

H5N1 highly pathogenic avian influenza in Southeast Asia

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Summary

Since the first H5N1 highly pathogenic avian influenza virus (HPAIV) infection in the region in August 2003, Cambodia, Laos, Malaysia, Myanmar, Indonesia, Thailand and Vietnam have all recorded outbreaks of the disease. The HPAIV continues to occur in some countries in Southeast Asia despite control programmes encompassing surveillance, vaccination and stamping out strategies. A number of strains have been circulating in the region since the first outbreaks in 2003, and although the source of the initial outbreaks in domestic poultry is not known, the continuing propagation of disease in the region is primarily the result of the movement of domestic poultry and poultry products, and people. A comprehensive approach using all the strategies available to break the chain of transmission of the virus in poultry will be needed to achieve lasting disease control.

Keywords

Avian influenza – Antigenic variant – Disease transmission – H5N1 – Marketing.

Introduction

Since the isolation of highly pathogenic avian influenza virus (HPAIV) subtype H5N1 from a domestic goose from Guangdong Province in China (*A/goose/Guangdong/1/96*) in 1996, H5N1 highly pathogenic avian influenza (HPAI) has been identified in domestic poultry and/or wild birds from 61 countries (15). The disease has also been confirmed in over 380 people, with more than 230 fatalities (4).

Between 2003 and 2008, seven of the eleven countries of the Southeast Asian region declared outbreaks of HPAI (Table 1). Official notification of mortality in chickens caused by H5N1 HPAIV infection was made first from Vietnam in December 2003 (8). Indonesia reported disease in January 2004, but retrospective assessment suggests that

outbreaks of the disease occurred in domestic poultry in Indonesia as early as August 2003 (9). Similarly, disease may have been present in Vietnam prior to December 2003 (8). High poultry mortalities due to other infections such as Newcastle disease are common in some Southeast Asian countries and this may have contributed to delays in detection and diagnosis of HPAI (8). Estimates in 2005 put losses of domestic birds in the region at 140 million, with a cost of approximately US\$10 billion (5).

Shortly after detection of HPAIV H5N1 in Vietnam, other countries in the region – Thailand, the Lao People's Democratic Republic (Lao PDR), Indonesia and Cambodia – made notifications in rapid succession. Outside Southeast Asia, China, Japan and Korea also reported outbreaks between December 2003 and January 2004. By the end of January 2004 almost all Thai and Vietnamese provinces were affected. A second wave of outbreaks began

Table 1
H5N1 outbreaks in Southeast Asia in 2006 and 2008 (completed with information from FAO AIDNews archives, 2006 to 2008)

Country	2006	Year 2007	2008
Brunei	–	–	–
Cambodia	February-April, August	April	December
East Timor	–	–	–
Indonesia	Outbreaks detected frequently in many areas	Outbreaks detected frequently in many areas	Outbreaks detected frequently in many areas
Lao PDR	July	February-March	February-March, August-September, October-November
Malaysia	February-March	June	–
Myanmar	March-April	March-September, November, December	–
Singapore	–	–	–
Thailand	July	January, March	January, October, November
Philippines	–	–	–
Vietnam	August, December	Outbreaks detected frequently in many areas	Outbreaks detected frequently in many areas

in June 2004, culminating in large numbers of outbreaks in Thailand at the end of 2004 and in Vietnam in early 2005. Malaysia reported its first cases of H5N1 in August 2004, but subsequently eradicated the disease by mass culling (3, 8, 11).

Multiple strains of HPAIV H5N1 were circulating in the region, complicating the epidemiological investigation of the epidemic. Most of the virus subtypes were derivatives of genotype Z, which was first identified in Hong Kong in 2002 and is itself derived from A/goose/Guangdong/1/96. It appears that this genotype is more virulent than its predecessors and is able to infect a wider range of species. Prior to this, six Asian lineage H5N1 genotypes (A, B, C, D, E and X₀) had been identified from aquatic and terrestrial poultry. Eight new genotypes, including Z, were identified after 2002 (7). Although the viruses causing outbreaks in the region were all genotype Z, also now called Asian-lineage H5N1, the subtype isolated from Indonesian outbreaks in 2003 and 2005 is now recognised as being different from those found in Thailand, Vietnam, Lao PDR and Cambodia. Genetic studies suggest that in the latter four countries the outbreaks were epidemiologically linked, with either a single introduction or multiple concurrent introductions from a common source (11). It was proposed that the initial spread occurred concurrently in a number of countries from wild birds to domestic poultry (9). However, the rapid spread of very virulent infectious bursal disease virus throughout Southeast Asia in 1990/1991 demonstrated that infections of poultry can spread quickly throughout the industry in that region, even without the involvement of wild birds. Subsequent spread of H5N1 HPAIV within the region has been

attributed to movement of domestic poultry and poultry products, and of people.

