Avian influenza in South East Asia

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Since the H5N1 virus first appeared in China in 1996, it has undergone dramatic evolution, both genetically and in its biological properties. This article discusses the evolution of H5N1 and the paradigm shift that has occurred in our understanding of the ecology and biology of avian influenza viruses as a result of the H5N1 experience.

The A/goose/Guandong/96 H5N1 virus was first identified in 1996 and quickly spread to Hong Kong and throughout southern China. It caused serious outbreaks in commercial poultry, resulting in the slaughter of over 2 million birds [1]. These outbreaks resulted in the introduction of one 'bird-free' day every month to the live birds markets in an attempt to control the spread of the virus [1]. This measure, together with culling and vaccination, slowed the spread of the virus.

In Hong Kong in 1997, the H5N1 virus sent shudders through the influenza virology community when it infected 18 humans, six of them fatally [1]. This was the first reported human infection of a virus that was derived directly from birds, without going through the pig as a mixing vessel. Subsequently, in 1999, a second influenza virus, H9N2, was transmitted directly to humans from birds, although no fatal infections were reported [1].

The goose/Guandong virus persisted in Asia relatively unchanged from 1996 until 2000 when a second genotype of virus appeared, incorporating genes from H9N2 and H6N1 influenza viruses derived from other aquatic birds [2]. Genes coding for the non-structural, matrix and polymerase proteins were introduced from the aquatic bird avian influenza virus gene pool through reassortment (Figure 1).

Between 2000 and 2003 multiple genotypes of H5N1 viruses were isolated, incorporating genes from other influenza A viruses. H9N2 viruses isolated in Hong Kong in 2003 were shown to have internal genes from H5N1 [2]. By 2004 most of these lineages were extinct and only the Z genotype was being isolated.

Evolution of H5N1 not only resulted in new genotypes but in viruses with different biological properties. In 2003 the H5N1 virus changed its receptor binding ability, acquiring a human cell receptor binding domain. The number of known human infections of H5N1 since 2003 has now exceeded 200, with over a 50% case fatality rate [3] (Table 1).

H5N1 is possibly evolving toward a pandemic virus with a broader host range, as demonstrated by its ability to infect mammals such as wild and domestic cats, dogs as well as mice and ferrets [4-6]. The tissue trophism of the later H5N1 viruses has also changed, expanding to cause nervous signs in infected animals [6].

Phylogenetic analyses of the H5 haemagglutinin genes from the 2004 and 2005 outbreaks show two different lineages. Clade 1 H5N1 viruses were isolated from Vietnam, Thailand and Cambodia, Laos and Malaysia. The more divergent Clade 2 viruses were isolated in China, Indonesia, Japan and South Korea. Clade 2 viruses have diversified into three sub-clades, one of which is related to the goose/Guandong/96 virus that re-emerged in 2004 and 2005 [7].

Genotype V viruses also re-emerged in 2005. The haemagglutinin genes from H5N1 viruses isolated from human specimens were closely related to genes from H5N1 viruses of avian origin. Human virus haemagglutinin gene sequences differ from the nearest gene from avian isolates from the same year by 2–14 nucleotides [7]. These findings are consistent with the epidemiologic data that suggest that humans acquired their infections by direct or indirect contact with poultry or poultry products.

H5N1 viruses have been isolated from many species of free ranging wild birds and have probably been circulating in these species since the first detection of the virus in geese in 1996. From 1999 onwards, H5N1 virus was detected in many avian species from Hong Kong. In particular, the number of virus isolations from ducks and geese increased from 1999-2001. In 2002 the first report of deaths of wild birds due to H5N1 were reported in Hong Kong [8]. In January 2003, the mortality extended to flamingos in Kowloon Park, Hong Kong and in May 2003 the H5N1 virus was also detected in Japan in imported duck meat [9]. In 1961 an H5N3 virus was isolated from dead terns in South Africa [10], but, apart from this one case, highly pathogenic avian influenza viruses isolated from chickens traditionally cause no disease in wild birds. However, recent H5N1 viruses have evolved the ability to cause disease in ducks and wild birds [8]. The clinical syndromes seen in H5N1 infected ducks range from unapparent infection, the traditional situation, to respiratory disease and to nervous disease with high mortalities.

