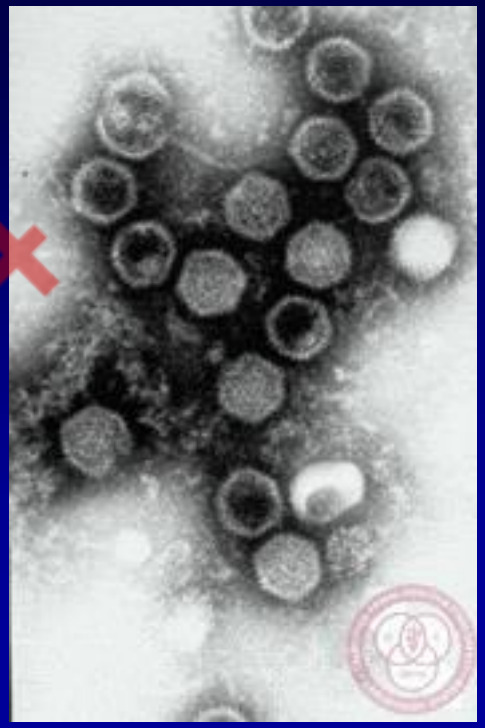
Influenza: navigating from seasonal to pandemic perspective



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Influenza virus: high mutational rate

Drift: small adaptive mutations (cause of seasonal epidemics)

Selective pressure favors the circulation of strains with partial cross-immunity against previously circulating strains

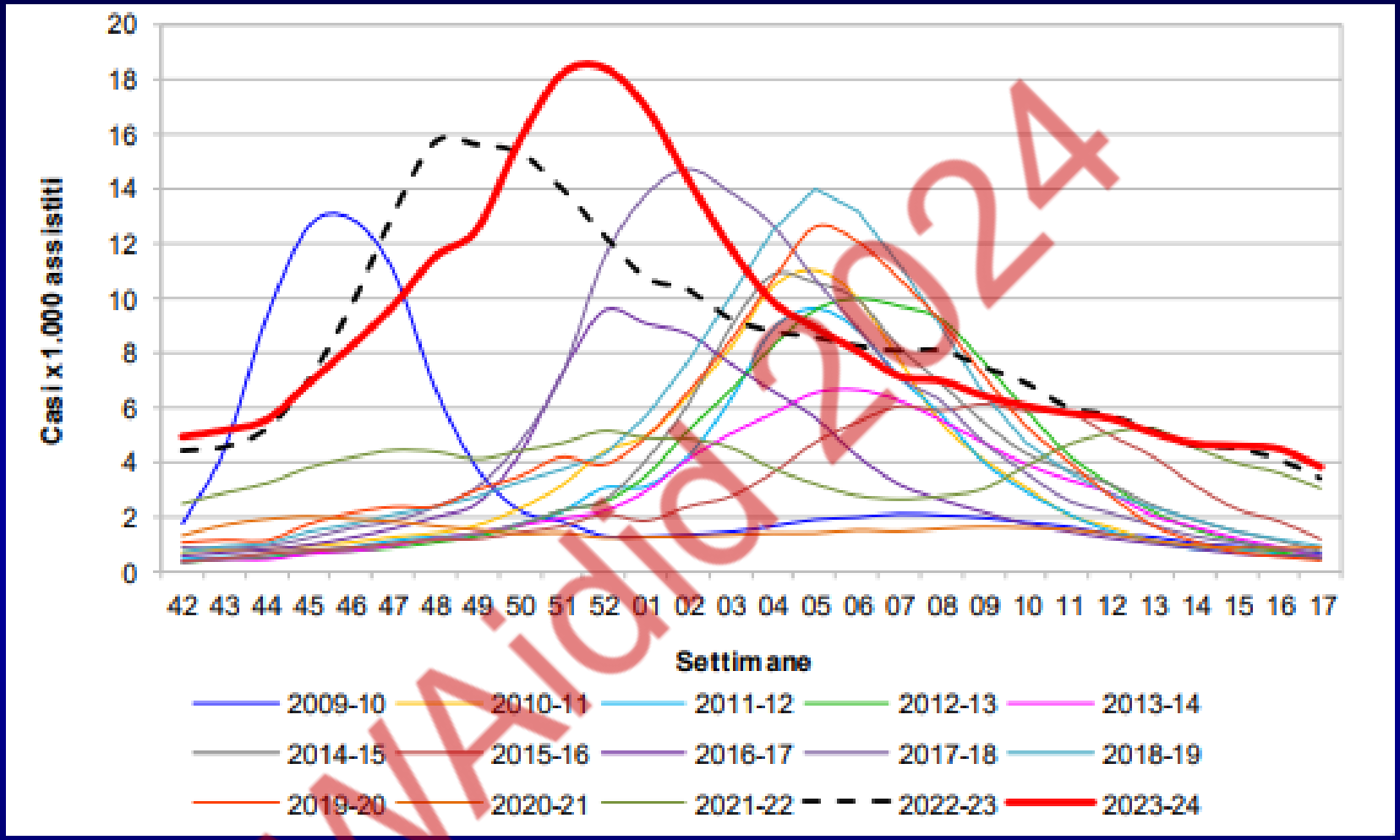
Shift: rearrangement with exchange of gene segments (cause of major – unpredictable – pandemics)