Propagation of the epidemic

Between 1999 and 2002 HPAIV H5N1 was isolated from healthy ducks in China and these viruses were shown to be antigenically similar to A/goose/Guangdong/1/96 (2). In 2001 a cross-sectional study of live bird markets in Vietnam found HPAIV H5N1 in healthy geese (10). In both cases the viruses were highly pathogenic for chickens. The H5N1 viruses found in 2001, however, differed genetically, antigenically, and in the resulting pathology, from those that later caused outbreaks in Vietnam in 2004 (9, 10).

Indonesia reported its first case of HPAIV H5N1 in poultry in January 2004 (16), although the epidemic is believed to have started in August 2003 (9). The disease is now considered endemic in many areas of the islands of Java, Bali and Sumatra, and in the southern Sulawesi (11, 13). As of December 2008, only two of Indonesia's 33 provinces had not reported outbreaks of the disease. On sequence analysis Indonesian viruses group to subclade 2.1 (Fig. 1).

As previously stated, the initial outbreaks in Thailand, Vietnam, Lao PDR and Cambodia occurred in late 2003, with a second wave in mid 2004 (8). Viruses in these outbreaks belonged to clade 1. Circulating viruses in the region today continue to belong to this clade, in addition to clade 2.3, suggesting a second introduction of HPAIV H5N1 in the region (Fig. 1). Subsequently, Thailand

