Possible Modes of Transmission of Avian Viruses to People: Studies in Experimental Models

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AI Virus Infections: Public Health Consequences

Potential Modes of Transmission:

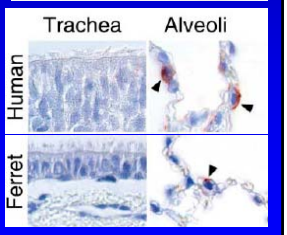
- **Inhalation:**
  - **Contaminated dust from rearing or slaughter**
  - **Fine water droplets generated during household/LPM slaughter process**
- **Contact with oral/nasal mucus membrane or conjunctiva:**
  - **Hand-transplantation of virus from contaminated surface, or dust/feathers to eye**
  - **Swimming/bathing in household pond**
- **Consumption of raw or undercooked infected poultry products?**
  - **H5N1 HPAI has not been a Food Safety issue**
- **Human to human transmission**
  - **Close, unprotected contact w/severely ill person**
  - **Respiratory secretions, body fluids & feces potentially infectious**

Mammalian Models for the Study Influenza Virus Virulence and Transmission

- Mouse
  - Susceptible to avian H5N1, but not human viruses
  - Suitable for virulence but not transmission studies
- Non-human primate
  - Susceptible to human and avian viruses
  - Suitable for virus-host response studies
- Guinea Pig
  - Susceptible to human and avian strains
  - Good model for transmission
  - Not optimal for virulence studies
- Ferret
  - Susceptible to human and avian influenza viruses
  - Best model to reflect virulence and transmissibility of influenza viruses as seen in humans
- Pig
  - Susceptible to swine, avian and human influenza viruses
  - Similar respiratory infections and lesions; no systemic disease

The Ferret Model as a Public Health Risk Assessment Tool

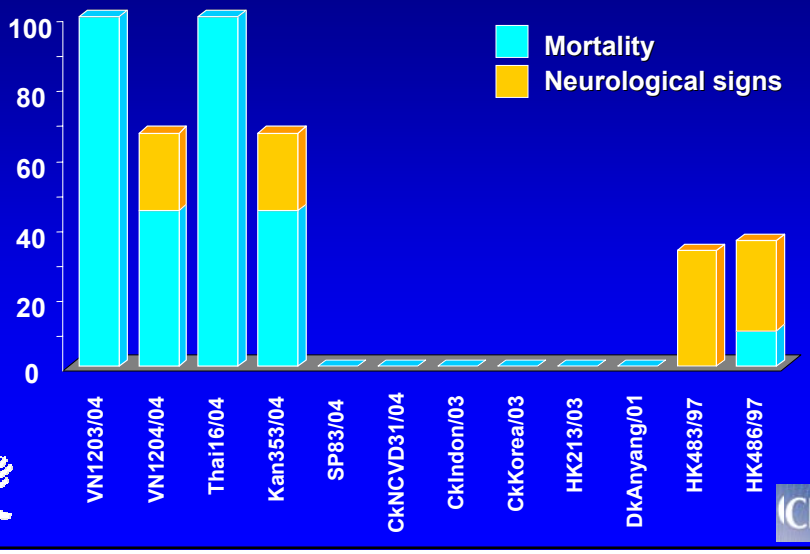
- Naturally susceptible to human and avian influenza viruses
  - Symptoms/course of infection similar to humans – virus strain dependent (asymptomatic, mild-severe respiratory, systemic disease)
  - Distribution of sialic acid receptors in the RT is generally similar to humans
- Study biologic and molecular properties that confer transmissibility
  - Large or small airborne respiratory droplets
  - Direct contact
- Assess risk of avian-human reassortment *in vivo*
  - Reassortment between H5N1 and H3N2



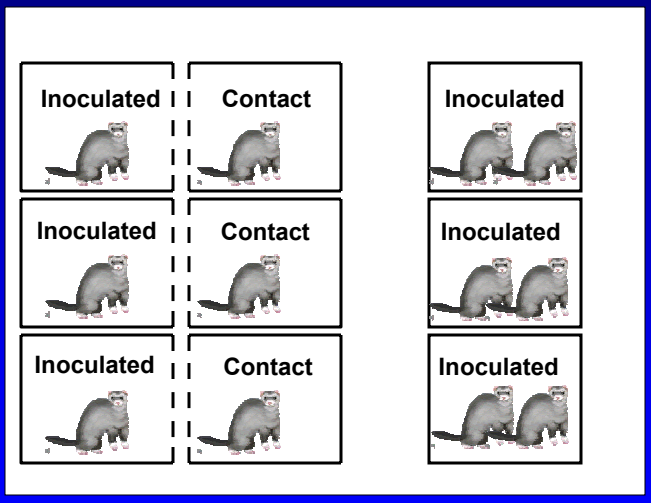
(van Riel et al., 2006)

