Prospective Influenza Vaccines

John Wood and Representatives of the World Health Organization Collaborating Centers on Influenza

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Prospective Infuenza Vaccines

- A vaccine of the same subtype as the newly emerged pandemic strain
- Will probably not match the pandemic strain antigenically
- Would probably not provide protection from infection
- Would hopefully modify the severity of infection
- Protection from death!

Influenza A Subtypes in Aquatic Birds

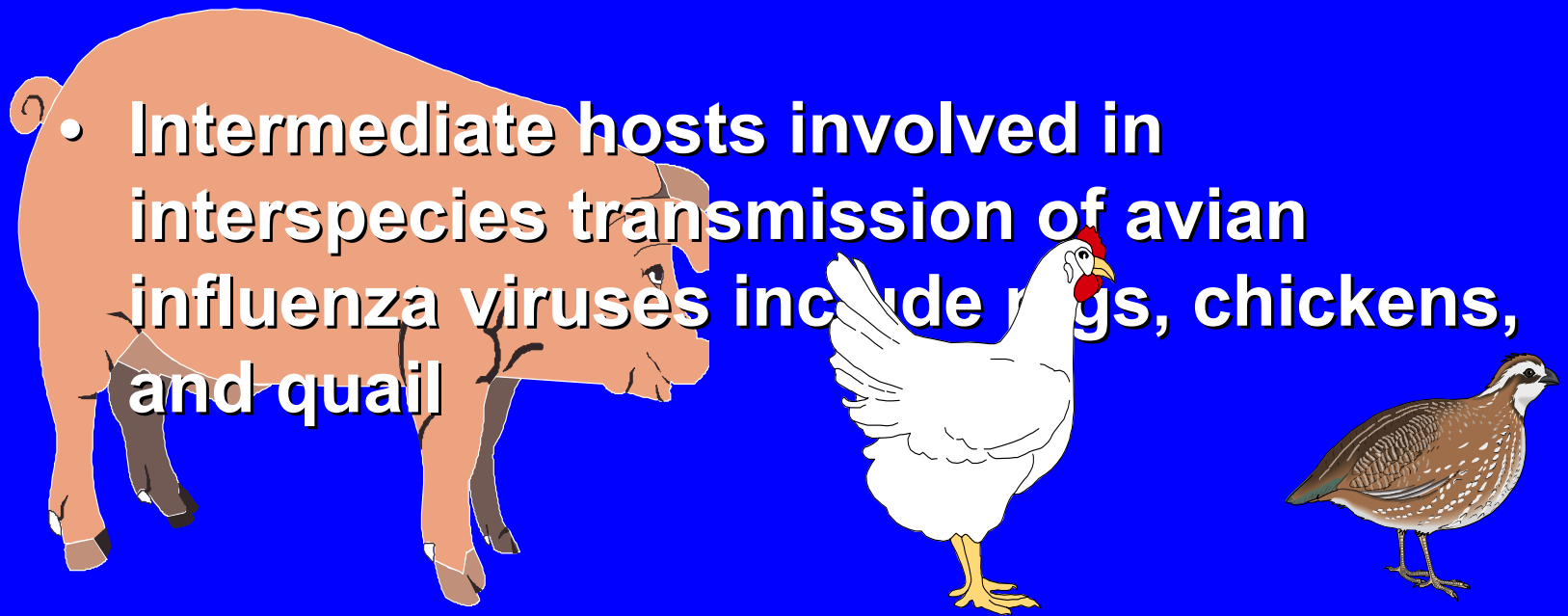
- 15 hemaggalutinin
- 9 neuraminidase
- How to prioritize?

The Ecology of influenza viruses

Dogma 7-8

- Most interspecies transmissions are transitory and do not result in stable lineages

- Intermediate hosts involved in interspecies transmission of avian influenza viruses include pigs, chickens, and quail



Highest Priority
H1, H2, H3

- Infection of humans and pandemic spread

High Priority
H5, H6, H7, H9

- Infection of humans but failure to demonstrate significant human to human spread (e.g. H5, H7, H9)

- Infection of domestic poultry and establishment of lineages in poultry (e.g. H6)

Lower Priority
H4, H10, H13

- Transitory infection of mammals and domestic poultry including pigs and chickens

Lowest Priority
H8, H11, H12, H14, H15

- Rarely found in land based domestic avian species (e.g. H8, H11, H12)
- Rarely found even in wild aquatic birds (e.g. H8, H14, H15)

