NOTHING TO BE SNEEZED AT

What is avian influenza and what dangers does it present for Australians and their birds?

BY ROB HEINSOHN, DAVID ROSHIER AND LEO JOSEPH

IN 1997, SHOCK waves hit the world with the first reported human fatality to avian influenza. The outbreak swept through the chicken farms and live bird markets of Hong Kong. The same deadly strain reappeared in 2002 and has since devastated the poultry industry in large parts of south-east Asia. In 2005, the virus struck migratory birds at Qinghai Lake, China, where amongst other victims it claimed an estimated 10 per cent of the global population of Bar-headed Geese. Since then, similar outbreaks among wild and domestic birds have been reported across Asia, Europe, the Middle East, and several African countries. By June 2008, this deadly strain (H5N1, see Box 1) had killed members of more than 60 bird species, and 385 cases of human infection and 243 human deaths had been reported in 14 different countries. Consequently, health authorities in many countries have devised contingency plans in case 'bird flu' becomes transmittable from human to human, which would greatly increase the risk of a pandemic.

Influenza pandemics are characterised by the worldwide spread of novel strains for which most of the human population lacks immunity. These pandemic strains typically drive previous strains of flu to extinction and cause heightened sickness and mortality. Historical records suggest that there have been 10 human influenza pandemics in the last 250 years. The last two, in 1957 and 1968, involved a combination of human and avian-adapted influenza viruses. Although pigs have always seemed a likely intermediary between birds and people, the apparently recent direct leap of the virus from bird to human suggests that rearrangement into a human disease can take place in humans themselves.

Whether the recent outbreak of the deadly H5N1 bird flu virus indicates that a human pandemic is imminent depends on a large range of factors, all of which relate to the ecology of the viruses and their original bird hosts, particularly how the viruses are spread. People living with (and moving) infected domestic birds appear to pose the greatest risk, but the potential role of migratory birds to spread flu viruses has also been in the spotlight.

Understanding the virus and its hosts

Before getting carried away by visions of high-flying, sneezing birds, it is useful to consider the different forms in which the avian influenza virus can occur, and how it is spread. In birds, most types of flu virus affect the digestive tract, not the respiratory system. Infected birds shed the viruses through their faeces rather than via the large volumes of mucus we normally associate with flu. There are many 'low pathogenic' subtypes of avian influenza (LPAI) which seem to cause little harm to wild birds, although other sub-types (see Box 1) can become deadly if transmitted to domesticated birds. The switch from low to high pathogenic status is achieved via modification of the part of the virus responsible for its replication. Interestingly, a recent study has confirmed

A large flock of Wandering Whistling-Ducks take to the air at Lake Murray in the Western province Papua-New Guinea. Though plentiful the birds proved difficult to capture for research into potential influenza pathways. Photo by **David Roshier**

In some ways bird flu is a misnomer because it affects the digestive rather than the respiratory tract and hence it is unlikely coughed or sneezed out in mucus. Here a perfectly healthy Crimson Rosella sneezes away water after drinking. Photo by **Raoul Slater**

that the H5N1 virus has shifted to become a disease of the respiratory tract in domestic ducks.

Scientists have also recently identified an essential difference between human and avian flu viruses that has so far helped to prevent large-scale human to human spread of H5N1, and hence a major flu pandemic. It seems that H5N1 viruses can only replicate in the lower part of the human respiratory tract; from there they have trouble making it into the mucus sprayed on the outside world via coughs and sneezes. Fortunately, multiple mutations in the viruses are required to allow them to bind to the tissue further up the tract from where (like regular human flu viruses) they can easily infect new victims.

As low pathogenic forms are the stock in wild birds that might lead to the more deadly strains, we need to understand the ecology of their hosts in order to assess the threat from this source. For example, many infected bird species are from wetlands and aquatic environments where the virus is shed in large amounts into the water. Other animals that drink the surface water, or use it for feeding, face a higher chance of infection. Thus, dabbling ducks, more than diving ducks, are particularly prone to LPAI infection because they feed at the surface. The virus seems to need water to survive for extended periods. It persists for longer in colder water: for example, only four days at 22°C, but 30 days at 0°C. Hence, the icy ponds and lakes of northern latitudes, where many migratory species congregate over summer, may be reservoirs for re-infection each year. However, the virus has trouble surviving in salty water, so that birds that feed in the sea seem relatively unaffected by it. Also, we know that juvenile birds that have not had prior contact with the bird flu viruses are most likely to develop symptomatic disease.