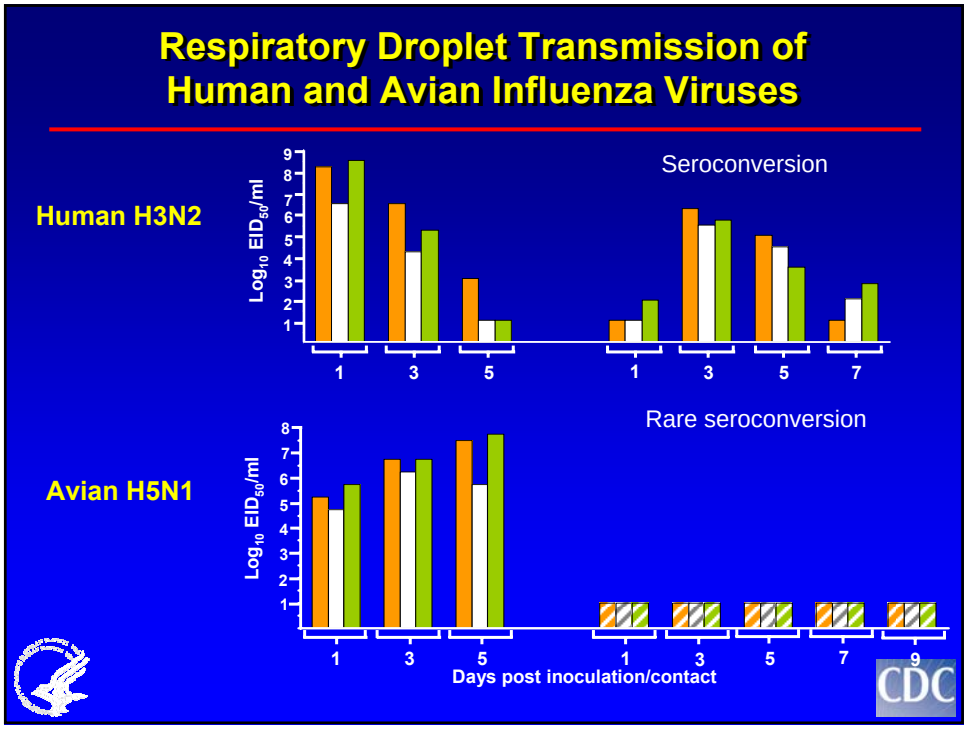
CDC

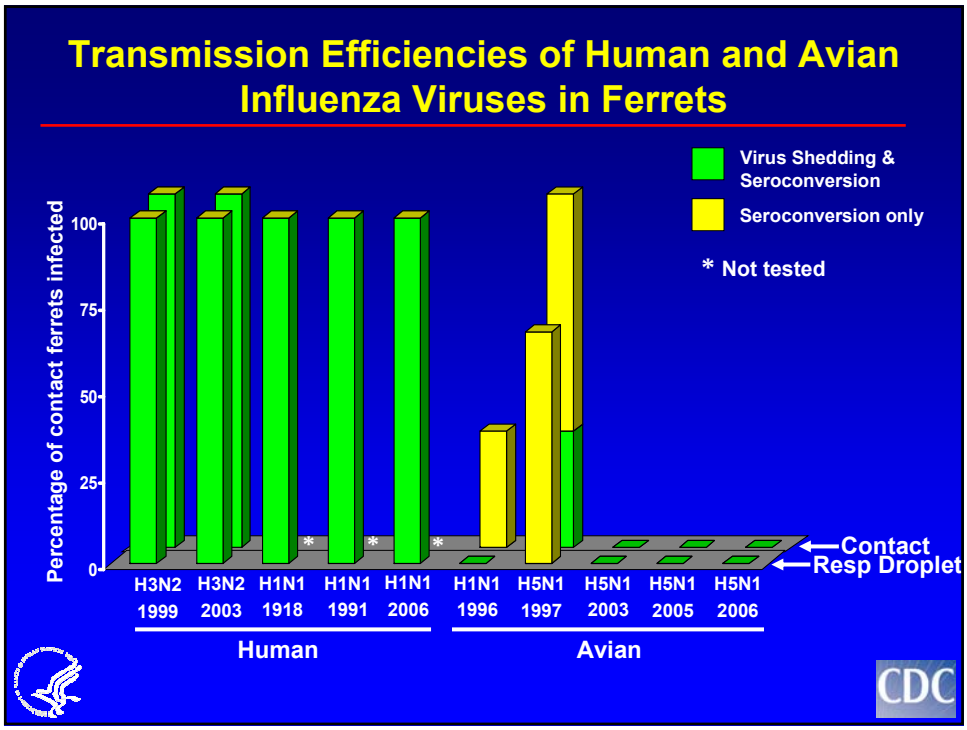
Risk Assessment: Understanding Virulence in Ferrets of HP H5N1 Viruses Isolated in Asia, 1997-2004



