

Protecting human and ecological health under viral threats in Asia

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Abstract Severe acute respiratory syndrome (SARS) outbreaked in 2003, and the avian influenza A (H5N1) also outbreaked in 2003 and continued to 2004. These pandemic viral diseases originated in South East Asia. Many human and animal lives were lost. Economic damages due to the pandemics were also very large. The question arises of why did the pandemics originate from South East Asian areas. Human influenza A consists of many sub-types of coronaviruses including the SARS virus and the avian influenza (H5N1) that are all variants of RNA of avian coronavirus. Variants are formed during infection of a coronavirus through not only birds but also mammals, including human beings. There are hot spots where viral infection rates are accelerated among birds, mammals and human beings. Suspicious areas are in South East Asia, where living conditions of birds, mammals and human beings are so close that there are always risks of viral infection. When we see the living conditions of farmers in southern China, northern Vietnam, Laos and northern Myanmar, they commonly raise ducks/chickens with pigs sharing ponds into which they discharge household wastewater, including human excreta, and pig excreta that are significant carriers of viruses. Bird faeces are also key carriers of the viruses. In the ponds, they raise ducks and conduct fish culture. Other important players are migrating birds from North Asia, which are principal vectors of avian influenza viruses. There is an urgent necessity of improving human and ecological health in South East Asia to control viral infection among birds, mammals and human beings. We can hinder the vicious cycle of virus infection through water contamination in ponds by providing good human, pig and chicken sanitation. It is easy to provide good sanitation practices for human, pigs and chickens, introducing collection and treatment of excreta. Our modern water technology can find good solutions for the problem.

Keywords Influenza A; H5N1; SARS; zoonosis; domestic animal sanitation; human sanitation

Introduction

Severe acute respiratory syndrome (SARS) outbreaked in 2003 and the avian influenza A (H5N1) also outbreaked in 2003 and continued to 2004. These pandemic viral diseases originated from South East Asia. Many human and animal lives were lost. Economic damages due to the pandemics were very large: the Asian Development Bank estimated 56 billion US dollars of losses among Asian countries including China, 17.9 billion the largest loss due to SARS incidents. Bird influenza consists of many sub-types of coronaviruses, including the SARS virus, that are all variants of RNA of avian coronaviruses. Variants are formed during infection of a coronavirus through not only birds but also mammals, including human beings. There are hot spots where viral infection rates are accelerated among birds, mammals and human beings. Suspicious areas are in South East Asia, where living conditions of birds, mammals and human beings are so close that there are always risks of viral infection. When we see the living conditions of farmers in southern China, northern Vietnam, Laos and northern Myanmar, they commonly raise ducks/chickens with pigs sharing ponds into which they discharge household wastewater (including human excreta) and pig excreta that are significant carriers of viruses. Birds' faeces are also key carriers of the viruses. The ponds are used for raising ducks and for aquaculture. Other important players are migrating birds from northern Asia, which are principal vectors of avian coronaviruses. There is an urgent necessity for improving

human and ecological health in South East Asia to control viral infection among birds, mammals and human beings. We can hinder the vicious cycle of virus infection through water contamination in ponds by providing good human and pig sanitation. It is easy to provide good sanitation practices for humans, pigs and chickens by introducing collection and treatment of the excreta. Our modern water technology can find good solutions for the problem.

Severe acute respiratory syndrome (SARS)

Severe acute respiratory syndrome (SARS) is a viral respiratory illness caused by a coronavirus, called SARS-associated coronavirus (SARS-CoV). The first severe and readily transmissible disease of the 21st century is believed to have originated in southern China at the end of 2002. From there it crossed into Hong Kong (China) in February 2003. It quickly transmitted to Viet Nam, Singapore, Canada and Germany, and then other parts of the world.

From November 2002 to July 2003, a cumulative total of more than 8098 probable SARS cases with more than 774 deaths were reported in 26 countries in North America, South America, Europe, and Asia—the vast majority of them in the Western Pacific (<http://www.cdc.gov/ncidod/sars/factsheet.htm>).