The virus appear as “new”. Human host populations completely susceptible

Determinants of seasonal variations in influenza epidemics

- Cold and dry air: higher virus stability
- Human behaviour: crowdy closed space
- (incidence peaks between Nov and Apr in the North emisphere and between May and Sep in the Southern emisphere)
- Virus migration (*"transequatorial swing"*) or persistence (small clusters during the hot season)?
- Tropics (hot/humid areas): epidemics all around the year with small variations

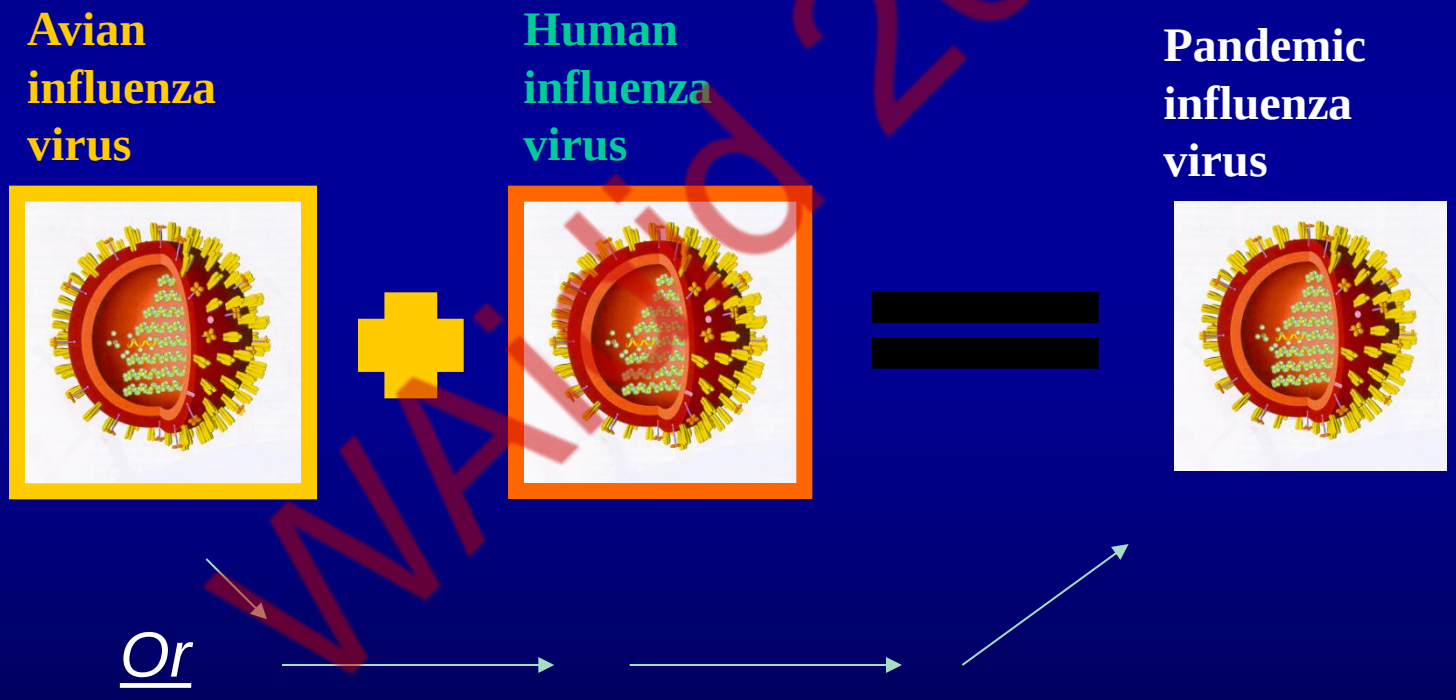
Incidence rate of ILI in Italy: 2009/2010-2023-2024