Migration has long been suspected to be a promoter of LPAI infection in birds. Long-distance migration is common in several bird groups, especially waterfowl and waders that travel very long distances up and down the globe. These migrants often form huge flocks at suitable stopover and wintering sites, which increases the likelihood of virus transmission between individuals. For example, the highest rates of LPAI infection in wild ducks in the temperate zone coincide with their frenzied aquatic feeding in large aggregations just prior to migration. Consequently, migration, aquatic life-style and surface feeding are the key ecological factors promoting LPAI transmission in the wild.

How are the deadly forms of bird flu spread?

The role of wild birds in the spread of the severe forms of bird flu is hotly debated, but the bulk of evidence so far suggests that the major spread of H5N1 in recent years is via the human trade in birds, especially poultry. After recombining into its deadly form in 1997, the H5N1 virus probably continued to circulate among domestic waterfowl in south-east Asia. In fact, surveillance of the virus in China has shown that it has continued to evolve into multiple genetic forms. The close proximity of farmers to their chickens and ducks and the wide-ranging trade in poultry probably played a key role in both its spread in the south-east Asian region, and its infection of humans. For example, the outbreak in south-east Asia in 2003 coincided with Chinese New Year when there is a peak in poultry trade and consumption.

Although many wild birds have become infected, some researchers argue that it is unlikely that sick individuals would have the energy to continue their migration. However, some bird species have been shown to be capable of carrying and shedding the virus without any signs of being diseased, and others may have partial immunity because of their previous exposure to the weakly pathogenic varieties. A recent study made it clear the same flu virus that migrating ducks can carry with little ill-effect can kill domestic chickens. The present situation in Europe, in which wild birds have been found

From left to right:

The wetlands of the Western Province of Papua-New Guinea, a staging area for waterbirds which may migrate to and from Australia. Photo by **Rob Heinsohn**

In search of ducks at Lake Murray. Photo by **Rob Heinsohn**

A Wandering Whistling-Duck captured at Lake Murray in the Western province Papua-New Guinea and fitted with a transmitter to track its movements. Photo by **Rob Heinsohn**

with the virus in countries that have not had outbreaks in their poultry, shows that wild birds can indeed be the first to carry bird flu to new areas. Among waterfowl, Mallards, both domestic and wild, may be of particular importance because they have been shown to carry virtually all of the bird flu sub-types.

Which wild birds are the natural reservoirs?

Birds in wetlands and aquatic environments, ducks, geese, and swans (Anseriformes), and gulls, terns and waders (Charadriiformes), especially, appear to form the major natural reservoir of bird flu viruses. The first recorded isolation of an influenza virus from a wild bird was from a Common Tern in 1961. The virus, in this case (H5N3), was responsible for an outbreak in South Africa where as least 1300 terns died.

Most gull species breed in crowded colonies in which quick infection via the large amounts of faecal material seems the most likely route to repeated infection. This differs from most dabbling ducks in which pairs breed separately but congregate in large numbers during moult and migration. Interestingly, flu viruses in gulls and terns appear to be genetically distinct from those in ducks, and less likely to cross the divide into humans. By contrast, the flu viruses of ducks and waders appear to be quite similar, to the extent that waders probably play an important role in their transmission to other species. Importantly, waders seem to have their highest infection rates during the spring migration suggesting that they can carry flu viruses long distances. This link between the two groups may explain the ultimate connection between wild birds, domestic poultry and humans. Waders travel the furthest of the migrating birds but rarely come in close contact with humans, although they do share wetland habitat with waterfowl. Wild ducks also move large distances, and in turn are more likely to spend time with domestic ducks in agricultural areas. Thus, an otherwise immobile strain of flu virus can make its way to poultry and humans almost anywhere in the world.

Is Australia threatened by its migratory connections to the north?

LPAI viruses have been isolated from at least 105 wild bird species, from 26 different families, some of which migrate to and from Australia (see Box 2). In considering the relevance of bird migration in the Australian region, some useful perspective comes from consideration of the biogeographical importance of Wallace's Line. This is the line that demarcates the Eurasian and Australo-Papuan biogeographical realms, as Alfred Russell Wallace realised in the 19th century. It reflects the largely independent evolutionary histories of the two regions. Much Australo-Papuan bird migration is east of Wallace's Line and thus within the region itself. No migratory waterfowl are known to cross Wallace's Line with any regularity. Some birds do migrate to Wallacea, the region about Wallace's Line, although, notably, no waterfowl are known to migrate between Australia and Wallacea.