The disease, which is normally transmitted through droplet spread from one person to another, begins with symptoms of fever (above 38 °C), myalgia and dry cough, and progresses to pneumonia. Approximately 10% of cases develop a severe respiratory illness. To date, there is no specific treatment for SARS, nor is there a speedy and reliable diagnostic test (<http://www.wpro.who.int/sars/docs/frontpage.asp>). The prevention and control measures against SARS were developed by WHO and health care agencies around the world. The key concept is early detection of patients and their isolation in hospitals. Home and community cares are also important to stop transmission. Those medical aspects of public health are bases, but there is as yet no information on the root cause of SARS. Coronaviruses have the distinction of containing the largest genome of all known RNA viruses. They are widespread throughout the animal kingdom, causing bronchitis (poultry), hepatitis (mice), enteritis (horses and pigs) and peritonitis (cats), but often infecting multiple sites. Known coronaviruses fall into three clades (members of two of which cause about 20% of common colds), but the SARS-CoV occupies a new fourth clade of its own. It is clearly a coronavirus, but not closely related to any previously sequenced virus. It presumably arose from an animal source in southern China, perhaps in a species with relatively little contact with man and in which viral disease has been little studied. The civet cat has been proposed as a possible source, but systematic studies of coronaviruses in a wide spectrum of wild and semi-domestic species are not yet complete. RNA viruses tend to evolve rapidly and coronaviruses frequently undergo homologous recombination, so that co-infection with an established human coronavirus and SARS-CoV could lead to emergence of new virus species combining various features of the parental strains (Openshaw, 2003). The first host of SARS has not yet been made clear. Wild animals such as raccoon dogs and civets were suspected to be original hosts, but not certain. However, the civets in Guangdong Province in China are not wild but raised and might be fed with infected ducks that might be original hosts.

Influenza A and the subtype H5N1

Influenza types A or B viruses cause epidemics of disease among human beings almost every winter. Getting a flu injection can prevent illness from types A and B influenza. Influenza type C infections cause a mild respiratory illness and are not thought to cause epidemics. Influenza B viruses are normally found only in humans. Although influenza

type B viruses can cause human epidemics, they have not caused pandemics. Influenza type C viruses cause mild illness in humans and do not cause epidemics or pandemics. These viruses are not classified according to subtype. The flu injection does not protect against type C influenza.

Influenza type A viruses are divided into subtypes based on two proteins on the surface of the virus. These proteins are called hemagglutinin (HA) and neuraminidase (NA). The hemagglutinin HA has 15 subtypes and the neuraminidase NA has 9 subtypes such that the combination of the two subtypes makes in total 135 subtypes of Influenza A.

The current subtypes of influenza A viruses found in people are A(H5N1), A(H1N1) and A(H3N2). Influenza A(H1N1), A(H3N2), and influenza B strains are included in each year's influenza vaccine, but not yet A(H5N1) (see <http://www.cdc.gov/flu/about/fluviruses.htm#three>).

The surfaces of influenza viruses are dotted with neuraminidase proteins. Neuraminidase, an enzyme, breaks the bonds that hold new virus particles to the outside of an infected cell. Once the enzyme breaks these bonds, this sets free new viruses that can infect other cells and spread infection (see Figure 1 and <http://www.niaid.nih.gov/factsheets/fludrugs.htm>).

Hemagglutinin of influenza virus A causes membrane fusion of the viral membrane with the host membrane. Fusion occurs after the host cell internalizes the virus by endocytosis. The drop of pH inside the host cell causes release of a hydrophobic fusion peptide and a large conformational change leading to membrane fusion (see <http://pfam.wustl.edu/cgi-bin/getdesc?name=hemagglutinin>).

Influenza A (H5N1) is a subtype of the Type A influenza virus. Wild birds are the natural hosts of the virus, hence the name avian influenza or bird flu. The virus was first isolated from birds (terns) in South Africa in 1961. The virus circulates among birds worldwide. It is very contagious among birds and can be deadly to them, particularly domesticated birds like chickens. The virus does not typically infect humans. In 1997, however, the first instance of direct bird-to-human transmission of H5N1 was documented during an outbreak of the avian influenza among poultry in Hong Kong; the virus caused severe respiratory illness in 18 people, of whom 6 died. Since that time, there have been other instances of H5N1 infection among humans. But so far, H5N1 viruses

