Overview of human cases of AI H5N1 since 1997

Dr Sylvie Briand
WHO Global Influenza Programme
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Review of the current H5N1 situation

- 387 cases and 245 deaths recorded since February 2003
- 15 countries affected in 3 continents (Africa, Asia, Europe)
  - Azerbaijan, Bangladesh, Cambodia, China, Djibouti, Egypt, Indonesia, Iraq, Lao People's Democratic Republic, Myanmar, Nigeria, Pakistan, Thailand, Turkey, Viet Nam
  - In 2008, 36 cases with 28 deaths reported in 5 countries. Most cases are in countries where the disease in animals is already considered entrenched.
- SARS outbreak: mid-March 2003- 5 July 2003
  - 8098 cases, 774 deaths
  - 26 countries affected
H5N1 Human Infection 2008

- 387 laboratory confirmed cases
- Primarily transmission from infected birds (poultry)
- Sporadic cases and small family clusters
- No evidence of sustained human to human transmission
- Limited un-sustained human-to-human transmission
  - Intimate prolonged contact at a critical stage of illness
  - Confirmed H2H, 3 generations, Pakistan, December 2007 - WER N°40, 3 October 2008

Increased geographical spread

- First signal:
  - May 1997. First human case with H5 N1 virus in Hong Kong.
  - December 1997.
    - Increase in the number of cases 18 cases / 6 deaths
    - Strong control measures: culling of poultry, closure of markets, no importation of poultry from neighbouring countries.

- February 2003: H5N1 comes back
  - Hong Kong - 3 cases/2 deaths reported in the same family coming from China.
  - Occurrence of the SARS outbreak at the same period

- End 2003 - end 2005: human infections reported in a number of countries in Asia

- Extension of the affected area since the end of 2005
  - European countries affected (Turkey Dec 2005)
  - Africa affected (Egypt March 2006)
  - Pakistan, Myanmar and Bangladesh in 2007-08
Distribution of A(H5N1) cases, deaths and CFR by country

<table>
<thead>
<tr>
<th>Country</th>
<th>All</th>
<th>Confirmed</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases</td>
<td>Deaths</td>
</tr>
<tr>
<td>Australia</td>
<td>91</td>
<td>3</td>
</tr>
<tr>
<td>Vietnam</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Cambodia</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Indonesia</td>
<td>108</td>
<td>49</td>
</tr>
<tr>
<td>Laos</td>
<td>20</td>
<td>2</td>
</tr>
<tr>
<td>Malaysia</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Mongolia</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Pakistan</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Philippines</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Thailand</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Viet Nam</td>
<td>641</td>
<td>14</td>
</tr>
<tr>
<td>Total</td>
<td>1432</td>
<td>68</td>
</tr>
</tbody>
</table>
Risk of pandemic?

The risk of pandemic has not decreased although a decrease in the yearly number of human cases is observed.

But

There are concerns about:
- countries with densely populated areas and ongoing circulation of A (H5N1) in poultry
- poor surveillance system

Laboratory-confirmed human avian influenza infections since 1999
Epidemiological review

There are differences between countries. A number of factors can explain the differences and it is difficult to disentangle them.

Country Profile
- Time
- Risk groups
- Mortality

- Behavioural factors & interventions
- Climate, seasons
- Gender
- Age
- Care

Animal

Virus clade

There are differences between countries. A number of factors can explain the differences and it is difficult to disentangle them.

Relationship between poultry outbreaks and human infections

- Viral circulation in poultry and occurrence of human cases are linked.

- Enhanced surveillance and integrated analysis at the human animal interface is needed to better understand the dynamic of avian and human infection
  - Country data (Egypt)
  - Dynamic patterns of avian and human influenza in east and southeast Asia
Seasonality of A (H5N1) infection in human cases by month of disease onset date, 2004-2007

The global epidemic curve for human cases of H5N1 suggests a "seasonal" pattern that peaks during the Northern Hemisphere winter and diminishes towards summer. Individual country data demonstrate this pattern most clearly in Egypt and Viet Nam.
Distribution of Human A(H5N1) cases over time

- Human cases occur throughout the year in Indonesia with a slight increase in January.
- The pattern of human cases of H5N1 is similar to that for "seasonal" influenza in Indonesia and Egypt.
- Factors involved in the increase of A(H5N1) infection in different period of the year: Role of climate? Co-infection with other influenza viruses? Link with poultry outbreaks?