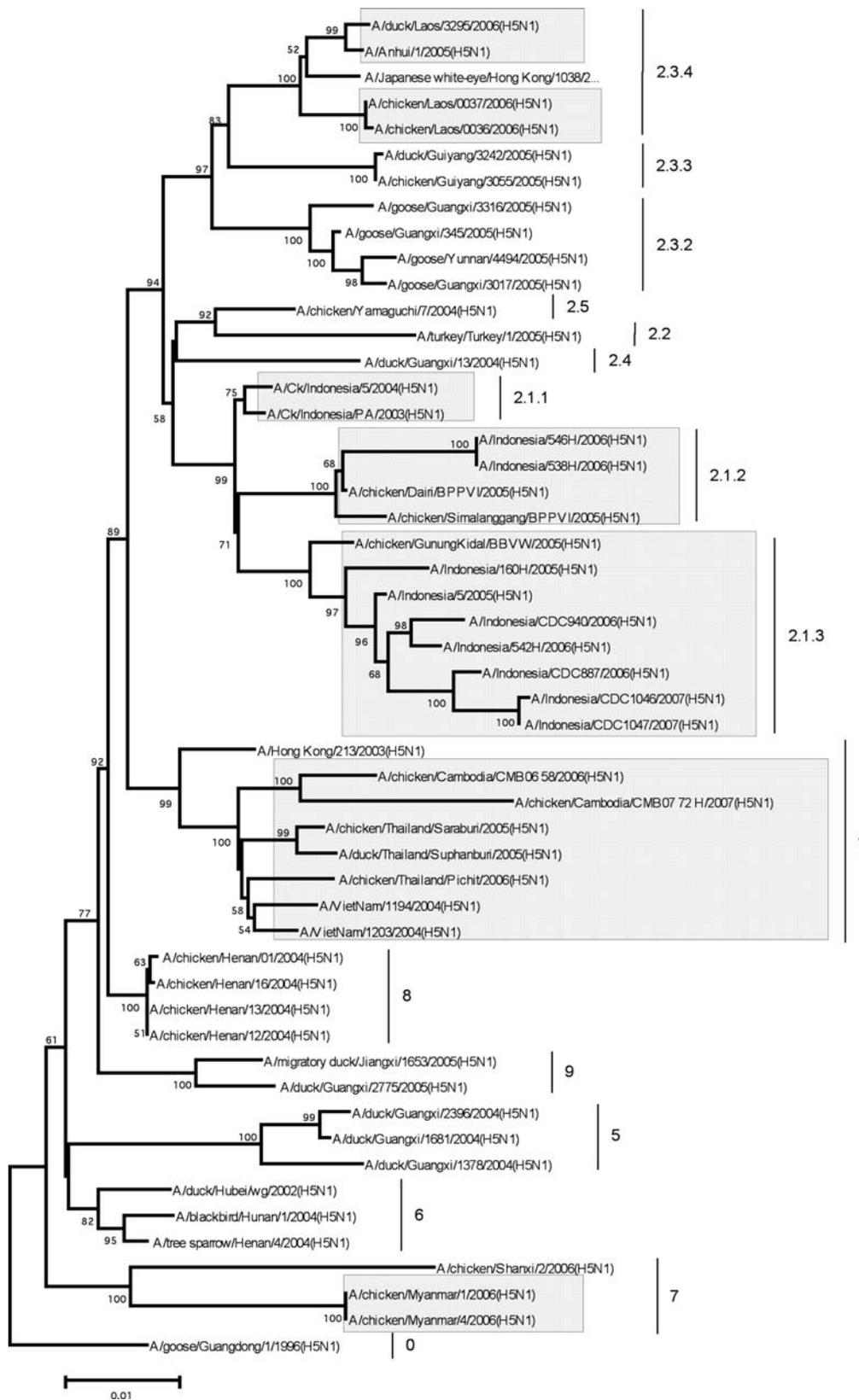


Fig. 1
Neighbour-joining tree of representative Southeast Asian highly pathogenic avian influenza virus H5N1 strains

The tree shows haemagglutinin clade relationship designations according to the World Health Organization (WHO) / World Organisation for Animal Health (OIE) / Food and Agriculture Organization (FAO) unified nomenclature system (WHO/OIE/FAO H5N1 Evolution Working Group and the Australian Animal Health Laboratory)

recorded outbreaks in July 2006, followed by an absence of disease until January and March 2007. Outbreaks were again detected in 2008, with notifications in January and October. Thailand has used intensive surveillance and stamping out programmes for disease control. It has also instigated legislation for duck rearing to minimise the role of domestic ducks in the spreading of H5N1.

In Vietnam, outbreaks have occurred intermittently from late 2006 through to the end of 2008 in many areas of the country. Control measures in Vietnam have relied heavily on vaccination, including vaccination of domestic ducks, but have also included restriction of duck rearing, closure of larger urban live bird markets and extensive campaigns to increase public awareness and initiate behaviour change of producers (6).

Outbreaks of HPAIV H5N1 occurred in Lao PDR from December 2003 or January 2004 to March 2004 (9). There have been intermittent outbreaks reported in recent years, including in 2008 (3). Initial phylogenetic analysis of isolates obtained from outbreaks in March and August/September 2008 suggests that the second outbreak was caused by a reintroduction of the virus, possibly from neighbouring China (4).

Initial outbreaks in Cambodia occurred between December 2003 and April 2004, with recurrences in September 2004 and January 2005. Outbreaks also reportedly occurred in August 2006, April 2007 and December 2008 (4).

In Myanmar, the first reported cases of HPAIV H5N1 occurred in March and April 2006, with disease present throughout much of 2007 and into January 2008 (16). Active surveillance detected seropositive ducks in 2008, but there were no recorded outbreaks during that year.

Malaysia's first reported outbreak was probably due to illegal importation of a fighting cock, and occurred on the Thai/Malaysian border (11). The country reported its second outbreak of HPAIV H5N1 in March 2006, and a subsequent infection in June 2007. There have been no reported cases from Malaysia in 2008.

Epidemiological considerations

The epidemiology of Asian H5N1 HPAIV differs in a number of ways from previous HPAIV:

- in late 2000/early 2001 there was an expansion of the host range of the HPAIV H5N1 to ducks, attributed to genetic changes in the virus, sometimes resulting in disease but often with asymptomatic infections. This is thought to be a significant factor in spread of the disease in the Southeast Asian region, particularly when combined with free-range duck rearing systems in some countries (8, 11, 12);

- the current Asian lineage HPAIV H5N1 appears to be circulating in several species of wild birds, an uncommon occurrence for HPAIV (9). An involvement of domestic ducks in the reassortment of H5N1 viruses and their phylogenetic similarities to wild aquatic species may have contributed to this phenomenon (11);

- there appears to have been a change in transmission from the faecal/oral route to the respiratory route in poultry and in some wild aquatic bird species. Recent studies using current strains of H5N1 found that in juvenile mallards and Pekin ducks, virus was present in higher titres in the trachea than the cloaca, both in inoculated and in contact birds (1, 12);

- as with other infectious diseases of poultry, continuing propagation of infection in the region has been attributed to trade and movement of live birds, free range duck rearing systems, live bird markets and minimal biosecurity in semi-intensive poultry production systems (6, 8, 11, 12).

