



Avian Influenza: Waiting for Godot?

SM Sapatnekar

“It is perfectly obvious that no one nor any single country can save the World from the horrors of tsunamis, hurricanes, earthquakes and winged influenza.”¹¹

... Richard Reeves

The spirit of the speech of Director-General LEE Jong-wook at the International Conference on Avian Influenza at Beijing, on 18 January 2006 was not different.⁹ Yes; Global challenges do need Global strategies, plan of action and endeavors. The threat of Avian Influenza (AI) reported widely as the “Bird Flu” in the lay press is no longer illusory. Today, there are eight known places on this *terra firma* where the disease is firmly entrenched. Cumulative number of laboratory confirmed human cases of Avian Influenza A/ (H5N1) reported to WHO as of 13th February 2006 is One hundred sixty-nine, of whom ninety-one have succumbed to the virus since 2003.¹³

| Date of onset | Cases | Total Deaths | Case Fatality Rate (%) |
|---------------|-------|--------------|------------------------|
| 2003 | 3 | 3 | 100.00 |
| 2004 | 46 | 32 | 69.56 |
| 2005 | 95 | 41 | 43.15 |
| 2006 | 25 | 15 | 60.00 |
| Total | 169 | 91 | 53.84 |

There are twenty countries where H5N1 infections have been reported to occur only in birds. India may be the latest entrant to the list since Navapur, a place 300 km.s from Mumbai has found H5N1 infection in the poultry that is confirmed by Animal Disease Laboratory at Bhopal.¹ Thus, there is no doubt about AI having established as an epizootic. Whereas Cambodia, China (Hong Kong), China (Mainland), Indonesia, Iraq, Thailand, Turkey, Viet Nam are the eight countries where human morbidity and mortality has been experienced in addition to the poultry.⁴ Reported cases and deaths in humans have demonstrated the multinational nature of AI. A trillion dollar question now is; will it be a long feared human pandemic; or worse still, how bad and how soon? The WHO’s Director General, Lee Jong-wook, is reported by the Times-online on 22nd Jan. 2006 to have warned that an outbreak in Britain was “inevitable and possibly imminent”.⁸ That rules out the question if and poses another – how soon?

Ex- Director, Haffkine Institute, Mumbai.

“The world may be on the brink of another pandemic. All countries will be affected. Widespread illness will occur. Medical supplies will be inadequate. Large numbers of deaths will occur. Economic and social disruption will be great”. This is not a citation from Prophecies of Nostradamus. These are five out of the “Ten things you need to know about pandemic influenza” by World Health Organization!¹⁴ These doomsday predictions sound alarming. But then the WHO website has 69 citations that carry the phrase inevitable and imminent (human pandemic), at least since 17 March 2003; and the good news is the pandemic has not occurred thus far.¹⁵

An interesting (and may be an entertaining) rejoinder to this anticipation of pandemic comes from ex-Cabinet minister of the Government of India, the renowned animal activist Maneka Gandhi.⁷ According to her, Bird Flu is the latest scam perpetrated by the American Government and pharmaceutical companies. She has cited two examples of major scares in the World in the last decade. First is the Y2K fear and another is the SARS phobia, which according to her were other bluffs. There is allegation now that the panic generated about AI by the media originated from USA. Her theory impleads Donald H. Rumsfeld, Defense Secretary in Bush’s Cabinet, who was Chairman of the Board of Gilead Sciences during 1988 to 2001. It is Gilead that holds marketing rights to the antiviral drug Tamiflu of Roche and there are millions of dollars involved. Thus Maneka Gandhi believes that Bush administration has now replaced Osama Bin Laden bogey with AI. This theory could have been shrugged off as a political statement and could have died its natural death. But then, expert views of renowned epidemiologists are equally divergent on the catastrophe envisioned.

Michael T. Osterholm, of CIDRAP from University of Minnesota asserts “Recent clinical, epidemiological, and laboratory evidence suggests that the impact of a pandemic caused by the current H5N1 strain would be similar to that of the 1918–19 pandemic. More than half of the people killed in that pandemic were 18 to 40 years old and largely healthy. If 1918–19 mortality data are extrapolated to the current U.S. population, 1.7 million people could die, half of them between the ages of 18 and 40. Globally, those same estimates yield 180–360 million deaths, more than five times the cumulative number of documented AIDS deaths.” On the other hand Dr. Peter Palese, Mount Sinai School of Medicine in New

York holds “The virus [H5N1] has been around for more than a dozen years, but it hasn’t jumped into the human population, I don’t think it has the capability of doing it”.⁵

The situation is akin to the famous tragi-comedy “Waiting for Godot” by Samuel Beckett wherein Vladimir and Estragon expectantly await Godot, who never turns up but apparently sends message that he will come the next day and the wait continues. Perhaps the World is anxiously awaiting human pandemic – hoping against the hope that it may never arrive.