The effect of social distancing:
Low flu actvity in the pandemic period
Higher activity in the post-COVID-19 era

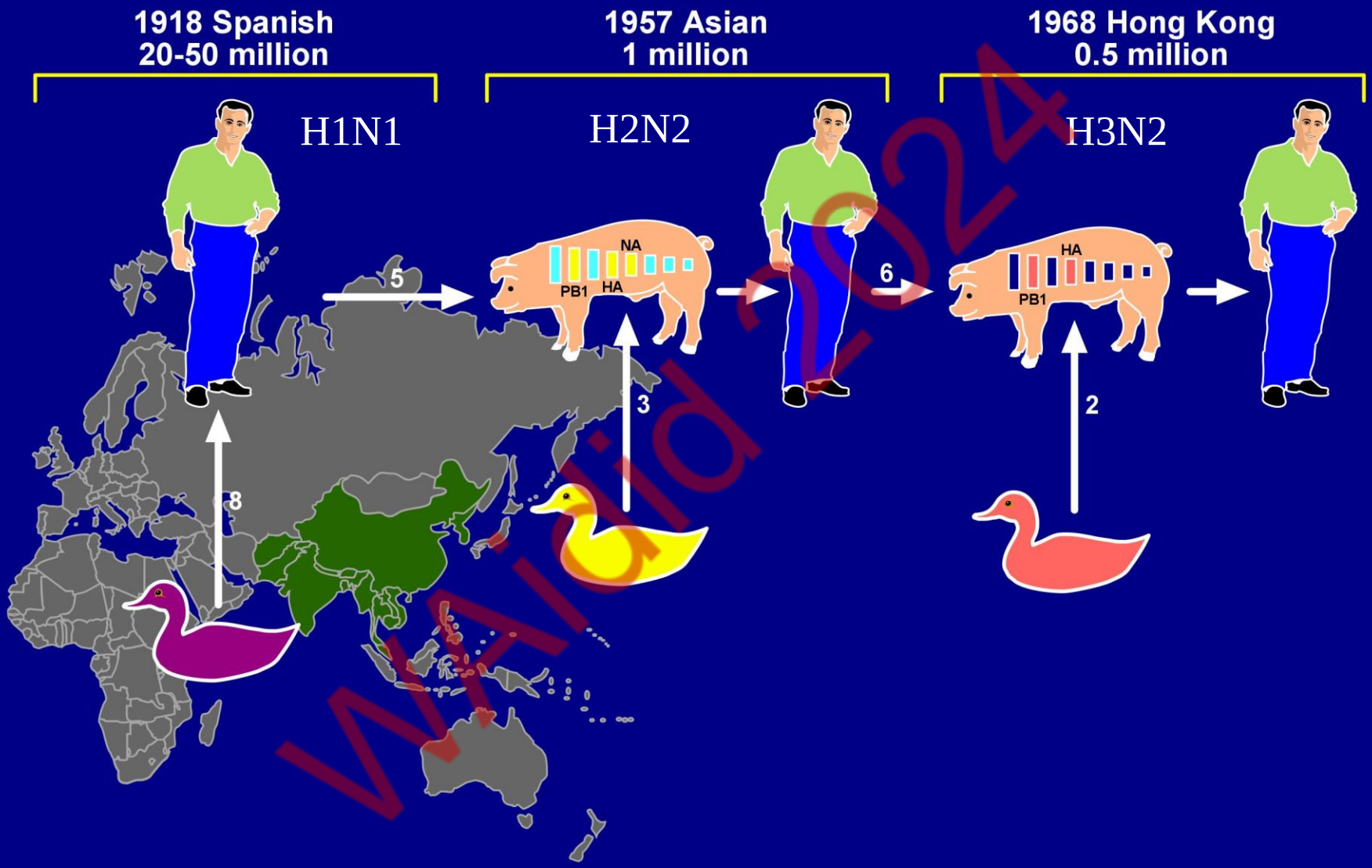
Pandemic potential of influenza A virus

Rearrangiament or direct trans-species passage

