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Potential for an avian influenza pandemic: Time for NZ to ramp up preparedness

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Michael Baker, John D. Potter, Nigel French, Jemma L. Geoghegan, Nick Wilson, Oz Mansoor, Sue Huang, Richard Webby

Summary

Influenza A(H5N1) virus, a major cause of highly pathogenic avian influenza (HPAI) or ‘bird flu’, is causing concern as it continues to evolve and infect new hosts, notably cattle for the first time. Although this virus is still not adapted for human-to-human transmission, its spread is a warning for Aotearoa New Zealand (NZ) to review and enhance our pandemic preparedness.

At a minimum, we need to immediately update our pandemic plan to incorporate lessons from past pandemic responses, notably the effective use of public health and social measures (PHSM) to delay entry and circulation of serious pandemic infections. We need to review systems to ensure timely supply of A(H5N1) testing, vaccine, antivirals, and infection prevention and control (IPC) equipment. And strengthen One Health approaches to reduce the risk of influenza emergence and spread in poultry, livestock, wildlife, and humans, along with effective surveillance and early detection and response systems covering these populations.

The continuing global spread of influenza A(H5N1) is causing international concern. A(H5N1) virus causes highly pathogenic avian influenza (HPAI) with high death rates in chickens and other birds.[1] This is the largest influenza panzootic (a pandemic in animals) of HPAI virus ever documented. An increasing number of mammals, most recently cattle, appear to be susceptible hosts for the virus. And a dairy farm worker was infected, the first known case of this virus jumping to humans from another mammal.[2 3]

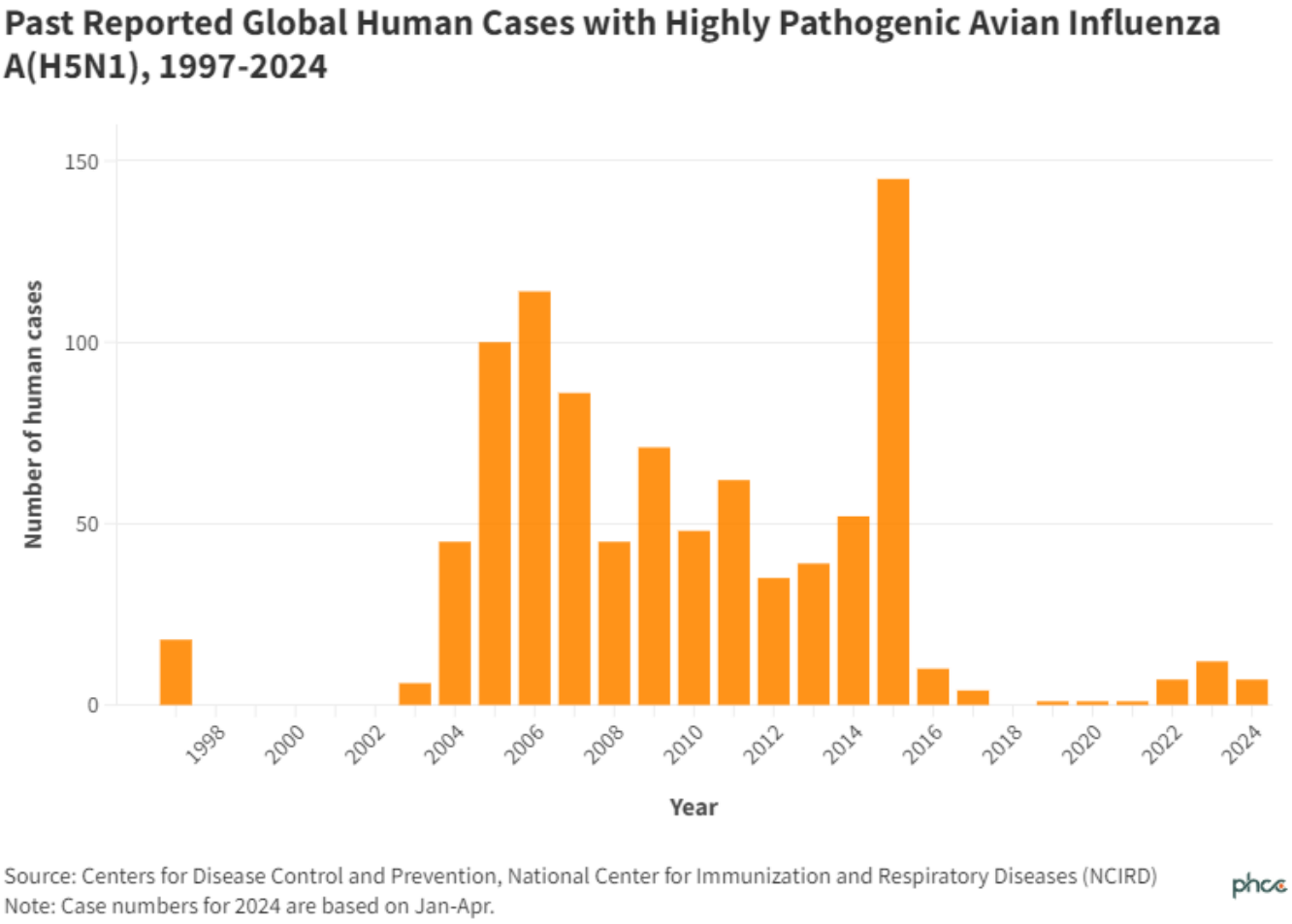
This Briefing provides a high-level risk assessment of the current A(H5N1) panzootic and comments on needed risk-management measures.