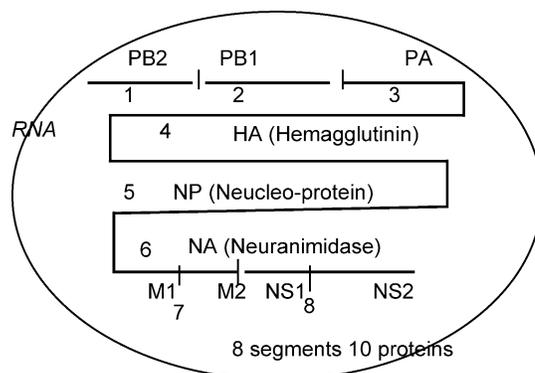


Figure 1 RNA codes of influenza virus A. RNA codes of influenza virus A consist of eight segments of gene blocks such as PB2, PB1, PA of RNA synthesis and transcription genes, HA (Hemagglutinin), NP(Nucleo-protein), NA(Neuraminidase), another block of M1 and M2, and the last block of NS1 and NS2. Infection ability consists of genetic types of HA (Hemagglutinin), and NA(Neuraminidase). Combination of types HA 1-15 and NA 1-9 makes 135 subtypes of Influenza A

have not been capable of efficient human-to-human transmission. Infected birds shed virus in saliva, nasal secretions and feces. Avian influenza viruses spread among susceptible birds when they had contact with contaminated excretions. It is believed that most cases of H5N1 infection in humans have resulted from contact with infected poultry or contaminated surfaces (<http://www.cdc.gov/flu/avian/outbreak.htm>).

The highly pathogenic avian influenza virus H5N1 caused heavy losses in poultry populations in the Chinese region in mid-2003. Starting in December 2003, eight countries and territories (Cambodia, China, Indonesia, Japan, Lao PDR, Republic of Korea, Thailand and Viet Nam) have reported confirmed outbreaks of Influenza A type H5N1. Since early February 2004 outbreaks have not been reported from additional countries. Japan ended control activities May 2004. However, the flu restarted in Vietnam, Thailand and China in July 2004.

The geographic distribution, rate of spread and severity of this epizootic are unprecedented. It is estimated that more than 100 million birds have died or have been killed in measures following OIE (Office International Epizooties) guidelines. The disease has had disastrous effects on the poultry industry through its impact on international trade and domestic consumption of poultry products. In some countries the disease situation is not clear, because of weaknesses in diagnosis, surveillance capacity and variable adherence to obligations for timely and accurate reporting. More frequent updates of the disease situation in animals is necessary to allow preventive measures in neighboring countries and to facilitate emergency preparedness for any necessary animal and public health interventions.

There are many epidemic and pandemic incidents due to other subtypes of Influenza A whose subtypes indicated with major incidents are as follows:

H1N1	1918	Spanish Influenza pandemic; 20million people died
H2N2	1957	Asian Influenza
H3N2	1968	Hong Kong Flu; Pigs infected from human, Hong Kong
H4N6	1999	Pigs were infected from birds, Canada
H5N2	1983	Chicken, USA; 1997, Chicken, Italy; 2003, Chicken, USA
H7N1	1999–2000	Chicken, Italy
H7N7	2003	Chicken, Netherlands and Germany

Strategic vaccination for influenza A

OIE organized a discussion of the use or non-use of vaccine that followed a presentation on the advantages and disadvantages of vaccines for avian influenza (FAO/OIE/WHO, 2004). The generally acceptable summary of that discussion is that: vaccine is a valuable tool in the control and elimination of avian influenza; however, vaccine alone is unlikely to lead to a successful eradication; vaccination combined with stamping out and adequate surveillance will likely lead to eradication in less time. Strategic vaccination in birds, if accompanied by appropriate surveillance will reduce the amount of virus excreted and lead to less viral exposure for humans.