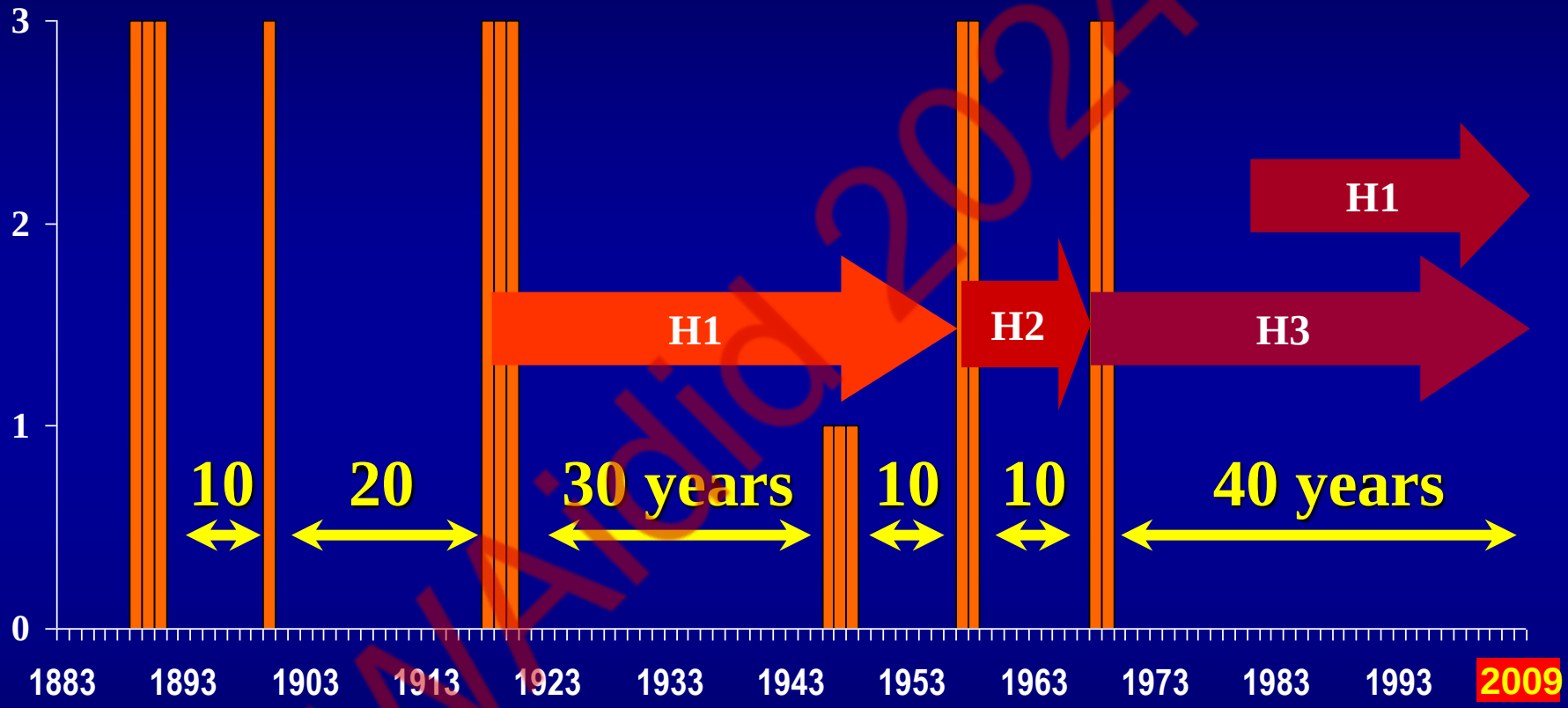


Courtesy of K. Stöhr

20° Century pandemics



Influenza pandemics



There is not a molecular clock for pandemics
They are completely unpredictable

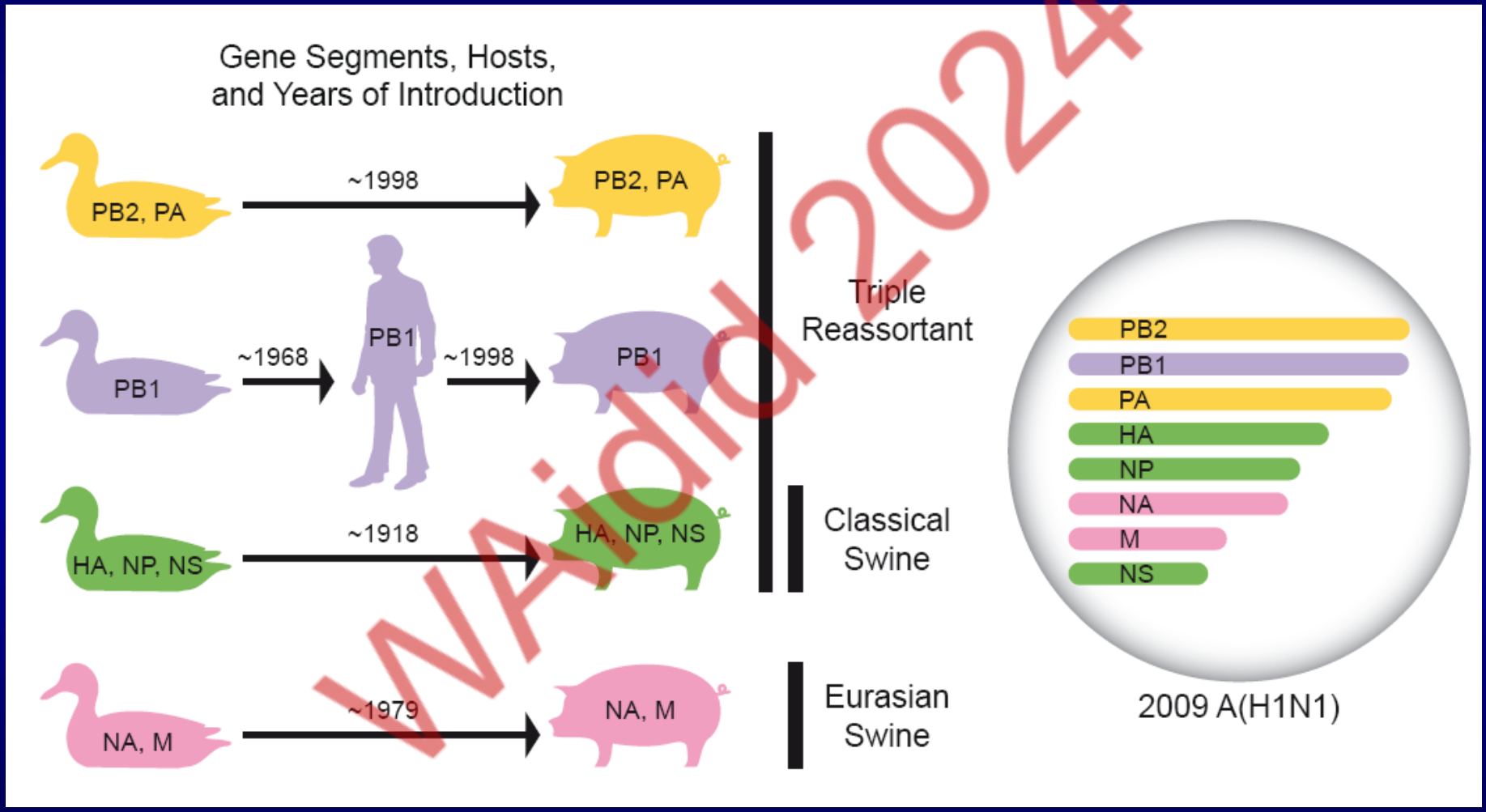
K. Stöhr (OMS)

Pandemics are not predictable
No seasonality

Winter:	**Jan 1830, Feb 1957**
Spring:	**Mar 1847, May 1889, Mar 1918 (*mild wave*)**
Summer:	**Aug 1857, Aug. 1918 (*severe wave*), July 1968**
Autumn:	**Oct/Nov 1732, 'Aug' 1781, Sep/Oct 1800**