After an intensive month of surveillance by the Thai Government at the end of 2004 (the 'X-ray survey'), a strong association between the distribution of HPAIV outbreaks and free-ranging ducks was observed. Other associated factors included the number of native chickens, the number of fighting cocks and the size of the human population. Outbreaks also occurred more commonly on lower plains than in more elevated regions (6). This correlation between duck rearing areas and poultry outbreaks was not seen in the initial outbreaks of late 2003 to early 2004 (8). The second wave of outbreaks in Vietnam was also correlated with the number of ducks in the region (6, 9).

Seasonally, the peak time for HPAIV H5N1 outbreaks in Southeast Asia is winter. Cooler temperatures (which increase virus survival time) and the increased demand for, and movement of, poultry for festivals have been considered contributing factors for this seasonality.

Under the World Health Organization (WHO)/ World Organisation for Animal Health (OIE)/ Food and Agriculture Organization (FAO) classification system, ten clades and many sub-clades of Asian-lineage H5N1 are now recognised (Fig. 1) (14). These clades are based on phylogenetic differences in the haemagglutinin (HA) gene, but do not differentiate genotypes or antigenic variants. As such, more than one genotype is seen in some of the phylogenetic clades (11). All Indonesian viruses are found in subclade 2.1, whereas those from Thailand, Vietnam, Lao PDR, Cambodia and Malaysia are predominantly from clades 1 and 2.3 (11, 17). In early 2006, Myanmar isolated a strain belonging to clade 7 and recently clade 7 has also been detected in northern Vietnam (14).

An important development relating to the control of HPAI globally has been the detection in Indonesia of isolates of HPAIV H5N1 against which the currently available vaccine strains are no longer protective. The discovery has led to a significant OFFLU (OIE/FAO Network of Expertise on Avian Influenza) coordinated response between Indonesian and international scientists under which the HA genes of over 200 isolates of HPAIV H5N1 from Indonesia have been sequenced, and the isolates analysed antigenically using cross-haemagglutination inhibition tests and antigenic mapping. These studies have confirmed that to date all of Indonesia's isolates belong to subclade 2.1, but with significant within-country variation now present. Clades 2.1.1 to 2.1.3 are now recognised, with some other isolates falling outside these subgroupings. The strains that are significantly different antigenically from vaccine strains have not yet been shown to be widely distributed, but progressive antigenic drift of the Indonesian isolates has been confirmed.

The development of antigenic variants has the potential to change the way vaccines for HPAI are developed, marketed, and used, and will certainly impose more rigorous requirements for monitoring and surveillance within the framework of vaccination programmes.

Opportunities for control

Control of H5N1 HPAI in Southeast Asian countries has been made difficult by the complexities of the poultry industry and by the huge poultry populations. For example, Indonesia has a commercial poultry population of up to 1.2 billion birds, and 300 million village chickens. Indonesia has a large free-range duck industry and village ducks are common. Vietnam and Thailand have even larger grazing duck industries, and this type of husbandry system is considered to present huge biosecurity problems. However, even farms commercially raising chickens, either broilers or layers, have not practiced any effective biosecurity in the persistently infected countries. In a country the size of Indonesia there are not enough financial resources to vaccinate all poultry, and vaccination has mostly been practiced in an *ad hoc* manner by interests seeking to protect commercial investments. However, such vaccination programmes have not been conducted under any system of coordinated monitoring.

The huge size of the poultry industries in less affluent countries also leads to situations where there are not sufficient funds to implement an effective culling and compensation approach to disease control. If infectious animal diseases are to be successfully managed, the blocking of the chain of transmission from infected to uninfected animals is an essential component of control programmes. Transmission is blocked by strategies such as culling of infected animals, and movement controls from

known infected premises or areas to uninfected areas or premises. Quarantine and farm-gate biosecurity are strategies designed to protect disease-free places, but are frequently not sufficient as stand-alone strategies. The control of the movement of infected birds is an essential complementary measure.