Risk assessment of influenza A(H5N1)

Influenza is considered the world’s most likely pandemic threat, for good reason (see Appendix for background).

General principles of pandemic risk assessment are based on key attributes of the emerging threat, notably its infectiousness, severity, controllability, and the certainty of knowledge and stability of the threat in question.[4]

A(H5N1) viruses are not currently being transmitted between people. It is still in the category of an uncommon ‘spillover’ infection, where people in close contact with infected birds and mammals become infected.[5] (see Figure). Severity varies, but the overall case fatality risk is high.[6]



A(H5N1) virus infection in birds is relatively well characterised, based on more than two decades of research. However, it is uncertain how it may evolve and adapt to other hosts, including humans.[7] Preliminary genomic evidence from the ongoing dairy cattle infections in the United States supports a single bird-to-dairy cattle transmission event with subsequent spread between cattle.[8] Despite potentially widespread transmission between dairy cows, the virus currently retains characteristics that are more avian virus-like than mammalian virus-like.[7] The virus isolated from the dairy worker did, however, have one mutation that has been associated with mammalian adaptation of A(H5N1) viruses.[2] There is potential that cows, like pigs, could become influenza 'mixing vessels' and/or promote the selection of mammalian virus traits enhancing zoonotic A(H5N1) virus transmission to people.[9 10]

NZ has systems to reduce the risk of importing A(H5N1) from animal populations overseas, including border biosecurity. However, the virus could be introduced by wild birds as NZ is on the migratory path of multiple species.[11] If the virus evolves to transmit in humans, we can expect rapid spread across the globe as with previous influenza pandemics, unless NZ and other countries applied vigorous control measures – see "risk management" below.

Risk management and upgrading our pandemic preparedness

There are international calls to strengthen preparedness for avian influenza.[12]

Effective surveillance for emerging infectious diseases is critically important. For zoonotic infections such surveillance needs to support early detection of A(H5N1) in wildlife, poultry, and livestock. Biosecurity New Zealand leads surveillance initiatives in this area. Members of the public have an important role in reporting sick or dead wild birds, poultry and sea mammals (see Biosecurity NZ for details).

Similarly, the human disease surveillance system has been extended to A(H5N1). HPAI is a separate notifiable disease (in addition to non-seasonal influenza). If the risk of importing A(H5N1) rises, NZ clinicians will need to be particularly vigilant, including considering the diagnosis in occupational groups who work with poultry, livestock, and wildlife and in arriving travellers.

Public health authorities in NZ need to update the national pandemic plan to cover the full range of A(H5N1) scenarios. The publicly available version is still the pre-Covid influenza plan from 2017.[13] The revised plan needs to fully support public health and social measures (PHSM): border management to exclude cases; case isolation, contact tracing and quarantine; ventilation upgrades; and masking and physical distancing.[14]

As was demonstrated during the Covid-19 pandemic, these measures were sufficient to interrupt disease transmission in multiple jurisdictions and to protect a sizeable proportion of the world's population from infection prior to arrival of a new vaccine.[15] Equity needs to be at the heart of pandemic responses.[16] NZ also has a responsibility to support measures to protect Pacific Island populations from pandemic diseases.[17] Enhanced pandemic planning will also help prepare NZ for other emerging threats such as bioengineered pandemics.[18]

One positive feature of A(H5N1) is that there is already production technology that can deliver effective vaccines.[19] The candidate vaccine viruses are a good match with circulating A(H5N1).[2] However, it would still take many months or longer to meet global demand.[20] There are small stocks of A(H5N1) vaccine available in NZ (though the online policy document has not been updated to describe the present situation).