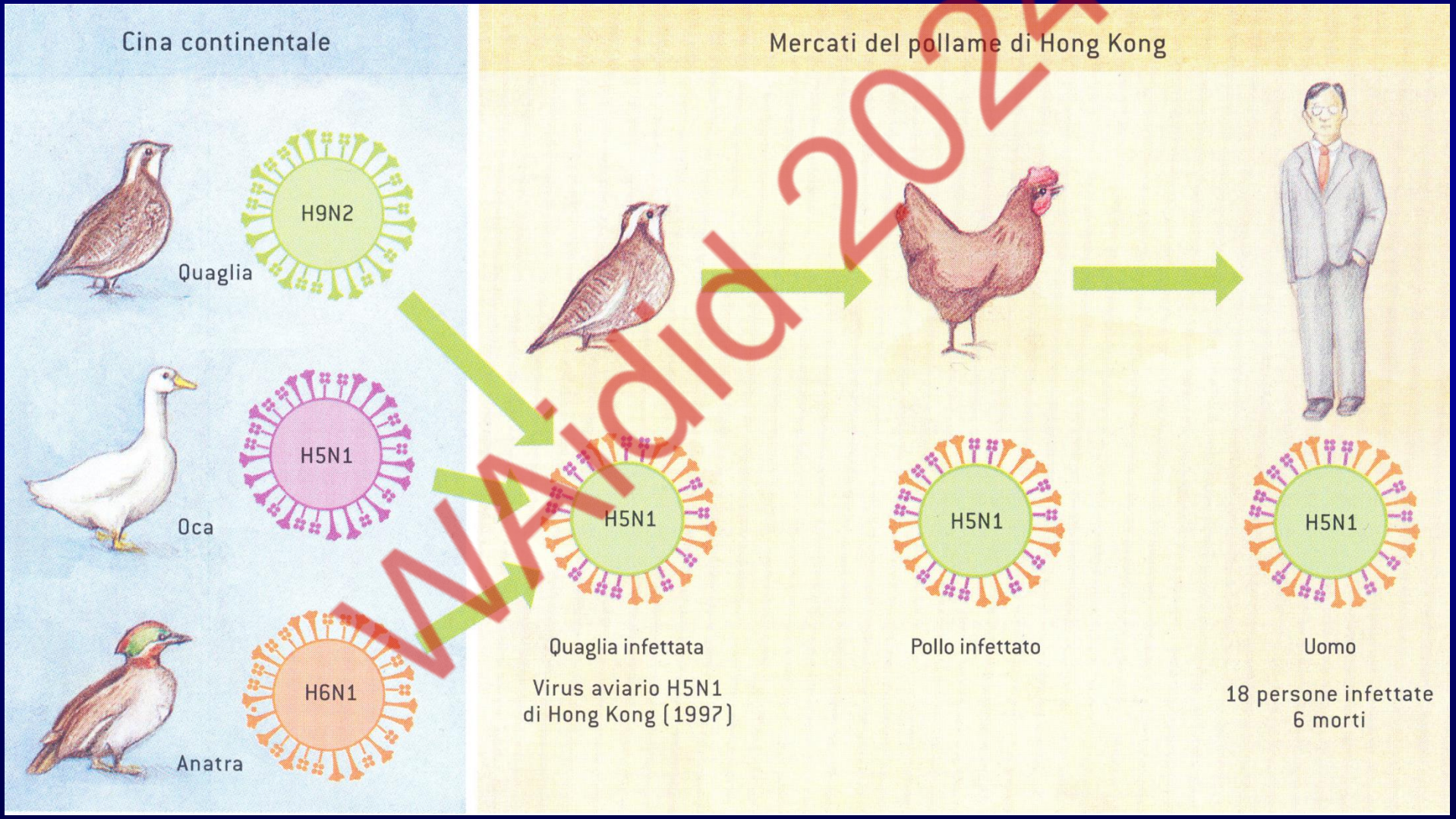
The 2009 «swine» A (H1N1v) flu

No avian virus from th East but a swine virus from the West



Pigs as a mixing vessel (triple reassortant virus)