Genesis of potentially pandemic influenza virus H5N1

Li *et al.* (2004) successfully demonstrated a series of genetic reassortment events traceable to the precursor of the H5N1 viruses that caused the initial human outbreak in Hong Kong in 1997 and subsequent avian outbreaks in 2001 and 2002 (Figure 2). The genetic reassortment events are accelerated by the infection rate among different host animals. These events finally converged to a dominant H5N1 genotype (Z) in chickens and ducks that was responsible for the regional outbreak in 2003–04. They indicated that domestic

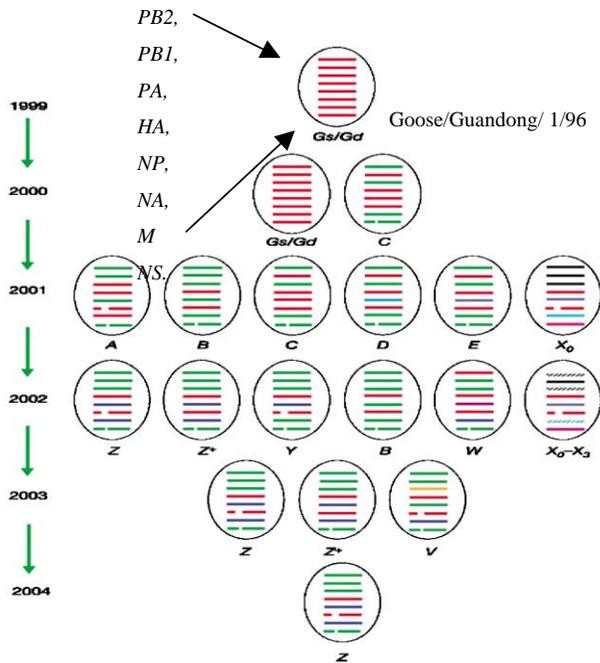


Figure 2 The genotypes of H5N1 influenza virus reassortants from Eastern Asia (Subscribers to the online version of Water Science and Technology can access the colour version of this figure from <http://www.iwaponline.com/wst>). The original genotype is Gs/Gd that means Goose/Guangdong/sample no.1/found in 1996. Eight gene segments of *PB2*, *PB1*, *PA*, *HA*, *NP*, *NA*, *M* and *NS* are shown with eight red (darker) bars. There was a new reassortant C emerged with green (paler) bars and a deletion of the green bar in 2000. There were other reassortants A, B, D, E, X₀ emerged in 2001. Color change with bars indicates significant changes in genetic sequences. Other genotypes Z, Z⁺, Y, W, X₁, X₂ and X₃ emerged in 2002. The genotype V emerged in 2003. Since January 2002, genotype Z, which contains both the NA and NS1 deletions, has become the dominant H5N1 virus in southern China. In February 2003, human H5N1 disease was diagnosed for the first time since December 1997. The human isolates (A/HK/212/03 and A/HK/213/03) had the same gene constellation as genotype Z but lacked the NA stalk deletion, and were designated genotype Z⁺. Sixty-two H5N1 virus isolates from 2003 were genetically sequenced and 60 of them belonged to genotype Z. All of the viruses that caused outbreaks in Indonesia, Thailand and Vietnam in late 2003 and early 2004 were genotype Z viruses

ducks in southern China had a central role in the generation and maintenance of this virus, and that wild birds may have contributed to the increasingly wide spread of the virus in Asia. Their results suggest that H5N1 viruses with pandemic potential have become endemic in the region and are not easily eradicable. These developments pose a threat to public and veterinary health in the region and potentially the world, and suggest that long-term control measures are required.

Wildlife management

OIE recommended wild life management (FAO/OIE/WHO, 2004). Massive killing of wild birds thought to be pests in the region led to massive famine and failed crops since the wild birds in fact were controlling crop pests more than being crop pests. Therefore wildlife not only warrants protection due to its aesthetic and cultural values, but also because of the ecosystem “services” provided at very low costs by animals and plants in the environment. As a result it was concluded that wild birds should not be depopulated in an attempt to control avian influenza but separation as much as possible should be attempted.

Reducing contact rates between wild birds and large commercial poultry operations aims to prevent wild waterfowl from direct or indirect contact. Village poultry health care programs, including possible vaccination programs and certainly health/husbandry education is the best approach to (1) provide an entree for surveillance operations, (2) reduce disease incidence, (3) improve rural livelihoods, and (4) reduce the threat or introduction of diseases into wild bird populations.