However, Science must look for answers beyond the wait. It needs an epidemiologic drill to answer these questions. AI in humans is essentially a zoonotic disease. Being primarily a disease of poultry birds, there is a species barrier for AI in mammals. Since 1959, instances of human infection with an avian influenza virus have occurred on only 10 occasions. Of the hundreds of strains of avian influenza A viruses, only four are known to have caused human infections: H5N1, H7N3, H7N7, and H9N2. Barring the H5N1, other viral strains result in a very mild illness.¹² Even in the bird population the virus is widely circulated all over the world, it rarely causes a severe infection. Yet, in its severe form, highly pathogenic avian influenza is characterized by sudden onset of severe disease, rapid contagion, and a mortality rate that can approach 100% within 48 hours. No wonder, when first identified in Italy in 1878, it was called as ‘chicken ebola’. To date, all outbreaks of the highly pathogenic form of avian influenza have been caused by viruses of the H5 and H7 subtypes that are associated with exceptional virulence.¹²

Like an intimidating enemy, this virus has a number of threatening features like high virulence, high pathogenicity, high transmissibility and high resistance to environmental stress. The virus can survive for more than a month in bird droppings in cold weather and for nearly a week even in hot summer temperatures.¹² Its primary hosts being highly mobile birds, poultry-to-poultry transfer is too easy. It is also carried easily by human attendants through their hands and clothes. Transcontinental bird migration is a routine annual event. So, the virus does not necessarily need a costly airplane for its global spread, except that it will be a faster mode if and when the pandemic prevails. The only consolation the virus offers is its longish incubation period in humans compared to the usual seasonal influenza. It ranges from 2 to 8 days and possibly as long as 17 days. Thus, there is some time margin for the clinicians and the public health authorities to intervene in the face of an epidemic.

Extensive studies of the human cases determined that direct contact with diseased poultry was the source of infection. Studies carried out in family members and social contacts of patients, health workers engaged in their care, and poultry cullers found very limited, if any,

evidence of spread of the virus from one person to another.¹²

To date, human infections with avian influenza A viruses detected since 1997 have not resulted in sustained human-to-human transmission.¹³ All evidence to date indicates that close contact with dead or sick birds is the principal source of human infection with the H5N1 virus. Especially risky behaviors identified include the slaughtering, defeathering, butchering and preparation for consumption of infected birds.¹² Yet, there are areas of our ignorance. For unknown reasons, most cases have occurred in rural and peri-urban households where small flocks of poultry are kept. Very few cases have been detected in presumed high-risk groups, such as commercial poultry workers, workers at live poultry markets, cullers, veterinarians, and health staff caring for patients without adequate protective equipment. Also lacking is an explanation for the puzzling concentration of cases in previously healthy children and young adults. Human infections ceased following the rapid destruction of Hong Kong’s entire poultry population, estimated at around 1.5 million birds. Some experts believe that that drastic action may have averted a pandemic.¹²

The World Health Organization has awarded a level 3 alert after having the risk assessed.¹⁷

| | | |
|--------------------------------------|---|---|
| Inter-pandemic phase | Low risk of human cases | 1 |
| New virus in animals, no human cases | Higher risk of human cases | 2 |
| Pandemic alert | No or very limited human-to-human transmission | 3 |
| New virus causes human cases | Evidence of increased human-to-human transmission | 4 |
| | Evidence of significant human-to-human transmission | 5 |
| Pandemic | Efficient and sustained human-to-human transmission | 6 |

With the evidence on hand, the ranking does not need to be disputed. WHO has also prescribed strategic actions phase-wise.¹⁹

1. Reduce opportunities for human infection
2. Strengthen the early warning system
3. Contain or delay spread at the source
4. Reduce morbidity, mortality, and social disruption
5. Conduct research to guide response measures.