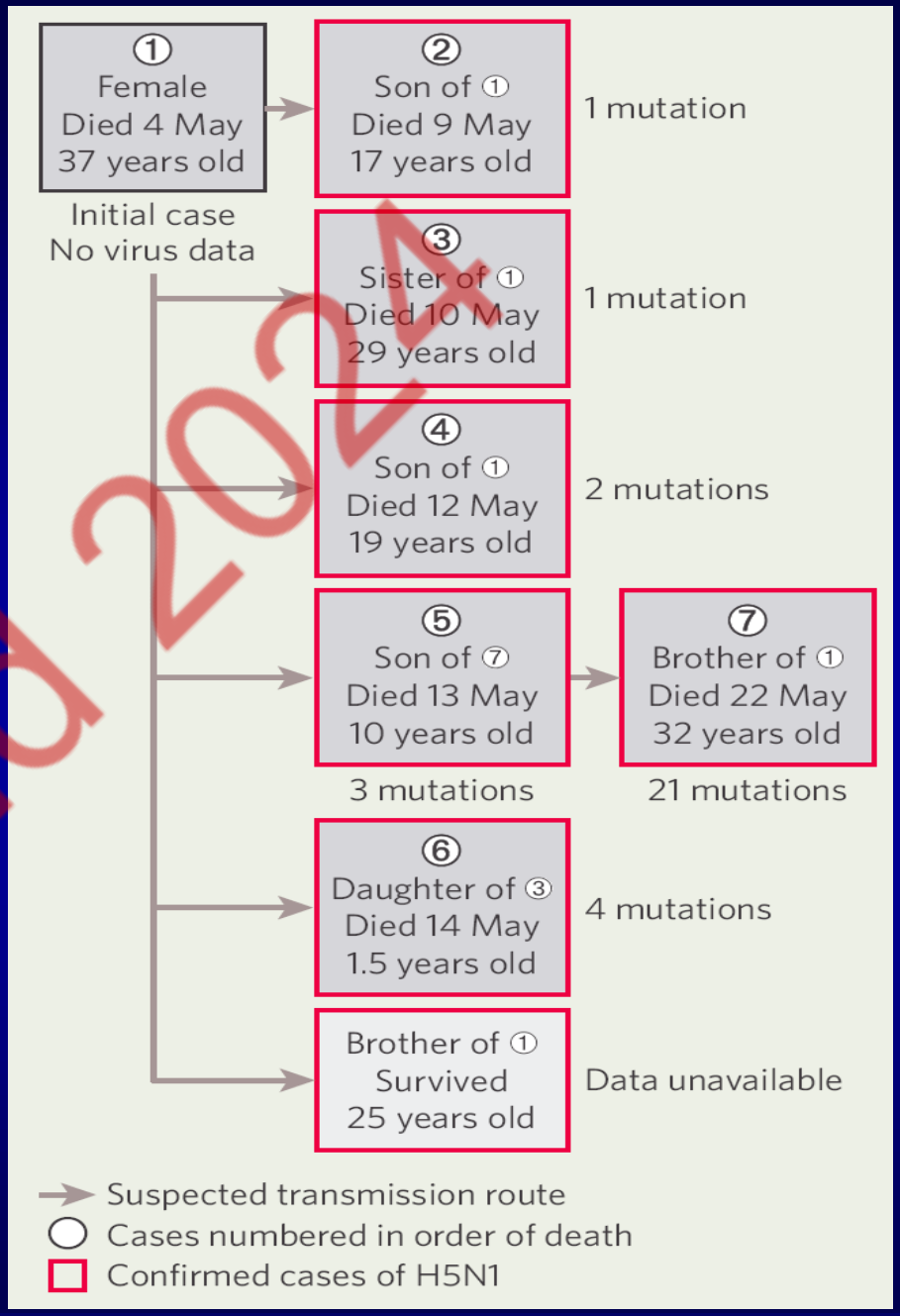
Avian Flu
Hong Kong 1997



H5N1 in birds and mammals

- **High levels of circulation in wild (migratory) birds and outbreaks among poultri since 2003**
- **Marine mammals** (dolphins, elephant seals and sea lions
- >48 **terrestrial mammals** species (i.e., polar bears, foxes, minks, cats, cows, a zoo tiger, and a pig)
- Around 900 **human cases** since 2003
- USA and Canada: outbreaks among cows with human cases (>20) spillover (mostly conjunctivitis but one severe case in a child)

