OPTIONS IX for THE CONTROL OF INFLUENZA
24-28 AUGUST 2016
Yuelong Shu, PhD
Professor
National Institute for Viral Diseases Control and Prevention, China CDC Beijing, P. R.China

I have no financial relationships with commercial interests to disclose.
The talk represents only the opinions of the presenter and does not necessarily represent the views of the National Institute for Viral Disease Control and Prevention, Chinese Centre for Disease Control and Prevention (China CDC).
The Market as an Influenza Risk Factor: The Animal Human Interface

Yuelong Shu
WHO Collaborating Center for Reference and Research on Influenza
Chinese National Influenza Center
National Institute for Viral Diseases Control and Prevention, China CDC
Beijing, P.R.China
25 August 2016
Live poultry market in China

Guan Y, et al, J Infect Dev Ctries 2013
Live poultry market in China

Guan Y, et al, J Infect Dev Ctries 2013
Live poultry market in Cambodia

Horm SV et al, Emerging Microbes & Infections, 2016
Live poultry markets

- Source of human infections
- Source of generation of novel avian influenza viruses
Live poultry markets & human infections with AIVs

- Exposure history investigation
- Molecular epidemiology evidences
- Serological evidences
- Effects of LPMs closure
Human infections with avian influenza viruses

**HPAI (H5)**
- 1997: 6/6GD, 2/HK, H9N2
- 1998-1999: 1/HK H9N2
- 2003-2004: 2/Egypt H10N7
- 2008-2009: 1/HK H9N2
- 2010: 7/Australia H10N7
- 2013: 1/Taiwan H6N1
- 2014: 2/HK H9N2
- 2015: 1/Hunan H9N2

**LPAI (H6, H9, H10)**

**HPAI (H7)**
- 1959: 1/USA H7N7
- 1977: 1/USA H7N7
- 1979-1980: 1/England H7N7
- 1996: 1/USA H7N7
- 2002: 89/Netherlands H7N7
- 2003: 1/Canada H7N3
- 2004: 1/Canada H7N3
- 2006: 4/Wales H7N2
- 2007: 1/Norfolk H7N3
- 2012: 2013~

**LPAI (H7)**
- 2013:
- 660/China H7N9
- 268 died
H5Nx
H7Nx
H6Nx
H10Nx
H9N2

Subclinical
Mild
Severe
Death

2016.isirv.org
Number of Confirmed Human H5N1 Cases
by month of onset as of 2016-07-21

- Azerbaijan (8)
- Bangladesh (8)
- Djibouti (1)
- Cambodia (56)
- Egypt (354)
- Canada (1)
- Indonesia (199)
- Iraq (3)
- Laos (2)
- Myanmar (1)
- Pakistan (3)
- Thailand (25)
- Turkey (12)
- Viet Nam (127)
4 waves
775 confirmed cases
316 cases died

Number of Confirmed Human H7N9 Cases and Deaths
by week as of 2016-7-14

Cases | Death

Weeks: 2013-2016
Counts: 0-40
More than 50% human infections with avian influenza viruses H5N1 (56%) or H7N9 (51%) due to live poultry market visiting

Investigation the source of Human infection with H5N1 viruses
Investigation the source of Human infection with H7N9
Investigation the source of Human infection with H7N9

Q Zhang et al., Science, 2013
Investigation the source of Human infection with H7N9

Figure 3: Phylogenetic trees for the haemagglutinin (HA1) (A) and neuraminidase (N) (B) genes of H7N9 viruses isolated from a patient and a chicken in Zhejiang, China

Geographic distribution of H7N9 human infection and H7N9-positive markets in Guangdong
(a) Human infection with H7N9 in Guangdong. (b) H7N9-positive markets in Guangdong.

Haojie Zhong., et al., Plos One. 2015
Clinical and epidemiological characteristics of a fatal case of avian influenza A H10N8 virus infection: a descriptive study

3 human cases
2 cases died
Phylogenetic analysis of HA (A) and NA genes recovered from the samples collected from the LPM which the index patient visited

Xiufeng Wan., et al., Infect Genet Evol. 2015
Phylogenetic analysis of PB2 (A), PB1 (B), PA (C), NP (D), MP (E), and NS (F) genes recovered from the samples collected from the LPM which the index patient visited.
✓ 14 confirmed cases
✓ 10 cases died
Aerosolized avian influenza A (H5N6) virus isolated from a live poultry market, China

The overall seroprevalence of H5N1 in Viet Nam was 4.0% in 2001 and 6.1% in 2011 respectively.

The A(H5N1) seropositive rate among LPM workers increased from 0% in 2013 to 37.8% in 2014 (P < 0.001) and the A(H9N2) seropositive rate increased from 10% to 55.6% (P < 0.001) in Hong Kong.

The positive rate of anti-H9 antibody among market poultry workers (51/600, 8.5%) was significantly higher than that among the general population (11/600, 1.8%).

The positive rate of anti-H6 antibody among market poultry workers was 0.4% (63/15689) in China.

The positive rate of anti-H7 antibody among market poultry workers was 3.2% in Italy.