Highly pathogenic avian influenza viruses usually evolve from low pathogenic viruses by the acquisition of multiple basic amino acids at the cleavage site of the haemagglutinin protein. The current

MICRO-FACT

The threat of pandemics from influenza A viruses is related to their capacity to infect other animal species, especially aquatic birds.

H5N1 virus is unusual in that no low pathogenic progenitor virus has ever been identified. All of the reported H5N1 virus isolates have been highly pathogenic for chickens.

In December 2003 and January 2004 outbreaks of H5N1 in commercial chickens and ducks were reported almost simultaneously in Vietnam, Indonesia, Korea and Japan. China reported outbreaks very soon after this, followed by Thailand, Malaysia and eventually Cambodia, Laos and Myanmar. Although the H5N1 virus continues to circulate in domestic poultry in the region, the role of wild birds in the epidemiology of H5N1 was unclear. In 2004 there was a mass mortality of bar-headed geese at Qinghai lake in central China [12]. Within months, the virus had spread westward into Central Asia, South Asia, the Middle East, Eastern Europe and eventually Western Europe and Africa [12, 13]. The majority of isolations were from wild birds but in several affected countries commercial poultry were also infected. Many human infections were reported, as well as infections of dogs and wild and domestic cats. As a result of the ongoing outbreak in Asia, FAO estimates that over 200 million birds have been culled in the region.