The threat of A(H5N1) is a further opportunity for NZ to strengthen and exercise its pandemic preparedness and response capacity.[21] The work of the NZ Royal Commission COVID-19 Lessons Learned is particularly important given its forward-looking focus on increasing NZ's preparedness for future pandemics. NZ should also consider use of simulation exercises to test national pandemic preparedness plans, as it has done in the past.[22] In addition, specific mitigation measures such as mask use could be implemented and evaluated for managing seasonal epidemics of respiratory infections.[23]

The One Health paradigm is useful for managing pandemic threats across the human, agricultural, and ecological domains.[24] Relevant organisations need to coordinate their work and consider a full range of scenarios including a sustained epizootic in poultry and dairy cattle. A New Zealand CDC-type organisation looks increasingly important to support the integration of science workforces and systems across these fields.[25]

This situation is a further impetus to strengthen collaborative international disease surveillance and control measures with the World Health Organization, including finalising revisions to the International Health Regulations (IHR) and Pandemic Accord. Strengthening cooperation with Australia (which is building new vaccine facilities) and capacity building in the Pacific will increase regional resilience.

What this Briefing adds

- Influenza has been a cause of human pandemics for centuries and is still the primary focus for pandemic preparedness (although there is growing concern about the threat of bioengineered pandemics).
- Influenza A(H5N1) has caused a global panzootic (a pandemic in birds and other animals) since 1997, with occasional and frequently fatal infections of humans but as yet no sustained human-to-human transmission.
- This virus is now infecting a wider range of birds and mammals, increasing exposure of humans to this infection and creating opportunities for mutations that could allow sustained human spread and trigger a pandemic.

Implications for policy and practice

- NZ needs to increase preparedness for a global influenza A(H5N1) pandemic, including: an updated plan that incorporates lessons from past pandemics (including the option of exclusion/elimination for a severe pandemic) and arrangements for supply of A(H5N1) testing, vaccine, antivirals, and appropriate protective equipment (notably respirator-grade masks).
- NZ needs to strengthen response capacities including One Health approaches to reduce the risk of influenza emergence and spread in poultry, livestock, wildlife, and humans, along with effective surveillance and early response systems.
- NZ should more actively support international approaches to reduce the risks of pandemics and improve their management, including an updated International Health Regulation and Pandemic Accord and capacity building in the Pacific region.

Author details

Prof Michael Baker, Department of Public Health, University of Otago Wellington, and Public Health Communication Centre

Prof John D. Potter, Research Centre for Hauora and Health, Massey University

Prof Nigel French, Distinguished Professor of Infectious Disease Epidemiology and Public

Health at Massey University

Prof Jemma Geoghegan, Webster Family Chair of Viral Pathogenesis, Department of Microbiology and Immunology, University of Otago.

Prof Nick Wilson, Department of Public Health, University of Otago Wellington, and Public Health Communication Centre

Dr Oz Mansoor, Medical Officer of Health, Tairāwhiti (on sabbatical with Public Health Communication Centre)

Prof Sue Huang, Director, WHO National Influenza Centre, Institute of Environmental Science and Research Ltd (ESR)

Prof Richard Webby, St. Jude Children's Research Hospital, and Director, World Health Organization Collaborating Centre for Studies on the Ecology of Influenza in Animals and Birds

Appendix: Background to the global rise in A(H5N1) influenza

History of influenza pandemics

Despite public sentiment, we have not yet seen the end of the Covid-19 pandemic.[26] It is therefore alarming to have to contemplate another pandemic threat, this time from influenza.