Zoonoses and the necessity of human and animal sanitary improvement

In addition to medical measures, including strategic vaccination for Influenza A, and wildlife management, there is another way to reduce the risks. *Li et al. (2004)* designated South China where there are hot spots where viral infection rates are accelerated among birds, mammals and human beings. Living conditions of birds, mammals and human beings are so close that there are always risks of viral infection. When we examine the living conditions of farmers in southern China, North Vietnam, Laos and north Myanmar, we see that, they commonly raise ducks/chickens with pigs sharing ponds where they discharge household wastewater including human excreta and pig excreta. The ponds are used for raising ducks and aquaculture. Other important players are migrating birds from north Asia, which are principal vectors of bird virus (*Figure 3*).

Since ducks are original hosts of all subtypes of Influenza A that do not harm ducks, duck feces discharged into duck ponds are the origin of dispersion of the virus, when the ponds are used as drinking waters for chicken and pigs. When pig feces are discharged into the duck pond water without proper treatment, this may transmit a reassorted virus into the pond where ducks are infected without significant disease symptom. Chicken farms feces might be discharged into water. Human excreta in China and Vietnam are traditionally used for agriculture without proper treatment. Here is the urgent necessity of common problems of sanitation for people and domesticated animals to control zoonoses such as influenza A virus and SARS virus. Good sanitary measures may not completely stop transmission of the viruses but would slow down the rate of reassortment of the viruses.

Ecological sanitation approach with modern technology can provide solutions

Discharge of urine and feces of animal and human without proper treatment must be stopped in those hot regions. Current practices of animal and human excreta discharge constitute a simple reuse of nitrogen and phosphate for agriculture, aquaculture and duck rearing. It is not a good solution to plan sewage works in the region, because it is simply financially impossible. It is relatively easy to provide urine and feces diversion toilets to

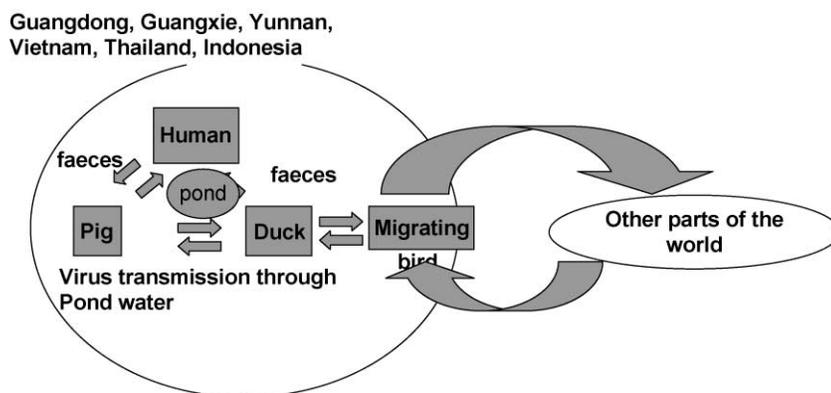




Figure 4 Urine and faeces separation toilets for ecological sanitation practice

people in the hot regions. North Vietnamese people are accustomed to use the diversion toilets because of their tradition of such type of toilet (Figure 4). Vacuum trucks collect separated urine and feces to bring to ecological plants. It is an easy practice for a municipality or another local authority to collect and transfer them. Collected urine can be easily converted to phosphate fertilizer in the form of magnesium ammonia phosphate (MAP) and ammonia sulfate, both of which are equivalent to chemical fertilizers in quality. Collected feces are easily fermented into methane that can provide heat and electric energy to operate the ecological plant. The fermented residue is disinfected in terms of virus pathogen and used as organic fertilizer. The same approach could be applied to pig farms where urine and feces separation is practiced by providing optimum living conditions to pigs in the pig house. The water from duck ponds must not be provided directly to pigs, chickens and quails for drinking. Drinking water for them must be treated to be virus free.

Conclusion

Severe acute respiratory syndrome (SARS) and the avian influenza A (H5N1) clearly showed typical zoonosis incidents in 21st century that remain at high risk of pandemic occurrence. The key animals are domestic ducks in southern China and Vietnam which have a central role in the generation and maintenance of the viruses, and wild birds that may have contributed to the increasingly wide spread of the virus in Asia. Good sanitary conditions with water to humans and domesticated animals in Vietnam and China are urgently needed to reduce the risk by slowing down the rate of reassortment of the viruses. An ecological sanitation approach can be introduced to Vietnam and China, easily compared to sewage works that are not affordable to reduce the risk in the hot regions.

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