Influenza Virus Transmission in Ferrets

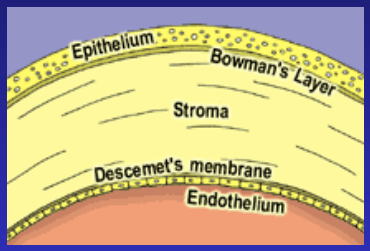



Respiratory Droplet Transmission of Human and Avian Influenza Viruses
Human H3N2
Seroconversion
Log10 EID50/ml
Avian H5N1
Rare seroconversion
Days post inoculation/contact
CDC


Transmission Efficiencies of Human and Avian Influenza Viruses in Ferrets
Virus Shedding & Seroconversion
Seroconversion only
* Not tested
Percentage of contact ferrets infected
Contact
Resp Droplet
H3N2 1999
H3N2 2003
H1N1 1918
H1N1 1991
H1N1 2006
H1N1 1996
H5N1 1997
H5N1 2003
H5N1 2005
H5N1 2006
Human
Avian
CDC

Ocular infection of mice with influenza A (H7) viruses: A site of primary replication and spread to the respiratory tract

Majority of human infections associated with H7 viruses have resulted in ocular and not respiratory disease



Human Tissue	SA Distribution in Tissues	Infection With Human Viruses	Infection With Avian Viruses
Lung	α2,6 and α2,3	H1, H2, H3	H5, H7, H9
Eye	mostly α2,3	rare but documented	H7, sporadic H5

(Jessica A. Belser, Jacqueline M. Katz, Terrence M. Tumpey, unpublished data)

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Corneal Scarification

Challenge 10^6 EID_{50}

Harvest Tissues → Lung, Nose, Eye → Viral Titers (EID_{50}/mL)

Day 0 — Day 3 — Day 6 — Day 14

Observe Daily → Morbidity/Mortality

- Generally, H7 seem to replicate more frequently and to higher titer in the eye; while H5, more frequently in the respiratory tract
- Pronounced morbidity and mortality w/ NL/219 (H7N7), HK/483 (H5N1), & Thai/16 (H5N1)

(Jessica A. Belser, Jacqueline M. Katz, Terrence M. Tumpey, unpublished data)

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Conclusions

- Various mammalian models have been used to study HPAIV pathogenicity and pathogenesis – model selection will vary with type of study
- Most studies have focused on determining infectivity, virulence, immunity and transmissibility; Ferrets are the best overall model
- Based on ferret model, contact and droplet transmission are inefficient for H5N1 HPAI viruses and other AIVs
- H7 and H5 viruses are both capable of replicating in ocular tissue, but *in vivo* H7 viruses display an ocular tropism while H5 viruses preferentially replicate in respiratory tissues
- H5N1 virus has been transmitted to ferret model when exposed to processing of asymptomatic infected chickens

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7th International Symposium on Avian Influenza

• Continuing Education Center, University of Georgia, Athens, Georgia
• April 5-8, 2009
• Sponsors: USAHA, USDA/APHIS, USDA/ARS, USDA/CSREES, AAAP
• Questions: ai.symposium@ars.usda.gov
• Registration: http://www.georgiacenter.uga.edu/conferences/