It is very likely that influenza pandemics have occurred regularly since humans settled into agricultural and then urban communities (eg, 5th century Greece, European Middle Ages).[27] [28] However, identifying, with certainty, that specific respiratory-disease outbreaks were influenza (eg, as opposed to coronaviruses or other pathogens) became possible only in the 20th century, when there were 3 pandemics: in 1918-19, 1957, and 1968.[28]

The influenza virus was discovered in 1933[29] and the first vaccine developed by 1945.[30]

Each of the 20th century pandemics was caused by a different influenza A subtype (respectively A(H1N1); A(H2N2); A(H3N2)).[28] The A(H1N1) virus responsible for the 1918-19 pandemic (“Spanish flu”) was an avian influenza virus that became fully adapted to humans, possibly through adaptation in other mammalian hosts.[31-33] The two later pandemics were the result of reassortment (swapping) of glycoprotein genes among viral strains with origins in wild birds—a common feature of avian influenza viruses.[34 35] The first influenza pandemic of the 21st Century was caused by the A(H1N1)pdm09 virus in 2009, which was a swine origin virus derived from reassortment of human, bird, and swine influenza viruses.[36]

Emergence of Influenza A(H5N1)

For the first time in 1997, direct evidence of the ability of avian influenza viruses to infect humans was found. Detection of 18 human cases of the newly described influenza A(H5N1) were identified in Hong Kong following serious outbreaks on chicken farms.[37 38] Six of the 18 people died; all were infected directly by chickens—there was no direct human-to-human transmission. The epidemic was halted following the slaughter of more than 1.5 million birds.[39]

Concerns again rose in 2003 regarding a possible epidemic of A(H5N1)[40 41] following an outbreak of bird flu among chickens in multiple southeast Asian countries and then evidence of limited human-to-human transmission in Vietnam in early 2004. There were 14 cases identified and 11 people died. Eight countries saw more than 20 million chickens slaughtered following expert advice that this was the only way to effectively extinguish the virus.[42] In all, more than 300 people were infected, of whom about 60% died.[41] The virus has also been sporadically detected in other mammals.[43]

In the last two years, the A(H5N1) clade 2.3.4.4b has spread explosively across most regions of the world following a reassortment event.[44-46] The increased prevalence of the virus in wild birds has led to infection of atypical bird species such as vultures[47] and also infection of multiple mammal species.[48-51] Most recently, it has been reported in dairy cattle in multiple US states[52-55] and has infected people.[56-58] Definable mutations are probably needed before this current A(H5N1) variant can adapt to cause sustained human-to-human transmission, given its failure to do so in the past. The virus isolated from the dairy worker did, however, have one mutation that has been associated with mammalian adaptation of A(H5N1) viruses.[2]

Spread in multiple mammal species may make it easier to develop the capacity for sustained human-to-human transmission and thus risk producing a human pandemic.[59] A 3 May 2024 preprint shows that human avian influenza A virus receptors are widely expressed in the bovine mammary gland, increasing the risk that cattle can act as a ‘mixing vessel’ for further viral evolution and possible development of the capacity for human-to-human transmission.[10]

From 2003 to 31 March 2024, there were 888 human cases of A(H5N1) influenza reported, of which 463 (52.1%) were fatal.[6] There have been very few human cases of the currently circulating lineage 2.3.4.4b, with 13 between 2022-24 of which two (15.4%) have died.[60] The majority were reported in Cambodia, China, Egypt, Indonesia, and Vietnam.This fatality risk may be overestimated because mild and asymptomatic infections in humans are less likely to be identified than severe disease, which would have shrunk the recorded denominator of total infections.

Influenza (and other) pandemics remain unpredictable in timing and severity. Previous documented pandemics have ranged from the intensity of seasonal influenza (as seen in influenza (H1N1) in 2009[61]) through to the 1918 influenza (H1N1) pandemic with a case fatality risk of about 2%.[62] For other respiratory pandemics the case fatality risk has been even higher, as was seen with SARS in 2003 where it was >10%.[62]

Details about influenza viruses

Influenza A(H5N1) virus causes HPAI outbreaks with high death rates in chickens and other birds (other HPAI viruses include A(H7N9), A(H5N8), A(H5N5), A(H5N6)).[1] It is distinguished from low pathogenicity avian influenza (LPAI) viruses, a more common form of the virus, which typically causes few or no signs in birds.