Mortality in A(H5N1) human cases

- Overall CFR: 63%
- Range from 44% in Egypt and 81.8% in Indonesia
- Time to presentation to health care facility is probably an important factor to explain higher mortality. However other factors cannot be discarded.
  - Surveillance bias
  - Virus virulence
  - Clinical management
  - Population characteristics
Mortality and health care

- Survival is closely linked to early hospitalization.
- However, a more systematic and consistent approach is needed when reporting information about hospitalization.
  - A case patient often visited more than one hospital and it was sometimes unclear which hospital admission date was reported.
  - In addition, data is not always available on treatment modalities.

Virus characteristics and mortality

- Virus A(H5N1) has changed since 1997 and continues to evolve (drifts)
- A(H5N1) clades (10 clades some divided in sub-clades)
  - Clade 1 Viet Nam, Thailand, Cambodia
  - Clade 2
    - 2.1 Indonesia
    - 2.2 Middle east, Europe, Africa
    - 2.3 Laos China
- Difference in virulence related to virus clade?
Distribution by age

- The overall median ages of cases: 20.0 years (range 3 months–81 years).
- The mean = 21.7 years.
- All age groups affected
  - Higher incidence in age group < 40 years
Egypt: 38 cases - 15 deaths

Indonesia: 106 cases - 85 deaths

Morbidity by age group in the most affected countries

Viet Nam: 100 cases - 46 deaths

Laboratory-Confirmed H5N1 Cases Age-Specific Incidence in Viet Nam (n=91) 25 Nov03 to 24 Nov06
Summary of distribution of A(H5N1) cases by gender

WER N°6, 2007, 82 41-48

- Sex ratio of male (n=157) to female (n=171) = 0.9
- Differences among countries
  - Egypt Sex ratio M/F=0.5 (12/26)
  - Thailand Sex ratio M/F =1.8 (16/9)
- No statistical difference in gender distribution among age group

In 2008, in Egypt, of the 50 laboratory confirmed cases in Egypt, 16 (32%) were male and 34 (68%) were female.

A(H5N1) Mortality and gender

<table>
<thead>
<tr>
<th>Country</th>
<th>Male</th>
<th>Female</th>
<th>Ratio M/F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azerbaijan</td>
<td>2</td>
<td>6</td>
<td>0.3</td>
</tr>
<tr>
<td>Cambodia</td>
<td>2</td>
<td>5</td>
<td>0.4</td>
</tr>
<tr>
<td>China</td>
<td>11</td>
<td>14</td>
<td>0.8</td>
</tr>
<tr>
<td>Djibouti</td>
<td>0</td>
<td>1</td>
<td>0.0</td>
</tr>
<tr>
<td>Egypt</td>
<td>12</td>
<td>26</td>
<td>0.5</td>
</tr>
<tr>
<td>Indonesia</td>
<td>54</td>
<td>62</td>
<td>1.0</td>
</tr>
<tr>
<td>Iraq</td>
<td>2</td>
<td>1</td>
<td>2.0</td>
</tr>
<tr>
<td>Laos</td>
<td>0</td>
<td>2</td>
<td>0.0</td>
</tr>
<tr>
<td>Nigeria</td>
<td>0</td>
<td>1</td>
<td>0.0</td>
</tr>
<tr>
<td>Thailand</td>
<td>16</td>
<td>9</td>
<td>1.8</td>
</tr>
<tr>
<td>Turkey</td>
<td>7</td>
<td>5</td>
<td>1.4</td>
</tr>
<tr>
<td>Viet Nam</td>
<td>51</td>
<td>49</td>
<td>1.0</td>
</tr>
<tr>
<td>All Countries</td>
<td>157</td>
<td>171</td>
<td>0.9</td>
</tr>
</tbody>
</table>

In Vietnam, the ratio of male to female was 0.67 (21/30 vs. 25/24), while in Egypt it was 0.083 (1/11 vs. 14/26).
Groups at risk?

- Poultry workers: Despite potentially high exposure, PW have develop the disease only on rare occasion.
- Health care workers: Nosocomial transmission exists but is very low compared to seasonal influenza viruses
- Family clusters: Genetic susceptibility to H5N1 virus infection? Common behaviours? Same Environment?
- Pregnancy
  - 6 cases in pregnant women
  - 4 deaths, 2 abortions

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