Highest Priority

Subtype H2

Rationale:

- Proven ability to cause pandemics
- Susceptible population <35 years of age
- Continues to circulate in wild aquatic birds

Candidates:

- A/Singapore/1/57/(H2N2) Ferret serum available
- A/Japan/305/57 (H2N2) Ferret serum available

Highest Priority

Subtype H5

Rationale:

- Proven ability to infect humans
- Potential for high pathogenicity in humans and birds
- Still circulating and causing diseases in SE Asia poultry and wild birds

Highest Priority

Subtype H7

Rationale:

- Proven ability to infect humans, horses, monkeys, seals
- Potential for high pathogenicity (in birds and humans)
- Cause outbreaks in poultry

Candidates:

- A/Netherlands/03 (H7N7)
- A/Ck/Italy/apathogenic (H7N1) (Ferret Serum available)
- Recent viruses from H7 outbreaks in Virginia/USA
- A/TK/Oregon/1/71 (H7N3)

Highest Priority

Subtype H9

Rationale:

- Proven ability to infect humans
- Possess α2, 3 and α2, 6 receptor specificity
- Genetically related to H5N1 virus (G1 lineage)
- Widespread circulation in Eurasia

Candidates:

- GI lineage A/HK/1073/97 (H9N2) (Ferret serum available) A/Quail/HK/G1/97 (H9N2) (Ferret serum available)
- G9 lineage A/Ck/HK/G9/97 (H9N2) [HGR with PR8 background exists] (Ferret serum available)
- A/Turkey/Wisconsin/66 (H9N2)

Highest Priority

Subtype H6

Rationale:

- H6N1 virus genetically related to H5N1 and H9N2 viruses
- Widespread circulation in SE Asia birds and recent increasingly widespread circulation in domestic poultry in North America

Candidates:

- A/CK/CA/465/2000 (H6N2)
- A/Teal/HK/97

  A/Turkey/Massachusetts/65 (H9N2)
- A/CK/Hong Kong/S40/99 (H6N1)

Lower Priority

Subtypes H4, H10, H13

Rationale:

- H4 ➔ Isolated from pigs and seals
- H10 ➔ Isolated from mink
- H13 ➔ Isolated from whales

Lowest Priority

Subtypes:

- H8
- H11
- H12
- H14
- H15

Rarely ever isolated even from wild aquatic birds. However, reference reagents are considered important in the repository

Neuraminidase Subtypes

- Highest Priority: N1, N2
- High Priority: N6, N7, N8, N9
- Lower Priority: N3, N4, N5

Selection of Viruses in a Subtype

- Screen viruses in a subtype for antigenic diversity
  - Hyperimmune sera - ferret sera
- Use phylogenetic analysis of HA sequences to detect diversity
- Most subtypes will require two or more vaccines

Influenza Surveillance at the Lower Animal/Human Interface

- Avian ➔ H5N1 humans, poultry (China)
  ➔ H7N7 humans, poultry (Europe)

- Pigs ➔ H1N1, H3N2, H1N1 triple reassortants

Highly Pathogenic Avian Influenza

Recent Events

- H7N7 Holland, Belgium, Germany
- H7N1 Italy
- H7N3 Chile
- H7N4 Australia
- H5N1 Hong Kong
- H5N1 Korea (duck meat)
- H5N1 Japan (duck meat)
- H5N1 Vietnam

Avian Influenza: Other Recent Events

- H7N2 U.S. Poultry Markets
- H9N2 Asia
- H6N1 Asia, U.S. (California)
- H6N2 Asia, U.S. (California)
- H3N2 Asia, U.S.

Highly Pathogenic AI in Holland (1)

Chickens: March 2003 - Holland
H7N7 - highly pathogenic
225 farms infected
30 million chickens killed

Humans: 347 persons with conjunctivitis
82 persons with confirmed H7N7
Spread to 3 contact persons
➔ One human died of H7N7 infection

Pigs: Serological evidence in pigs

Swine Influenza: Recent Events

- H1N1, H3N2, H1N2 and reassortants
- Dominance of viruses with avian internal genes
- Transmission of H3N2 viruses to turkeys
- H1N2 viruses with avian genes in Korea
- H1N2, H3N2 “classical” strains in Hong Kong

