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)
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

Avian H5N1

Transmission Efficiencies of Human and Avian Influenza Viruses in Ferrets

- Virus Shedding & Seroconversion
- Seroconversion only

* Not tested
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

<table>
<thead>
<tr>
<th>Human Tissue</th>
<th>SA Distribution in Tissues</th>
<th>Infection With Human Viruses</th>
<th>Infection With Avian Viruses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>α2,6 and α2,3</td>
<td>H1, H2, H3</td>
<td>H5, H7, H9</td>
</tr>
<tr>
<td>Eye</td>
<td>mostly α2,3</td>
<td>rare but documented</td>
<td>H7, sporadic H5</td>
</tr>
</tbody>
</table>

(Jessica A. Belser, Jacqueline M. Katz, Terrence M. Tumpey, unpublished data)

Corneal Scarification

- 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)
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 chicken

7th International Symposium on Avian Influenza

• Continuing Education Center, University of Georgia, Athens, Georgia
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