Our scant knowledge of Australian waterfowl movements is cause for concern. Australo-Papuan waterfowl are among the birds that move between Australia and the island of New Guinea, where outbreaks have occurred in West Papua, so it is critical that we improve knowledge of our northern connections (Box 2). Of as much concern are the roughly three million shorebirds, from 35 species, that regularly migrate across Wallace's Line to Australia each year along the East-Asian Australasian flyway from as far away as northern Siberia and Alaska. Some of the larger species fly thousands of kilometres in single 'hops' (e.g. from Australia to the Yellow Sea in China) while others have important

Box 1: Avian influenza

To many people bird flu (avian influenza) conjures up images of thousands of chickens being slaughtered to stop the spread of the disease. Others imagine high-flying, sneezing birds shedding an aerosol of infected droplets on a helpless human population. As an infectious and potentially deadly disease, it pushes our buttons and has at times been grossly over-hyped by the media.

The reality is that avian influenza circulates every year through domestic and wild birds, just as human flu circulates in human populations. It is caused by Type A strains of the influenza virus, which can infect birds, humans and a range of other mammals. It is divided into sub-types described by combinations of the proteins H (haemagglutinin) and N (neuraminidase): haemagglutinin allows the virus to attach to the surface of a cell, whereas neuraminidase allows it to be released into the cell. At present there are 16 known H sub-types and 9 N sub-types. Human flu is based on a small number of sub-types (mostly H1, H2, and H3, and N1 and N2), but bird flu can involve all of H1 to H16 and N1 to N9.

The two previous influenza pandemics resulted from reassortment (exchanging of genes) between human and bird-adapted viruses. The 1957 pandemic involved the avian H2N2 virus and the human H1N1 virus, and in the 1968 pandemic there was reassortment between the avian H3Nx virus and the human H2N2 virus. It was originally thought that the viral reassortment took place in pigs because avian influenza viruses usually have trouble replicating in humans, whereas pigs have receptors for both bird and human flu. However, the recent cases of H5N1 and H9N2 avian influenza virus in humans suggest that reassortment can take place in humans without the need for any intermediate host.

In wild birds, the H and N sub-types appear to be stable, but they can mutate and have the potential for rapid replication and severe disease when they infect chickens and turkeys. But most strains of bird flu are not virulent—these are referred to as low-pathenogenic influenza (LPAI). The low virulence of these types probably reflects a long co-evolution during which the viruses were selected not to destroy their hosts. The highly pathogenic (HPAI) varieties are not maintained for long in wild bird populations. This reflects the unfavourable conditions for such highly virulent diseases; for example, the low density of hosts (because of fatalities) and strong competition from LPAIs. To date, wild birds have only been known to contract two of the highly pathogenic forms of bird flu (the current H5N1 virus and H5N3 in Common Terns).

Flu viruses in wild birds (usually LPAI) are important because of their potential to infect poultry and humans. They are most likely to mutate into deadly forms when poultry is kept in large, closely packed populations, as in south-east Asia. During outbreaks of HPAI among poultry the situation becomes more difficult when the virus acquires the capacity to remain inactive in some individuals. These healthy carriers can spread the virus over long periods and over large distances, which is currently the situation in south-east Asia, where some domestic ducks are healthy carriers, whereas chickens and turkeys always suffer higher mortality.

The economic losses to the poultry industry have been staggering, but there is also the possibility that if humans become infected by both human and avian strains, a new lethal sub-type with pandemic qualities may emerge.

Although Australia has already had five outbreaks of bird flu in its poultry (in 1976, 1985, 1992, 1994, and 1997, including the sub-types H7N7, H7N3, and H7N4), we have not yet encountered the lethal H5N1 found in south-east Asia. The nearest known outbreak of H5N1 was in poultry at Timika in south-western New Guinea (West Papua, Indonesia) in August 2006.

stopovers in the region enroute. The importance of this flyway becomes clear when one considers that at least some of the destinations and stopovers include countries that have had confirmed HPAI outbreaks. On arrival in Australia many waders congregate on coastal floodplains and wetlands and interact with Australian duck populations.