Schultsz C et al., Plos One 2005
Tham C et al., WPSAR 2014
To KK et al., J infection 2016
Xin L et al., EID 2015
Di TL et al., Avian Dis 2012
Serological studies suggested a substantial risk of mild H7N9 infections in live poultry markets.

Jinquan Cheng., et CID 2014
Serological studies suggested a substantial risk of mild H7N9 infections in live poultry markets

Jinquan Cheng., et CID 2014
First survey: poultry workers (36/501=7.2%) general population(0/417)

Second survey: poultry workers(56/375=14.9%), general population(0/408)

Of 96 individuals who participated in both surveys, 52 (54.2%) workers had a ≥4-fold rise in H7N9 antibody

In a multivariable analysis, female sex and ≥10 years of occupational exposure were identified as risk factors for infection.

Serological studies suggested a substantial risk of mild H7N9 infections in live poultry markets
The closure of LPMs reduced the mean daily number of infections by 99% in Shanghai, 99% in Hangzhou, 97% in Huzhou, and 97% in Nanjing.
Live poultry markets

- Source of human infections
- Source of generation of novel influenza viruses
The genesis of H10N8 avian influenza viruses in poultry markets

Shu et al, Scientific Report, 2015
Frequent reassortment events of H7N9 AIVs
Dissemination of H7N9 AIVs

Frequent reassortment events of H5N6 AIVs
Poultry farm

emergence of novel viruses
Poultry farm --- emergence of novel viruses

Ck13188-like (H7N9) + Ck13200-like (H9N2) → New genotypes of H7N9 virus

Jilin10117 (H7N9)
Poultry farm --- emergence of novel viruses

Table. Homology among influenza viruses closely related to avian influenza virus A/chicken/Jilin/SD020/2014(H7N2) from Jilin, China, 2014*

<table>
<thead>
<tr>
<th>Gene</th>
<th>Virus</th>
<th>Homology, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>HA</td>
<td>A/chicken/Zhejiang/S4135/2013(H7N9)</td>
<td>99.6</td>
</tr>
<tr>
<td>NA</td>
<td>A/chicken/Jilin/SD001/2014(H9N2)</td>
<td>99.1</td>
</tr>
<tr>
<td>PB2</td>
<td>A/chicken/Zhejiang/S4135/2013(H7N9)</td>
<td>99.9</td>
</tr>
<tr>
<td>PB1</td>
<td>A/chicken/Zhejiang/S4135/2013(H7N9)</td>
<td>99.5</td>
</tr>
<tr>
<td>PA</td>
<td>A/chicken/Hunan/SD015/2014(H7N9)</td>
<td>99.7</td>
</tr>
<tr>
<td>NP</td>
<td>A/Shanghai/02/2013(H7N9)</td>
<td>99.8</td>
</tr>
<tr>
<td>M</td>
<td>A/Shanghai/5190T/2013(H7N9)</td>
<td>99.7</td>
</tr>
<tr>
<td>NS</td>
<td>A/chicken/Jilin/SD001/2014(H9N2)</td>
<td>100</td>
</tr>
</tbody>
</table>

*HA, hemagglutinin; NA, neuraminidase; NP, nucleoprotein; M, matrix; NS, nonstructural; PA, polymerase basic; PB, polymerase basic.

Shi et al, EID, 2014
Genetic tuning promote the interspecies transmission

Wang D et al, Eurosurveillance, 2014
Interspecies transmission of influenza A viruses
What we could do?

LPM surveillance
Sustained LPM surveillance in China

- 250,000 were collected from live poultry markets and farms
- More than 40,000 viruses isolated
- 1000 whole genome sequenced
Sustained LPM surveillance contributes to early warnings for human infection with AIVs
Production system | Vaccination | live poultry market

H9N2 H5N1 H7N9 H10N8 H5N2 H5N6 HxNy

✗ ? ✗ ✗
Surveillance, always surveillance

63 network labs
197 sentinel hospitals

411 network labs
556 sentinel hospitals

- 2 millions clinical specimen collected during 2011-16
- 100,000 viruses isolated
- 30,000 viruses were antigenically characterized
- 12,000 viruses test the antiviral sensitivity
- 2,000 whole genome were sequenced
Summary

- LPAI
- Domestic ducks/geese
- Wild waterfowl
- Terrestrial poultry
- Human

AIVs: H5N1, H7N7, H9N2, H7N2, H10N7, H7N9, H6N1, H10N8, H5N6, et al.
SAVE THE DATE: 14-16 June 2017

The 5th isirv-AVG Conference

Prevention and Treatment of Respiratory Virus Infections: Antivirals, Traditional Therapies, Probiotics and Host-Directed Interventions

Regal East Asia Hotel, Shanghai, China, 14-16 June 2017

This Conference will be of interest to research investigators, clinicians and Public Health experts. It will focus on the progress in combatting respiratory virus infections (RVIs) with vaccines and therapeutics, including novel antiviral approaches, and will address regional issues, like the impact of RVIs in Asia and the use/effectiveness of traditional Chinese medicines. A special symposium on novel coronaviruses (SARS/MERS) will be featured.
Thank you for your attention!