Coping with pandemic avian influenza

Avian influenza, or "bird flu", is a contagious disease of animals caused by viruses that normally infect only birds and, less commonly, pigs. While all bird species are thought to be susceptible to infection, domestic poultry flocks are especially vulnerable to infections that can rapidly reach epidemic proportions. The disease in birds has two forms. The first causes mild illness, sometimes expressed only as ruffled feathers or reduced egg production. Of greater concern is the second form, known as "highly pathogenic avian influenza". This form, which was first recognized in Italy in 1878, is extremely contagious in birds and rapidly fatal, with a mortality approaching 100%. Birds can die on the same day that symptoms first appear. The disease can spread from farm to farm within a country as also be carried by migratory fowl across the world. The avian flu viruses spread through poultry flocks either via respiratory secretions or contact with contaminated faeces. A single gram of contaminated faeces has enough viruses to infect one million birds.

The current concern amongst public health officials is prompted by the fact that most major outbreaks of Avian flu recently reported have been caused by the highly pathogenic H5N1 strain. There is mounting evidence that this strain has a unique capacity to jump the species barrier and cause severe disease, with high mortality, in humans. A bigger concern is the possibility that the present situation could give rise to another influenza pandemic in humans. Scientists are aware that avian and human influenza viruses can exchange genes when a person is simultaneously infected with viruses from both species. This process of gene swapping inside the human body can give rise to a completely new subtype of the influenza virus to which few, if any, humans would have natural immunity. And, an alarming situation would rise if person-to-person transmission resulted in successive generations of severe disease with high mortality. This was the situation during the great influenza pandemic of 1918–1919, when a completely new influenza virus subtype emerged and spread around the globe, in around 4 to 6 months. Several waves of infection occurred over 2 years, killing an estimated 40–50 million persons.

Currently the H5N1 strain has resulted in a few cases of humans being infected with the virus. However these cases have been due to factors like close proximity to the fowl or eating improperly cooked meat prepared from affected poultry. The cumulative number of confirmed cases of Avian Influenza (H5N1) reported to WHO as on 09 November 2005 stands as under [Table 1]:

The World Health Organization has offered the following classification for the various phases [Table 2] in an avian flu pandemic situation.[4]

Currently most countries affected are in the pandemic alert period of phase 3 where there is still no clear cut evidence of human to human transmission. WHO has also outlined the overarching public health goals for these phases which are enumerated as above.

So, do we have a threat of human pandemic influenza now? While no one can predict accurately when the pandemic will happen there is no doubt that we are on the threshold of a human flu pandemic. The WHO mentions that best case scenarios modeled on the mild pandemic of 1968 project global excess deaths in the range of 2 to 7.4 million.[5] There are others who mention that clinical, epidemiological and laboratory evidence suggest that a pandemic caused by the H5N1 strain would be more likely to mimic the 1918 pandemic than those that occurred more recently, resulting in far higher mortality.[3]

To reach the critical phase of the human pandemic the virus must satisfy three components. (1) an ability to infect human beings, (2) a vulnerable population without innate immunity and (3) rapid efficient person-to-person transmission. H5N1 has met the first two criteria. It is only a matter of time before the H5N1 virus picks up the genes necessary for rapid person-to-person transmission. When this occurs, quarantine will not halt the spread of the virus. The disease can be transmitted before symptom onset and is highly contagious during...
It is also expected that rapid global spread of H5N1 will occur through air travel.\(^5\)

This brings us to the all important aspect dealing with the prevention and control of such a pandemic. It has been shown that while the H5N1 virus is resistant to antiviral compounds which are M2 inhibitors, the virus is susceptible to the class of antiviral neuramidase inhibitors (Oseltamivir and Zanamivir).\(^6\) These class of drugs are however quite expensive and in a pandemic there may not be enough supplies to go around unless the drugs are manufactured locally in India. The world is also waiting for the production of a vaccine which will be effective against the H5N1 strain. Manufacturing capacity for influenza vaccines is concentrated in Australia, Europe, Japan and North America but it seems unlikely that vaccines will be available till a few months into the first few days of the illness.\(^4\) It is also expected that rapid global spread of H5N1 will occur through air travel.\(^5\)