H5N1: low efficiency of inter-human transmission

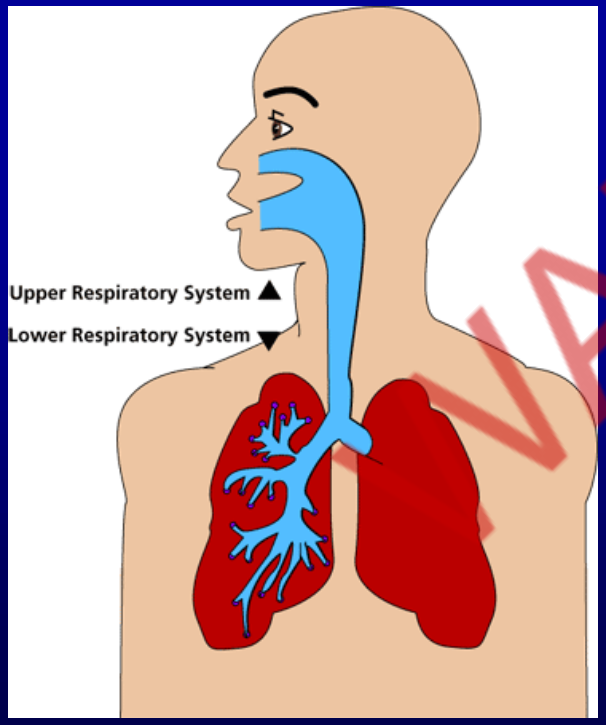


Indonesia: *family cluster* , 2006

Receptors for human and avian viruses and H5N1 affinity

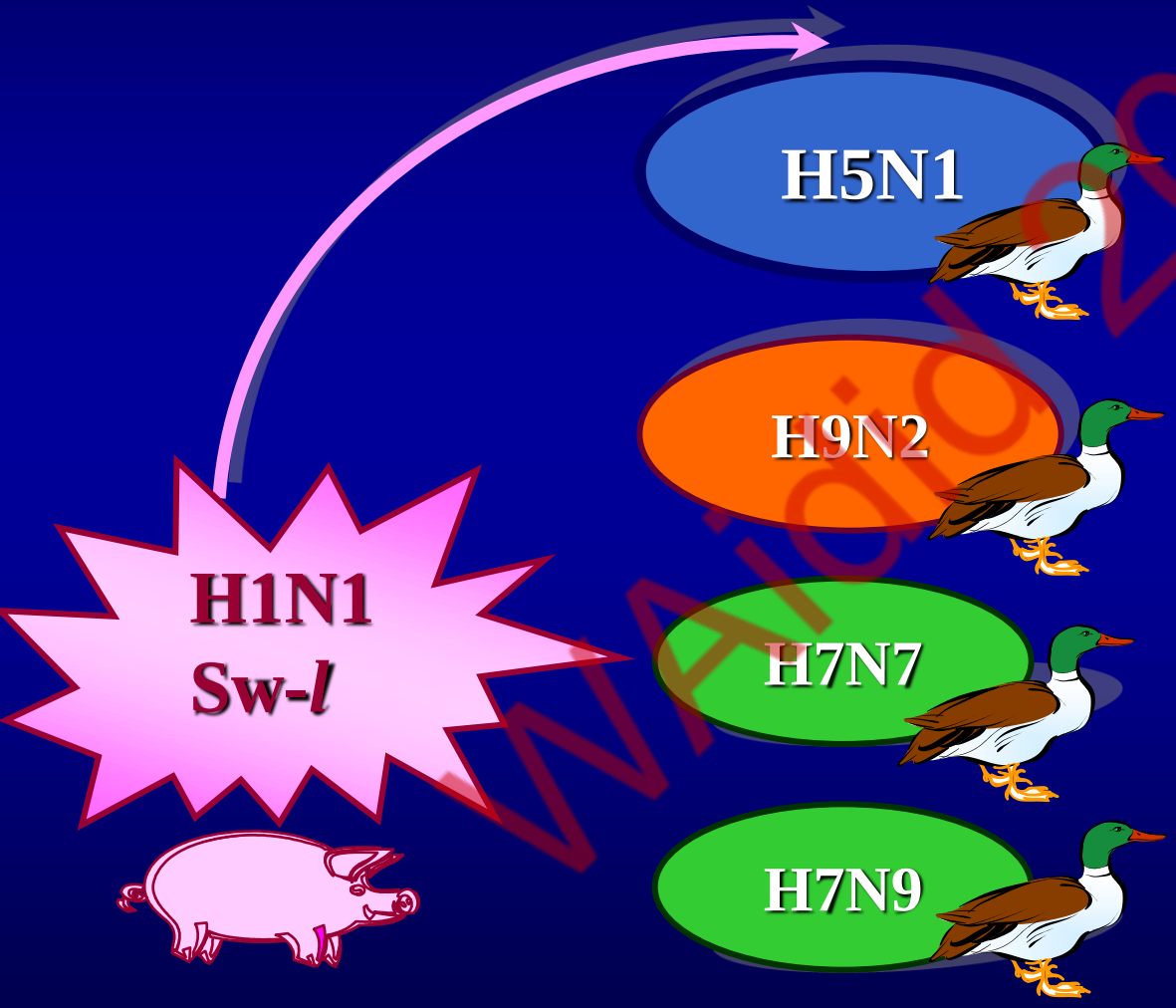
Receptors for avian flu viruses (α2,6) located in conjunctiva and high respiratory tract)

Receptors for human flu viruses (*α2,3-linked sialic acid) located* in the low respiratory tract)



Unsolved issues:
High case-fatality rates reported so far (but not in the US): mild cases undetected?
May mutation leading to change in receptor affinity affect virulence?

The potential pandemic "Hit List"



What we don't know about the next pandemic flu virus

- When it will emerge
- What virus (H5 or other avian virus, swine virus, avian/swine/human rearranged, etc.)
- Where it will emerge
- How aggressive the new flu virus will be

We need to be ready: support R&D on pre-pandemic vaccines to make them available at the global level within 100 days