Thus, a practicing clinician, irrespective of his specialization, will be required to contribute to the extent of having high index of suspicion for diagnosis, prescribing antiviral therapy and notification of cases and deaths to local authorities – if and when they do occur. The H5N1 virus that has caused human illness and death in Asia is resistant to amantadine and rimantadine, two antiviral medications commonly used for influenza. Two other antiviral medications, oseltamavir and zanamavir, would probably work to treat influenza caused by H5N1 virus, but additional



Fig. 1 : Risk of pandemic

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Fig. 3 : Risk of spread

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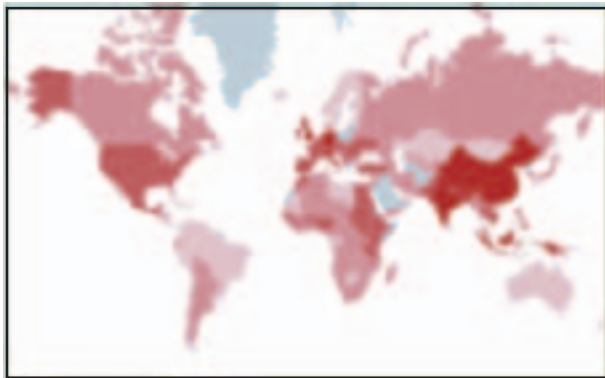


Fig. 2 : Risk of emergence

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Fig. 4 : Capacity to contain.

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Maplecroft.net Limited Global map of pandemic risk

studies still need to be done to demonstrate their effectiveness.³

An effective vaccine is the genuine answer to any communicable disease. There currently is no commercially available vaccine to protect humans against H5N1 virus. Researchers from the University of Pittsburgh, Penn say that they have genetically engineered an avian flu vaccine that completely protected mice and chickens from infection in a study.²⁰ That indeed is good news. Whether H5N1 will show the courtesy not to change its antigenic character before development of human vaccine remains to be seen.

An interesting website has displayed preparedness of various countries to counter the threat of AI. Depending on various tangible factors, a score is awarded that weighs risk of emergence, risk of spread and the capacity to contain an outbreak.¹⁰ There are no

bonus marks for guessing that India has extreme risk of emergence and score poorer even than Pakistan regarding the capacity to take control of the situation. A poorer score for UK is no consolation as population density and intensity of international travel adds to its risk. A table of comparison is carved out from the international ranking exercise.

The state of affairs is not surprising. First, the infrastructure is certainly poor if it exists. “Infectious diseases” has not been developed as a specialty in India ever. Infectious Diseases Hospitals if they exist – are invariably municipal; which means these will have leaking roofs, dangling wires, peeling paint and demoralized staff. For every impending epidemic, we need to look westwards either for guidance or else for endorsement. Even today, the issue “whether it was plague or not at Surat” remains a controversy. The acute

| | Risk of emergence | | | Risk of spread to and within the Country | | | Risk of Incapacity to contain an outbreak | | | Pandemic Risk Index | | |
|----------|-------------------|------------|---------|--|------------|---------|---|------------|-------|---------------------|------------|---------|
| | Value | World Rank | Level | Value | World Rank | Level | Value | World Rank | Level | Value | World Rank | Level |
| Pakistan | 3.56 | 42 | High | 8.71 | 135 | Low | 3.33 | 51 | High | 4.40 | 68 | High |
| Belgium | 0.03 | 3 | Extreme | 2.02 | 5 | Extreme | 8.96 | 150 | Low | 2.75 | 32 | High |
| U.K. | 1.46 | 9 | Extreme | 0.63 | 1 | Extreme | 8.58 | 148 | Low | 2.49 | 25 | Extreme |
| India | 2.49 | 26 | Extreme | 5.08 | 42 | Medium | 2.61 | 40 | High | 1.40 | 6 | Extreme |

Note: Values are in the range of Zero to Ten. Lower the value score and lower the World rank, higher is the risk.

panic disorder witnessed at all levels of administration then has cost the country about 600 million US\$, since imports from India were banned. The situation was not different ten years later when SARS was feared to affect India. Authorities again fumbled about a case admitted to Infectious Diseases Hospital in Mumbai. On the brighter side is visible change in responsiveness in some states in India. On the darker side is spread of rumors, lack of ownership by authorities, blame game and media-trials.

The human host has no immunological memory of encounter with H5N1. Corollary, there is no herd immunity. The epizootic has set-in. Human toll is inching towards a century. Only ray of hope is that chain of transmission from person-to-person has not occurred even where there have been clusters of human infection. Thus, in the eternal epidemiological triad, the HOST is highly susceptible and the ENVIRONMENT is conducive for transmission of infection. It is now up to the AGENT (H5N1) to set the spark to ignite the pandemic. Will that be?

