

for health, it is gradually becomes that of the people itself. "Poverty is the inability to command events that affect our lives." Thus learning those skills is central to solutions.

Healthy Municipalities had led the way, to new health.

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## Avian flu

# Avian influenza: a human pandemic threat?

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## Another influenza pandemic in humans is inevitable

In January 2004, the most serious outbreak of avian influenza in terms of the number of human deaths (22 deaths out of a total of 33 cases in Vietnam and Thailand) began. This outbreak was caused by the viral subtype H5N1 (H (haemagglutinin) and N (neuraminidase) are viral surface proteins that define specific subtypes) and, to date, constitutes the largest epidemic in commercial poultry,<sup>1,2</sup> affecting a number of Asian countries (that is, Cambodia, China, Indonesia, Japan, Lao People's Democratic Republic, and the Republic of Korea, in addition to Thailand and Vietnam), where more than 100 million birds either died or were culled in the first two months of 2004.<sup>3,4</sup> The high case fatality rate, together with the potential occurrence of human epidemics, have created great public health concern, given the viruses' high pathogenicity in humans. The question that remains unanswered, and that is the basic cause of such concern, is: "Will this avian virus be able to cause a large scale epidemic among humans after mutation or reassortment?"

To answer this question, we have to consider what we already know. The natural reservoir of avian influenza viruses is wild aquatic birds, which may be infected with "avirulent" or "low pathogenic" strains of the virus and present with only mild symptoms or no symptoms at all. Low pathogenic viruses can infect domestic poultry and other intermediate hosts and develop into highly pathogenic viruses (usually the H5N1 subtype), which cause a highly lethal disease, once defined as "fowl plague" (fowl plague was first identified in 1878 by an Italian scientist, Edoardo Perroncito, who described an outbreak of a contagious disease affecting domestic birds in farms near Turin, Italy).<sup>5</sup> Influenza viruses are secreted from the intestinal tract into the faeces

of infected birds, and the modes of transmission may be either direct or indirect. Transmission from animals to humans is apparently rare: avian influenza viruses do not replicate efficiently in humans, and receptor specificity is a determinant of a certain host range restriction.<sup>6</sup>

The first recorded instance of direct transmission to a human host occurred in Hong Kong in 1997 and involved different strains of the same subtype implicated in the current outbreaks (H5N1). Of the 18 persons infected, six died, with the case fatality exceeding 30%.<sup>6,7</sup> The avian influenza subtype, H9N2, crossed the species barrier in 1999, causing mild illness in two children in Hong Kong.<sup>8</sup> In February 2003, two members of a family, returning to Hong Kong after having travelled to southern China, became ill, and one of them died, again from H5N1 avian influenza.<sup>9</sup> In April 2003, another avian influenza viral subtype, H7N7, which had caused an extensive epidemic among poultry, caused the death of a veterinarian and an outbreak of conjunctivitis or mild influenza-like illness among 85 persons who had handled infected chickens, in addition to family members.<sup>10</sup> In mid-December 2003, H9N2 infection was detected in a child in Hong Kong hospitalised with influenza symptoms, later recovering.<sup>11</sup> Finally, in early 2004, during a poultry outbreak attributable to another H7 influenza strain, the H7N3 subtype, in British Columbia, Canada, two laboratory confirmed human cases with conjunctival and upper respiratory symptoms were reported, and at least 10 other poultry workers developed similar symptoms.<sup>12</sup> This chronology of event indicates that avian to human transmission, although apparently rare, can occur, and that at least four different subtypes are involved.

Regarding human to human transmission of avian influenza strains, little evidence is available. In addition to the family members of poultry workers who acquired H7N7 in the Netherlands, the results of a serosurvey conducted in Hong Kong showed that one of the 54 healthcare workers tested had increased antibody titres, suggesting that transmission of H5N1 from infected patients may occur,<sup>13</sup> whereas inter-human transmission was not confirmed in a family cluster investigated in Vietnam during the 2004 H5N1 outbreak. Finally, there was no evidence of human to human transmission of H9N2 in Hong Kong in 1999.<sup>14</sup>

Although this evidence suggests that human to human transmission is inefficient, the potential for viruses to mutate must be considered. Influenza A viruses are known to undergo small or large antigenic changes (that is, drifts and shifts), and major changes can result in worldwide pandemics, such as those of "Asian" flu in 1957 and "Hong Kong" flu in 1968. These changes are often attributable to the reassortment (in pigs or even in coinfecting humans) of avian with human influenza strains. In stochastic terms, the higher the frequency of inter-species passage the higher the risk of humans becoming suitable hosts, as the risk of a reassortment event is proportional to the number of hosts coinfecting with human and avian strains.<sup>15</sup>

Based on the above information, it is not possible to predict whether or not a large scale epidemic of avian influenza virus among humans is in the making. None the less, we must consider the potential for this to occur. Obviously, the response to this threat of an epidemic must be prompt and efficient. Because of the size of the population of the wild bird reservoir, avian influenza is not an eradicable disease. At present, the most that can be done is to prevent interspecies passage to pigs or humans during fowl epidemics through the mass culling of infected or exposed poultry, which proved to be effective in halting the epidemic in Hong Kong in 1997.<sup>16,17</sup> To prevent the re-emergence of avian viruses, other initiatives can be adopted, although in Hong Kong the re-emergence of H5N1 was not completely prevented by the elimination of live aquatic birds (for example, ducks and geese) and intermediate hosts (for example, quails) from wet markets (live animal markets), or by the active

surveillance and use of inactivated vaccines in poultry farms.<sup>16</sup> In fact, the role of these vaccines remains controversial.<sup>18</sup> The best option for preventing re-emergence, and thus interspecies passage, would definitely be that of eliminating live poultry markets, which provide optimum conditions for the amplification of influenza viruses. However, the elimination of wet markets is not a realistic goal, at least for the near future, given that these markets are an integral part of the food culture of Asian countries, where older generations do not buy frozen or refrigerated products.<sup>16-19</sup>

If the virus were to become capable of efficient human to human transmission, traditional public health measures, such as quarantine and contact tracing and isolation, as well as travel restriction, which were successful in controlling the epidemic of SARS, would not be likely to work, as influenza might have a considerably higher basic reproductive rate,  $R_0$  (that is, the average number of secondary cases generated by an infected host).<sup>20</sup> However, some models have predicted an initial adaptation of a new pandemic virus, with limited initial efficiency in terms of human to human transmission.<sup>21</sup> In such a case, traditional public health measures, triggered by early recognition of the infection (that is, through good surveillance and the availability of rapid and reliable diagnostic tests), along with the use of prophylactic antiviral treatment (neuraminidase inhibitors), as occurred in the Netherlands,<sup>22</sup> might help to reduce further transmission, allowing more time for a vaccine to be developed.<sup>23</sup> To this end, stockpiling of sufficient quantities of antiviral drugs should be considered in preparedness plans. Although an effective vaccine could feasibly be developed, large scale

production would not be easy, and the decision to perform mass vaccination, which must obviously be timely, could be affected by past experience, such as the costly 1976 swine flu campaign in the United States, where the epidemic turned out to be a false alarm.<sup>24</sup>

Although another influenza pandemic in humans is inevitable, we cannot predict when it will occur. In the meantime, we must do everything in our power to avert this threat, which means improving our responsiveness to a pandemic alert through implementation of all possible preventive strategies.

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