Poultry marketing systems are complex in Southeast Asia, and vary from totally informal arrangements in villages and with smallholder producers to more regulated requirements for the commercial sector that are usually not effectively implemented. The management of potentially infected birds through the marketing system is a facet of the industry that is receiving increasing attention among countries in the region. There is anecdotal information that a component of risk management in poultry raising in some areas has involved rapidly disbursing birds to market at the first signs of ill health in a flock. Studies of birds in the market chain confirm high levels of infection, and by inference, of transmission. Success in dealing with such issues will be an essential component of H5N1 management in the region.

There has been a huge international response to the challenge of H5N1 in Southeast Asian countries, particularly with the objective of reducing human exposure to infection and, consequently, the number of human cases. This is seen as an essential component of managing the risk of a pandemic outbreak of H5N1 influenza in people. The collaborative programmes throughout the region have seen significant gains in capacity building in the participating countries, in terms of public and veterinary laboratory diagnostic capability, Veterinary Services, public and veterinary disease management systems, surveillance, biosafety, public awareness and policy development.

However, the future of the prolonged HPAIV H5N1 epidemic in Southeast Asia remains unclear. The disease has been described as 'entrenched' in some countries. Countries which showed promising early success in its control, such as Thailand and Vietnam, continue to experience further outbreaks. Countries such as Indonesia have made considerable advances in developing surveillance and diagnostic capabilities, but are faced with enormous challenges due to the size of the poultry industry, its complexity and the limited resources available in proportion to the scale of the problem. The uncertainty regarding viable strategies for long-term use of vaccines adds to the problem. Attention is being focused on actions that will physically interrupt the chain of transmission of infection, such as poultry industry restructuring, changes to marketing practices and improvements in the biosecurity of commercial premises. It is only through a comprehensive approach employing multiple interventions that H5N1 infection may be brought under control.

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L'influenza aviaire hautement pathogène due au virus de sous-type H5N1 en Asie du Sud-Est

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Résumé

Depuis sa première apparition dans la région en août 2003, des foyers d'influenza aviaire hautement pathogène due au virus H5N1 ont été notifiés au Cambodge, au Laos, en Malaisie, au Myanmar, en Indonésie, en Thaïlande et au Vietnam. Malgré les programmes de lutte mis en place, axés sur la surveillance, la vaccination et l'abattage sanitaire, le virus de l'IAHP continue de circuler dans certains pays du Sud-Est asiatique. Plusieurs souches circulent dans la région depuis les premiers foyers de 2003 ; bien que l'on ignore l'origine des premiers foyers qui ont affecté les volailles domestiques, il est établi que la cause de la propagation ininterrompue de la maladie dans la région réside dans les mouvements de volailles domestiques et de produits avicoles, ainsi que dans les déplacements humains. Une démarche intégrée faisant appel à toutes les stratégies disponibles pour briser la chaîne de transmission du virus chez les volailles est indispensable si l'on veut réussir à maîtriser durablement la maladie.

Mots-clés

Commercialisation – H5N1 – Influenza aviaire – Transmission – Variant antigénique. ■

Influenza aviar altamente patógena por H5N1 en el Sudeste asiático

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Resumen

Desde que en agosto de 2003 se declaró la primera infección por virus de la cepa H5N1 de la influenza aviar altamente patógena (IAAP), se han registrado brotes de enfermedad en Camboya, Laos, Malasia, Myanmar, Indonesia, Tailandia y Vietnam. Pese a la aplicación de programas de control que incluyen estrategias de vigilancia, vacunación y sacrificio sanitario, la IAAP sigue presente en algunos países del Sudeste asiático. Desde los primeros brotes ocurridos en 2003, varias cepas han venido circulando por la región, y aunque se ignora el origen de los primeros brotes en aves domésticas, la continua diseminación de

la enfermedad en la región se debe principalmente al movimiento de personas y de aves domésticas y sus derivados. Para lograr un control duradero de la enfermedad hará falta un planteamiento global que combine todas las estrategias existentes a fin de romper la cadena de transmisión del virus en las aves de corral.

Palabras clave

Influenza aviar – H5N1 – Marketing – Transmisión de enfermedad – Variantes antigénicas.



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