Unlike their cousins from the northern hemisphere, Australian ducks do not undertake predictable seasonal movements. Instead, many populations move in direct response to flooding and drought, which occur irregularly. Several species, such as Grey Teal, are nonetheless very wide-ranging and travel well beyond our northern borders. Magpie Geese, Wandering and Plumed Whistling-Duck, Radjah Shelduck, Green Pygmy-Geese and Pacific Black Duck all occur on the floodplains of southern New Guinea. Documenting their movements both beyond our shores and within the continent is essential for understanding their potential role in transmitting bird flu and other viruses. An important example of this can be seen with recent results from satellite tracking of ducks in New Guinea. Within a few weeks, a pair of Wandering Whistling-Ducks captured and released at Lake Murray in the Western province Papua-New Guinea in August 2007 travelled hundreds of kilometres into West Papua (Indonesia), where the nearest outbreak of H5N1 to Australia occurred.

Ultimately, wild birds will continue to traverse the globe whatever our human health concerns. Bird migration is one of the wonders of the natural world and huge sums of money are spent to encourage the preservation of key breeding, stopover and migration habitats for many species. However, birds, like all animals, carry microbes and some of these become virulent and deadly to poultry. Humans are occasionally infected by a small number of these diseases when they live closely with domestic stock.

In summing up the threat from wild birds, two key facts should be remembered. First, most of the global spread of H5N1 can be traced to human trade of bird products, rather than wild bird migration. Second, modern crowd-epidemic diseases like influenza only take off once they have mutated into new forms for which we do not already have immunity. When this happens, as it has repeatedly in our past, it is person-to-person contact that really matters. Crowd diseases like influenza A spread like wildfire through large populations, and in the modern era are more likely to arrive with a sneezing person on a jumbo jet than in the faeces or phlegm of a high flying duck.

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Box 2: Understanding our northern connections

Australia has expanded its surveillance effort for avian influenza through increased testing of wild birds and investigating wild bird disease events. A wide variety of low pathogenic avian influenza subtypes have been identified within Australia. However, in 13 disease investigations involving waterfowl no highly pathogenic influenza virus was found. Instead botulism was identified as the most common cause of these disease outbreaks.

Among the birds that potentially could bring highly pathogenic (HPAI) varieties of avian influenza to Australia (see table) we know most about the origins and migration of the many waders that visit our shores each summer. However, waterfowl are the natural reservoir for avian influenza and we understand considerably less about their likely origins and movements in our region. In 2007 the authors commenced a project to investigate movement and connectivity in bird populations either side of Torres Strait and the Arafura Sea.

Over the next few years we will be collecting blood and feather samples from waterfowl at sites up the west coast of Cape York, in Papua New Guinea, and across the Top End, as well as using the resources of the Australian National Wildlife Collection in Canberra and colleagues in Indonesia. Genetic markers, stable isotopes and trace elements will be used to assign individuals to populations and infer the connectivity between them. In the first instance, our target species are Grey Teal, Pacific Black Duck, Wandering Whistling-Duck, and Magpie Goose. The first two species are widespread across Australia, New Guinea and Indonesia, whereas Wandering Whistling-Ducks are a vagile tropical species. The Magpie Goose is a coastal species that is dispersive in the dry season, including to New Guinea. In time the analyses will be extended to lowland forest species such as Rainbow Bee-eater, Pied Imperial-Pigeon and Metallic Starling that migrate annually from the forests of New Guinea to mainland Australia to breed.

We have also fitted satellite transmitters on Wandering Whistling-Duck to observe directly the nature and extent of movement in this non-obligate migrant. The birds were trapped and released with transmitters at Lake Murray in the Western Province of Papua New Guinea. The transmitters are solar powered, weigh just 12 g and have an operational life of several years. We are hopeful of getting movement data for the next two years or more. The movements of the tagged Wandering Whistling-Ducks can be followed by downloading a data file, for viewing with Google Earth, at: http://csusap.csu.edu.au/~droshier/wanderers.png.html.

Bird groups with potential to carry avian influenza (AI). That is, groups which have some members that move between Australian and Asia and have been shown to carry avian influenza somewhere in the world

Common name	Occurrence of AI
Waterfowl (ducks and geese)	Common
Turnstones/sandpipers/phalaropes/plovers (shorebirds/waders)	Occasional
Gulls/terns	Occasional
Shearwaters/petrels	Rare
Cormorants	Rare
Herons/Bitterns	Rare
Ibises	Rare
Pigeons/doves	Extremely rare
Bee-eaters	Extremely rare
Starlings	Extremely rare

Adapted from Tracey, J.P., Woods, R., Roshier, D., West, P. and Saunders, G.R. (2004). The role of wild birds in the transmission of avian influenza for Australia: an ecological perspective. *Emu* 104: 109–124.

Left: David Roshier, with transmitters at the ready, and local assistants at Lake Murray. Photo by **Rob Heinsohn**