### Table 1: Total number of cases includes number of deaths. WHO reports only laboratory-confirmed cases

<table>
<thead>
<tr>
<th>Date of onset</th>
<th>Indonesia</th>
<th>Vietnam</th>
<th>Thailand</th>
<th>Cambodia</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>cases</td>
<td>deaths</td>
<td>cases</td>
<td>deaths</td>
<td>cases</td>
</tr>
<tr>
<td>26.12.03-10.03.04</td>
<td>35</td>
<td>24</td>
<td>23</td>
<td>16</td>
<td>12</td>
</tr>
<tr>
<td>19.07.04-08.10.04</td>
<td>9</td>
<td>8</td>
<td>4</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>16.12.04- to date</td>
<td>9</td>
<td>5</td>
<td>65</td>
<td>22</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>92</td>
<td>42</td>
<td>20</td>
<td>13</td>
<td>125</td>
</tr>
</tbody>
</table>

### Table 2: WHO classification of phases in avian flu pandemic

<table>
<thead>
<tr>
<th>NEW PHASES</th>
<th>OVERARCHING PUBLIC HEALTH GOALS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Interpandemic period</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Phase 1.</strong> No new influenza virus subtypes have been detected in humans. An influenza virus subtype that has caused human infection may be present in animals. If present in animals, the risk of human infection or disease is considered to be low.</td>
<td>Strengthen influenza pandemic preparedness at the global, regional, national and subnational levels.</td>
</tr>
<tr>
<td><strong>Phase 2.</strong> No new influenza virus subtypes have been detected in humans. However, a circulating animal influenza virus subtype poses a substantial risk of human disease.</td>
<td>Minimize the risk of transmission to humans; detect and report such transmission rapidly if it occurs.</td>
</tr>
<tr>
<td><strong>Pandemic alert period</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Phase 3.</strong> Human infection(s) with a new subtype, but no human-to-human spread, or at most rare instances of spread to a close contact.(^b)</td>
<td>Ensure rapid characterization of the new virus subtype and early detection, notification and response to additional cases.</td>
</tr>
<tr>
<td><strong>Phase 4.</strong> Small cluster(s) with limited human-to-human transmission but spread is highly localized, suggesting that the virus is not well adapted to humans.(^b)</td>
<td>Contain the new virus within limited foci or delay spread to gain time to implement preparedness measures, including vaccine development.</td>
</tr>
<tr>
<td><strong>Phase 5.</strong> Larger cluster(s) but human-to-human spread still localized, suggesting that the virus is becoming increasingly better adapted to humans, but may not yet be fully transmissible (substantial pandemic risk).</td>
<td>Maximize efforts to contain or delay spread, to possibly avert a pandemic, and to gain time to implement pandemic response measures.</td>
</tr>
<tr>
<td><strong>Pandemic period</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Phase 6.</strong> Pandemic: increased and sustained transmission in general population.(^b)</td>
<td>Minimize the impact of the pandemic.</td>
</tr>
</tbody>
</table>

\(^a\) The distinction between phase 1 and phase 2 is based on the risk of human infection or disease resulting from circulating strains in animals. The distinction is based on various factors and their relative importance according to current scientific knowledge. Factors may include pathogenicity in animals and humans, occurrence in domesticated animals and livestock or only in wildlife, whether the virus is enzootic or epizootic, geographically localized or widespread, and/or other scientific parameters.