Influenza A viruses have been described as sloppy, capricious, and promiscuous.¹⁹ As for the day, the Global stage is set for a tragic melodrama. The epizootic has been an international success. The script for a human pandemic is ready. The producer of the show and lead actor- H5N1 -is in the green room for a make up that will make him pathogenic to Humans. He does not seem to have made up his mind yet, though the bells of curtain rise have sounded twice!

Acknowledgement

This Editorial has relied heavily on the references from the official website of the World Health Organization for latest facts, statistics and strategies. Experience from SARS episode has shown that informal networking of epidemiologists and contributors works wonders under the threat of impending epidemic. Hence the links for respective websites are furnished. Pandemic risk ranking from Maplecroft website at reference 10 above is with kind permission. It may be further cited only with express permission of Maplecroft.net Limited; it is under a Copyright. Both the sources are gratefully

acknowledged. Website at reference 17 above is worth visiting periodically for timely updates for various infectious diseases and emergencies.

REFERENCES

1. Agashe Ashish; Bird flu in India; Asian age; 19 Feb.2006; Page 1 & 2
2. Centre for Disease Control and Prevention; Key Facts About Avian Influenza (Bird Flu) and Avian Influenza A (H5N1) Virus; <http://www.cdc.gov/flu/avian/gen-info/facts.htm>; February 7, 2006
3. Centre for Disease Control and Prevention; Avian Influenza Infection in Humans; <http://www.cdc.gov/flu/avian/gen-info/avian-flu-humans.htm>
4. Flu Wiki Science; Basic Scientific Information; <http://www.fluwikie.com/index.php?n=Science.Science#Influenza>
5. Flu Wiki Science; Expert Opinions about a Flu Pandemic; <http://www.fluwikie.com/index.php?n=Science.OpinionAboutAFluPandemic>
6. Fox Maggie; Alertnetnews; 20 Jan 2006; Alerting humanitarians to emergencies; <http://www.alertnet.org/thenews/newsdesk/N20130277.htm>
7. Gandhi Maneka; THE SCARE OF EPIDEMICS: What is the reality of the avian flu? http://www.abolitionist-online.com/article-issue02_maneka.gandhi.shtml
8. Henderson Mark; Britain at highest risk from avian flu pandemic; The Times January 12, 2006 www.timesonline.co.uk/birdflu
9. Lee Jong-wook Director General, WHO; Speech at Beijing; International Pledging Conference on Avian and Human Pandemic Influenza; 18 Jan.2006; http://www.who.int/dg/lee/speeches/2006/flumeeting_beijing/en/index.html
10. Maplecroft.net Limited Global map of pandemic risk(Copyright © Maplecroft.NET Limited, 2005) <http://maps.maplecroft.com/showtext?issue=56&topic=interpret> (cited with permission)
11. Reeves Richard; Opinion Column; uexpress dt.21 Oct 2005; http://www.uexpress.com/richardreeves/?uc_full_date=20051021
12. WHO fact sheet; Avian influenza (" bird flu") - Fact sheet February 2006; www.who.int/entity/csr/disease/avian_influenza/en/ - 24k - 21 Jan 2006
13. World Health Organization; Epidemic and Pandemic Alert and Response; Cumulative Number of Confirmed Human Cases of Avian Influenza A/ (H5N1) Reported to WHO; 13 February 2006; http://www.who.int/csr/disease/avian_influenza/country/cases_table_2006_02_13/en/index.html
14. World Health Organization; Epidemic and Pandemic Alert and Response; 14 October 2005; <http://www.who.int/csr/disease/influenza/pandemic10things>
15. World Health Organization; FIFTY-SIXTH WORLD HEALTH ASSEMBLY; Influenza- Report by the Secretariat; A56/23; Provisional agenda item 14.14; 17 March 2003; paragraph 7
16. World Health Organization; WHO/CDS/CSR/GIP/2005.8; Communicable Disease Surveillance and Response; Global Influenza Programme; Responding to the avian influenza pandemic threat
17. World Health Organization; Epidemic and Pandemic Alert and Response; Current WHO phase of pandemic alert; http://www.who.int/csr/disease/avian_influenza/phase/en/index.html
18. World Health Organization; Responding to the avian influenza pandemic threat; Recommended strategic actions; WHO/CDS/CSR/GIP/2005.8; page 5
19. World Health Organization; Avian influenza: assessing the pandemic threat; January 2005; Page 12; http://www.who.int/csr/disease/influenza/WHO_CDS_2005_29/en/print.html
20. World Science; Jan. 28, 2006; Vaccine gives "100 percent" bird flu protection in animal study; http://www.world-science.net/othernews/060128_flufirm.htm



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