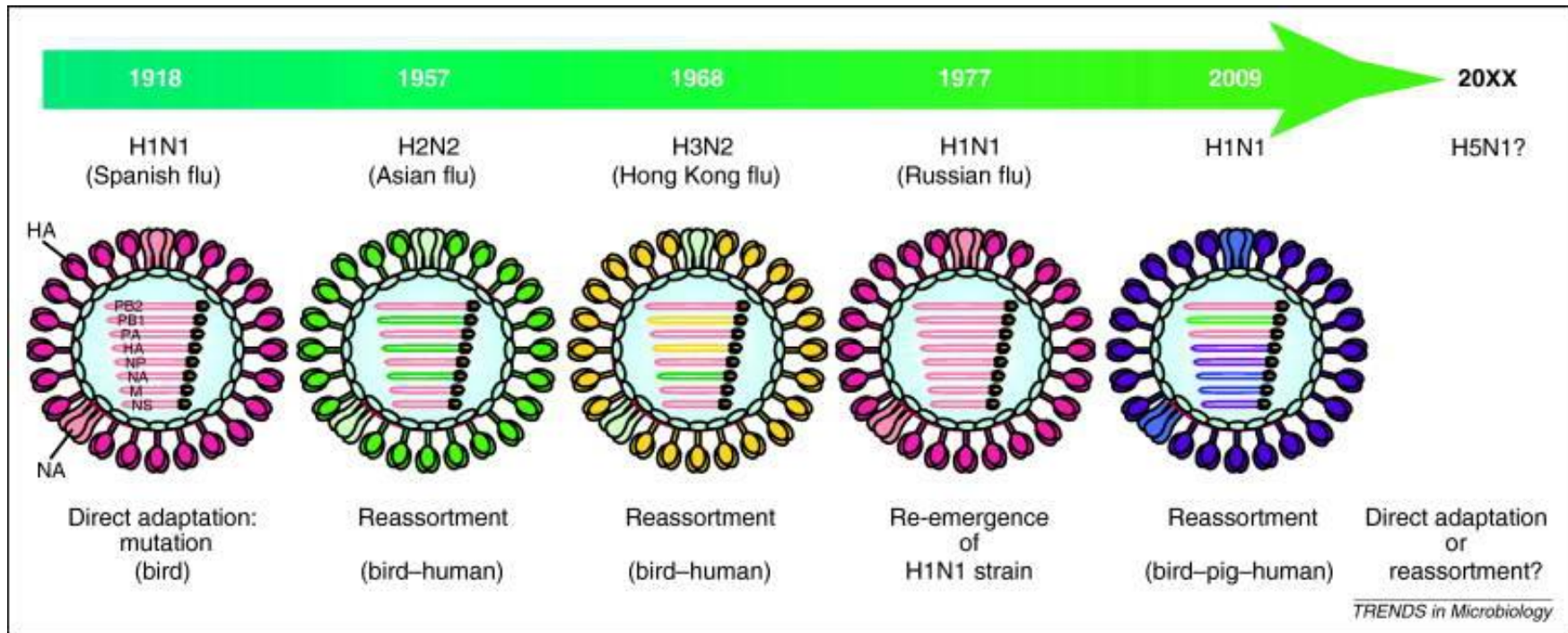


Easily spread  
Rarely fatal

H5N1



Spreads slowly  
Often fatal



# Take home points

- Influenza is genetically diverse and can mutate into new strains by spontaneous mutations or reassortment
- Avian and Human influenza strains have specific propensities for sialic acid residues which affects efficiency of transmission and pathogenicity
- HPAI Avian Influenza in humans skips traditional mixing vessels (pigs) and are highly pathogenic due to propensity for lower respiratory sialic acid residues

**Thank you**