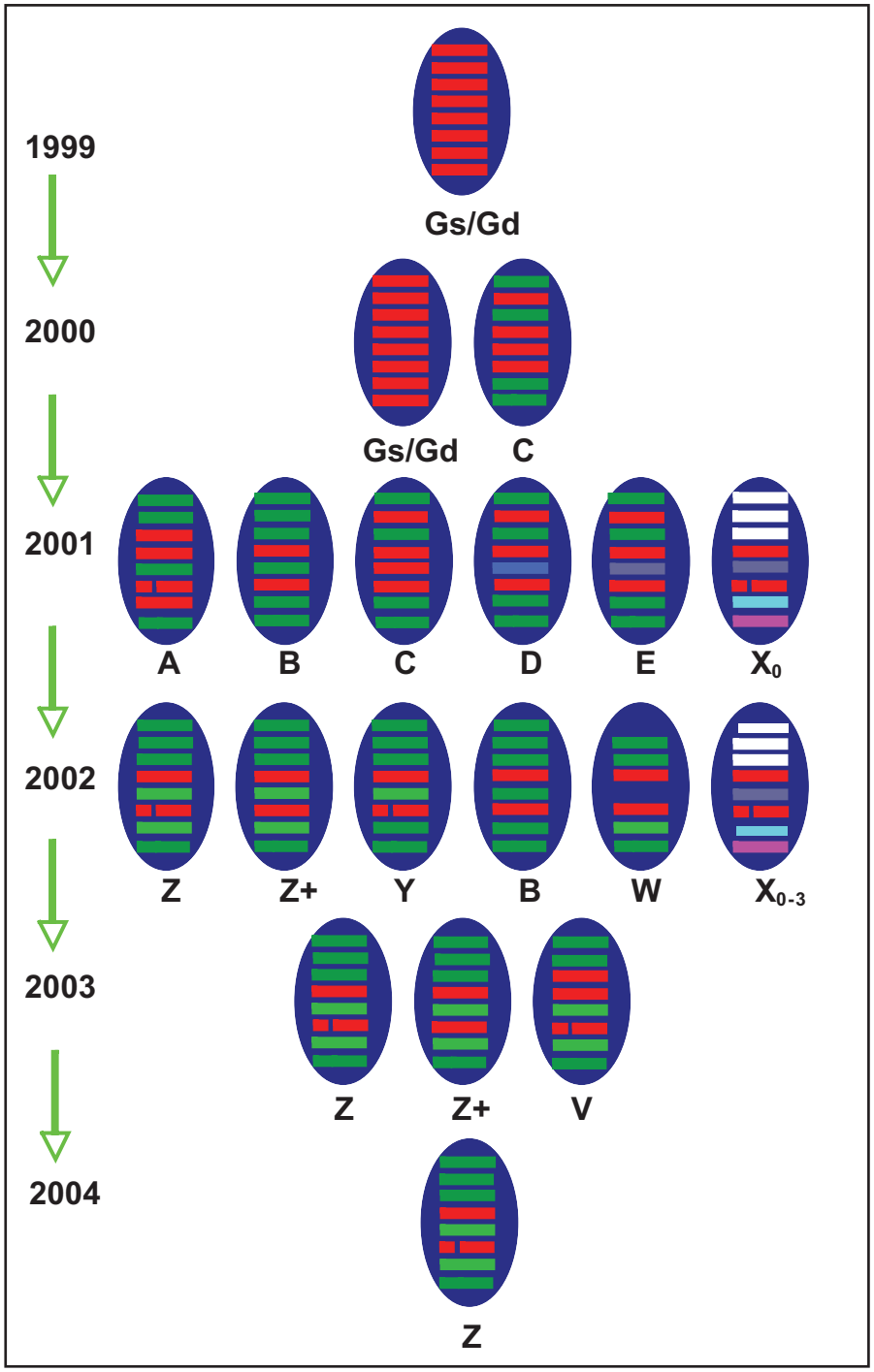

Figure 1. Evolution of H5N1 viruses between 1999-2004 [2].

MICRO-FACT

The manufacture of most influenza vaccines involves the use of very large numbers of fertile chicken eggs.

While it has been demonstrated that migrating birds can carry the virus over long distances, in Siberia, Eastern and Western Europe, it is not clear whether wild birds can act as long-term reservoirs of H5N1 viruses or if the virus originates in domestic poultry. In most European countries where the virus has appeared, it has been in the wild birds. In East and Southeast Asia, the disease was probably spread by a combination of domestic and wild birds, while in Africa the poultry trade and traffic was largely responsible. Despite advances in the diagnosis and control of H5N1, evolution of the virus suggests that the problems will persist for many years to come.

Table 1. Cases of H5N1 infection in humans and associated mortalities (World Health Organization, Geneva).

Country	Infections	Deaths
Azerbaijan	8	5
Cambodia	6	6
China	21	14
Egypt	14	6
Indonesia	61	46
Iraq	2	2
Thailand	24	16
Turkey	12	4
Vietnam	93	42
Total	**241**	**141**

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ASM joins APACE

The Australian Professional Acknowledgement of Continuing Education (APACE) is a voluntary continuing education programme for medical scientists designed and administered by the Australian Institute of Medical Scientists (AIMS)

Recently the Australasian Association of Clinical Biochemists (AACB) and the Australian Society for Microbiology (ASM) signed a memorandum of understanding with AIMS to allow AACB and ASM members to also participate in the APACE programme.

AIMS will continue to administer the APACE programme. ASM members will be able to enrol in the programme for an annual fee of $25.00 (non-member rate $184.80). Applications from ASM members wishing to enrol in APACE will be processed initially by the ASM National Office. Application forms will be available shortly on the ASM website and joining APACE will be an option for members when paying their annual membership subscription.

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The healthcare industry is undergoing rapid changes and there is now a requirement for medical scientists, especially those in supervisory positions, to continually develop their knowledge and skills in relation to their professional practice through participation in a continuing education programme. By joining APACE, all medical scientists will have access to the same continuing education programme. To gain APACE accreditation, participants will be required to accumulate a minimum of 100 CEU credits within a maximum submission period of 2 years (3 years for rural members).

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