\(^b\) The distinction between phase 3, phase 4 and phase 5 is based on an assessment of the risk of a pandemic. Various factors and their relative importance according to current scientific knowledge may be considered. Factors may include rate of transmission, geographical location and spread, severity of illness, presence of genes from human strains (if derived from an animal strain), and/or other scientific parameters.
the onset of the pandemic. The use of reverse genetics for rapid development of influenza vaccines as a means to respond to pandemic threat seems to offer an appropriate technology that can cope with demand for vaccines in the event of a pandemic.\(^7\)

From the perspective of a practicing occupational health physician in charge of the health of all employees in an industry we can take the following steps to prevent / control avian influenza.

1. Vaccinate all employees with the current available strain of influenza vaccine. While this will not protect against the avian flu it will ensure that in the event of any outbreak any case of influenza in the vaccinated populace should be viewed with suspicion - which can then help in decision making vis-à-vis treatment with the antiviral drug *Oseltamivir* (Tamiflu). Companies should also advise suppliers / 3Ps on the best practice in this area for them to take appropriate action at their end.
   - If a vaccine against the specific strain of H5N1 becomes available then industries should offer this protection to all employees. At present there is no vaccine available against Avian flu. While trials are still going on, it is likely that the vaccine will be available only a few months after the onset of the pandemic.
   - From a public health perspective groups prioritized for vaccination should be (1) health care workers most at risk (2) essential services workers (3) at risk groups (4) enclosed communities and (5) general population.\(^8\)

2. During the phase of the human pandemic it is recommended that employees with fever of > 38 degrees C. stay away from work till they are symptom and fever free. Such cases should be reviewed by appropriate medical personnel (The industry local medical advisor would be able to coordinate this).

3. A health education and hygiene awareness campaign be started to cover all employees.

4. It would be useful to have in place guidelines covering the following:
   - Who will be eligible to receive the antiviral drug *Oseltamivir*? e.g. treatment modality
   - Travel restrictions and their scope
   - Evacuation of non-essential staff
   - Policy on absenteeism
   - Personal protective measures

5. With respect to the specific aspect of treatment, since the drug *Oseltamivir* will be in short supply the recommendation is to prioritize the drug delivery to:
   - Individuals in close contact with known cases of Avian flu
   - Individuals who have been in contact with poultry
   - Health care providers
   - Diagnosed / confirmed cases of Avian flu
   - Un-immunized people in high risk groups: to ameliorate illness and reduce complications, hospital admissions and deaths
   - Immunized people: if emerging information suggests that the vaccine is not effective at reducing serious illness, complications or deaths

It must be mentioned here that this drug is likely to be effective if taken in the very early phase (within two days of the condition). Therapy with *Oseltamivir* (Tamiflu or a local equivalent) should start within 48 hours after the onset of influenza symptoms and the current recommended dosage is 75 mg tablets twice daily for five days. As a prophylaxis the current view is that the drug can be taken for a maximum period of 6 weeks while in a pandemic the “waves” could last for 8 – 12 weeks. The recommended dosage for prophylaxis is 75 mg. once a day. For severe cases the inhaled *Zanamivir* (Relenza) is also advocated.

The current advice from various health authorities is to stockpile supply of *Oseltamivir* for 30% of the staff. In the event of a pandemic there will be immense pressure on operating companies and they should have clear plans with respect to:
   - Business Continuity
   - Ensuring availability of the antiviral drug *Oseltamivir* (Tamiflu or a locally made equivalent )
   - Laid down policy to deal with an outbreak

Apart from the specific medical interventions, key non-medical interventions should include stress on personal hygiene, wearing of appropriate masks (N-95 or N-100 with exhalation valve). At the population level contact tracing and screening of travelers at both the national and international levels are essential to prevent transmission. The country’s health system will be stretched to its limit with respect to both preventing cases as well as taking care of the affected people.

The threat of the pandemic is real. We as occupational health physicians have a significant role to play to mitigate the morbidity and mortality arising out of such a pandemic. It will be essential for companies to put in place a comprehensive pandemic preparedness plan as well as business continuity plans. Close co-operation with governmental health agencies is also essential. It must be mentioned here that the Indian health authorities are seized of the potential pandemic and are gearing up to meet this threat.
REFERENCES


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