Novel features of 2002-2003 H5N1 viruses form SE Asia

- Re-emergence in humans
- Antigenic drift in HA
- Lethality for aquatic birds
- Continuing circulation and evolution

H5N1 Influenza Outbreak – Kowloon Park, Hong Kong


Puna Teal Duck


Wood Duck


Bar-headed Goose


Common Shel duck


Ruddy Duck


Coscoroba Swan


Rosybill Duck


Greater Flamingo

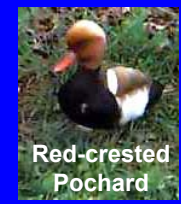

Tufted Duck


Bahama Pintail


White-faced Whistling Duck


Black-necked Swan


Brazilian Duck


Red-crested Pochard


Chiloe Wigeion Duck

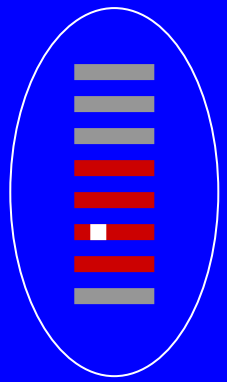

Victoria Crowned Pigeon


Ringed Teal Duck


Hawaiian Goose

H5N1 Genotypes Hong Kong: December 2002

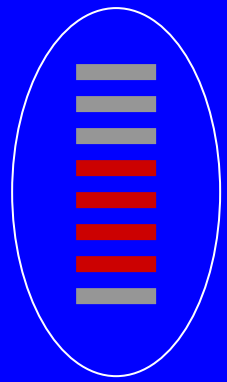
2002Z



Grey Heron

Kowloon Park, Farm, Markets since Dec. 10, 02

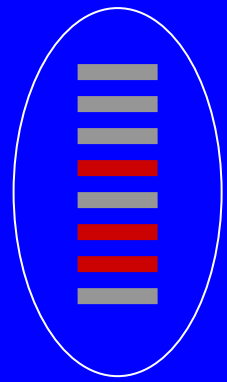
New Genotype 1



739.2
739.3
757.3

Penfold Park Viruses from Migratory Birds

