Research Issues in Animal Surveillance and Pandemic Planning

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SURVEILLANCE
Spread of H5N1 Influenza in Asia 2004

100s of millions of birds culled

Human Cases: 70
Human Deaths: 47

Vietnam: 33 deaths
Thailand: 12 deaths
Cambodia: 2 deaths
The Difficulty of Obtaining Avian H5N1 Viruses

- Trade embargos
- National pride
- Intellectual property
- Different missions for FAO, OIE and WHO
- Absence of infrastructure
The Hong Kong Model

No H5N1 influenza in poultry or humans in 2004, 2005
The 1997 H5N1 Outbreak in Hong Kong

FIRST BUILD THE INFRASTRUCTURE

Nov. 1997 1 small lab, 1 ancient hood

Dec. 1997

- The brightest and best trained young virologists flown in
- Laminar flow cabinets flown in
- Temporary isolation lab established
- Staff stay on the ground

No human infections: virus availability

- Collaboration Agriculture, Health Department, University, WHO
Current Advice to Countries with Poor Infrastructure

• After SARS and laboratory infection of humans
  – Do not attempt to isolate viruses
  – Use molecular analysis – RT PCR
  – Send samples to expert laboratories
Changes in Poultry Marketing in Hong Kong

- Two clean days per month
- Inactivated H5N1 vaccine
  - *Sentinal birds*
- No H5N1 2004, 2005
Why is the Hong Kong H5N1 Control Strategy Not Copied?

- Too expensive!
- Reluctance to accept agricultural vaccines
- Lack of promotion by international agencies
- Lack of political will
Agriculture Vaccines

- Not standardized for antigen content
- Required to induce HI antibody in poultry
- There are good and bad agricultural vaccines
## Vaccines for use in Poultry (Traditional)

<table>
<thead>
<tr>
<th>Country</th>
<th>Type</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hong Kong</td>
<td>Commercial</td>
<td>A/CK/Mexico/232/94/ (H5N2)*</td>
</tr>
<tr>
<td>China</td>
<td>Commercial</td>
<td>A/DK/England/N-28/73 (H5N2)</td>
</tr>
<tr>
<td>Indonesia</td>
<td></td>
<td>A/CK/Indonesia/03 (H5N1) [H.P]</td>
</tr>
</tbody>
</table>

*Homology of HA $\approx 94\%$ with current H5/04
Recent Developments in Poultry Vaccines

<table>
<thead>
<tr>
<th>Virus</th>
<th>Host</th>
<th>Backbone</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fowlpox – H5</td>
<td>China, US</td>
<td></td>
<td></td>
</tr>
<tr>
<td>r.g. -- H5N1</td>
<td></td>
<td>H9N2</td>
<td>China</td>
</tr>
<tr>
<td>r.g. -- H5N3</td>
<td></td>
<td>PR8</td>
<td>US</td>
</tr>
<tr>
<td></td>
<td></td>
<td>backbone</td>
<td></td>
</tr>
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<td></td>
<td></td>
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</tbody>
</table>

Poultry Vaccines (The Good Ones)

- Provide protection despite antigenic drift
- Mechanism unresolved
- Do not provide sterilizing immunity
- Can reduce virus load below level of transmission
Poultry Vaccines
(The Bad Ones)

• Protect against disease signs
• Birds shed transmissible levels of virus
• Promotes spread of virus in live markets and antigenic drift
Missing Information

The role of domestic ducks
Ducks Vietnam

- 60 million – many free range
  - Reduce to 40 million (commercial hatching ban)
- Peak numbers in May, October
  - Rice Harvest
Continuing Evolution of H5N1 in Ducks in Asia

- Nov. 2002: H5N1 kills waterfowl in Hong Kong
- 2003: Majority of H5N1 isolates are highly pathogenic in ducks
- 2004: Many duck H5N1 isolates are non-pathogenic in ducks
Vaccine – Reverse Genetics

A/PuertoRico/8/34 (H1N1)

Hoffmann 8 Plasmid System

A/CK/Vietnam/C59/04 (H5N1)

removal of connecting peptide

A/DK/Germany/1215/73 (H2N3)

PB2

PB1

PA

NP

NS

M

Vero cell

HA

NA
# Lethality of H5N1/04 Viruses for Ferrets

<table>
<thead>
<tr>
<th>Isolated from</th>
<th>No. Tested</th>
<th>Severe</th>
<th>Mild</th>
</tr>
</thead>
<tbody>
<tr>
<td>Humans</td>
<td>4</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Duck</td>
<td>3</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Chicken</td>
<td>4</td>
<td>0</td>
<td>4</td>
</tr>
</tbody>
</table>
Trends in Duck Populations (FAOSTAT 2001)

- **China:**
  - 1961: 700,000
  - 1998: 500,000

- **Thailand:**
  - 1961: 25,000
  - 1998: 15,000

- **Viet Nam:**
  - 1961: 60,000
  - 1998: 10,000

- **Indonesia:**
  - 1961: 35,000
  - 1998: 5,000

Countries: China, Thailand, Viet Nam, Indonesia
Duck Population -- Asia

~ 2 BILLION domestic ducks
10 to 100 times more domestic than wild ducks
An outbreak of deadly bird flu in North Korea could wipe out its fledgling chicken breeding industry and deprive the impoverished country of its main source of animal protein, animal experts said yesterday.
Summary

\textbf{The immediate issue}

- Reduce the likelihood of human to human transmission by reducing virus load in poultry
  - Stamping out
  - Vaccination
- Quality vaccines for poultry needed
Summary

Unresolved issues

• Transmissibility
• Pathogenicity
• The Asian Host
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