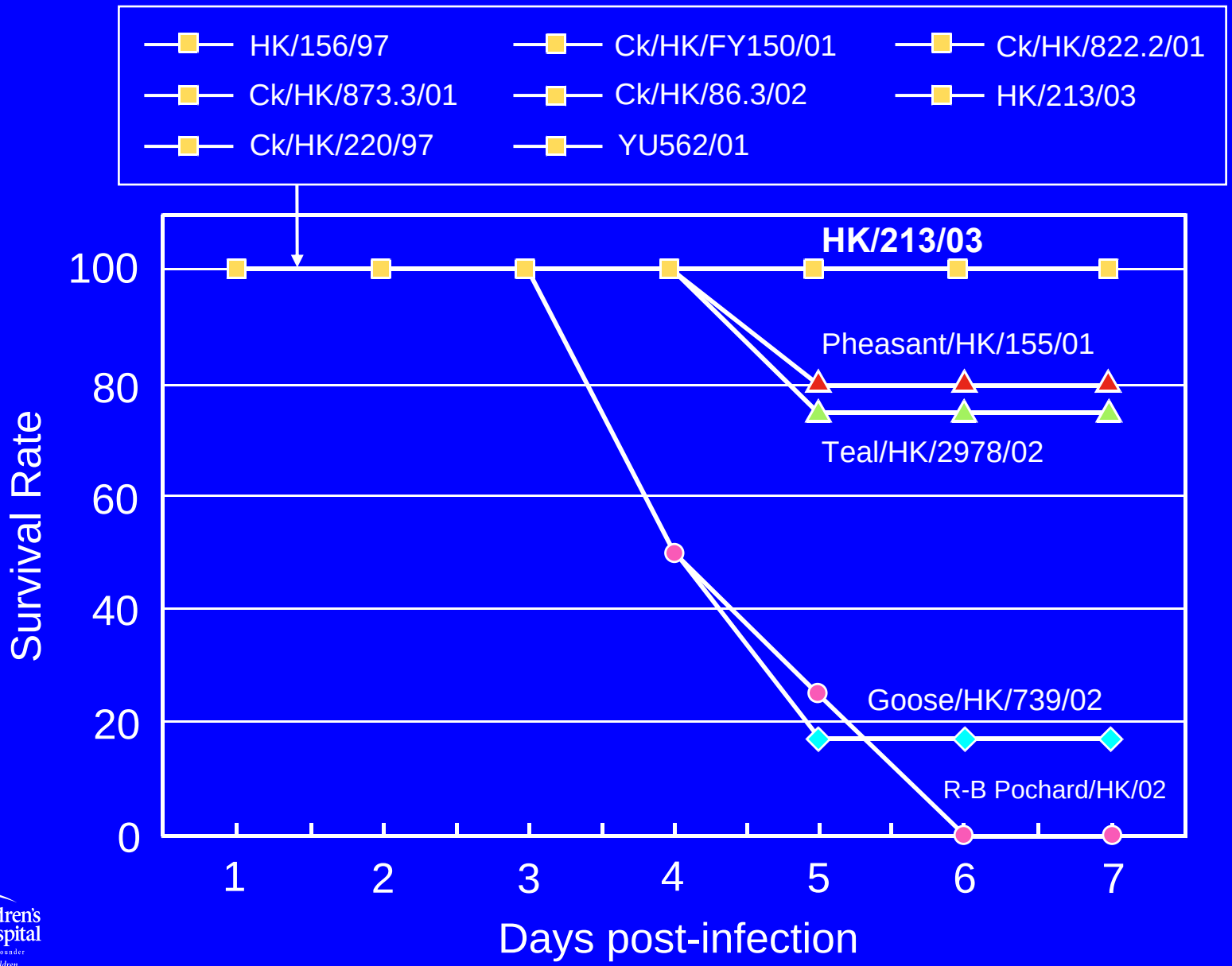
New Genotype 2



SV2978.1
SV2978.3

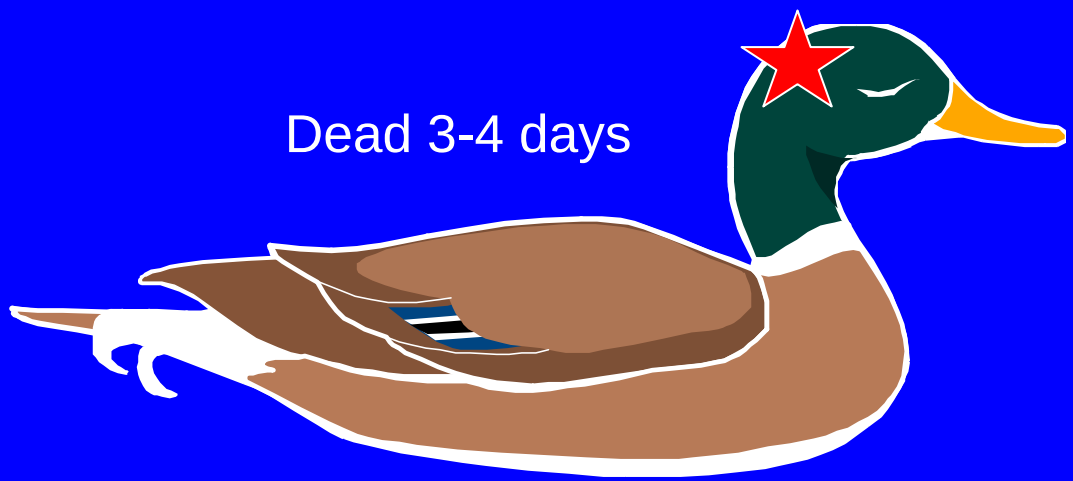
Smuggled Teal Isolates

Evolution of duck-lethal H5N1 Viruses



St. Jude Children's Research Hospital
ALSAC • Danny Thomas, Founder
Finding cures. Saving children.

Lethality of H5N1/02 in Ducks



Dead 3-4 days

Oral Transmission

Severe neurological symptoms.

Survivors spread virus for >10 days.

Influenza A Viruses From Hong Kong Poultry Markets 2003

Number per Month								
Subtype	**Jan**	**Feb**	**Mar**	**Apr**	**May**	**June**	**July**	**Aug**
H5N1	**5**	**1**	**5**	**10**	**7**	**2**	**0**	**0**
H6N1	**0**	**1**	**3**	**0**	**3**	**0**	**0**	**0**
H9N2	**4**	**7**	**1**	**3**	**19**	**8**	**25**	**41**

Prospective Infuenza Vaccines

- Have been talked about for the last 30 years
  - –“The time for talking is over.”

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