The two glycoproteins on the influenza virus membrane, hemagglutinin (HA) and neuraminidase (NA), enable entry and exit of the virus, respectively. HA mediates entry by binding to sialic acids on target cells and NA mediates exit by destruction of these bonds. The sialic acid receptors preferred by avian and human adapted influenza viruses differ slightly in chemical composition. HAs are a principal determinant of the pathogenicity of influenza A viruses. In addition to mediating binding to host cells, HAs initiate infection by inducing fusion between host cell and virus membranes. The capacity to fuse is dependent on the activation of HA by enzymatic cleavage by host proteases. There are striking differences between highly pathogenic and low-pathogenic avian influenza viruses in their sensitivity to these host proteases and as a consequence their intrinsic ability to cause systemic disease, particularly in gallinaceous poultry.[63] After virus replication occurs in the host cells, the receptor-destroying virus enzyme, neuraminidase, removes the sialic-acid residues from the surfaces of the infected cells, releasing the newly made viruses to infect more cells.[64]

The 1980 WHO system of nomenclature of influenza viruses consists of two parts: a type (A, B, C, D) and strain designation and, for influenza A viruses, designation of the antigenic subtypes, based on the characterisation of the surface antigens that determine infection: HA antigens initially were classified as having 12, but now 18, subtypes, H1-H18, and NA antigens initially 9, now 11, subtypes, N1-N11.[65-68] These designations give rise to the HxNy classification of the influenza viruses. There are further divisions of subtypes based on the mutation-driven evolution of the virus.[69]

One Health approach to understanding and managing the A(H5N1) threat

A(H5N1) poses a risk to humans, wildlife, and poultry/livestock, and as such benefits from a One Health approach.[24] This infection could be devastating to native birdlife and marine mammals as seen internationally.[70] It is also a severe threat to poultry.[71] The current outbreak in livestock in the US shows its broader threat to agriculture.[2] For example, infected dairy cattle can shed virus in milk and potentially transmit infection to other mammals via unpasteurised milk.[3] On one north Texas dairy farm in March 2024, >50% of approximately 24 domestic cats became ill and died after being fed raw milk from sick cows. Laboratory testing of bovine milk samples and specimens from two autopsied cats confirmed they were infected by the same strain of A(H5N1).[3]

While A(H5N1) remains in non-human populations, Biosecurity New Zealand (Ministry of Primary Industries) is the lead agency for assessing and managing the threat. Given the threat to wildlife, the Department of Conservation (DOC) is also involved. These agencies also work with the Ministry of Health and Te Whatu Ora/Health NZ which is actively

monitoring a range of pandemic threats. Those agencies are working together to develop response options that represent the best approach for NZ to protect our unique native species, mitigate the impact on the poultry sector and take preventative measures to protect human health.

Organisations working across the human health, agricultural, and ecological domains as well as those concerned with occupational health and safety, will need to consider a full range of scenarios including a sustained epizootic in dairy cattle in NZ. In the event of an outbreak in poultry and/or livestock, there are a range of possible actions that would be taken. These include movement control, vaccination, or depopulation, depending on the species infected and the location.

Biosecurity New Zealand is actively monitoring the international spread of A(H5N1) viruses. This virus first appeared in South America in late 2022,[70] the sub-Antarctic island of South Georgia in late 2023, and the Antarctic Peninsula near South America in February 2024. So far, Australia, NZ, the Pacific Islands and much of Antarctica remain free from the A(H5N1) virus. The virus has been detected in most other regions of the world.

Diagnosis of A(H5N1) depends on collecting suitable specimens for specialist testing at two Wallaceville laboratories: the WHO National Influenza Centre for human specimens and the Animal Health Laboratory for animal specimens.

Biosecurity New Zealand leads several streams of surveillance, aimed at detecting A(H5N1) should it arrive in NZ or the Ross Sea region:

- Passive surveillance via Biosecurity NZ's Exotic Pest and Disease hotline. Material has been circulated to the veterinary profession to highlight the clinical signs of A(H5N1) and the poultry industry is in a state of heightened awareness;
- Surveillance of migratory birds and shorebirds not displaying clinical signs of A(H5N1) via a contract between MPI and Dunedin Wildlife Hospital, began in September 2023. Dunedin and other wildlife hospitals will continue to report birds with suspected avian influenza symptoms via the 0800 number.
- Study of the ecology and evolution of Low Pathogenicity Avian Influenza viruses (LPAI) viruses circulating in NZ, run by MPI's Animal Health Laboratory, involving the sampling and testing mallard ducks in conjunction with a Fish and Game New Zealand annual banding programme to track duck numbers;
- Poultry export testing for avian influenza to meet Overseas Market Access Requirements (OMAR) and enable export of day-old chicks and hatching eggs. Managed by the poultry industry, with lab results being provided to MPI. All non-negative samples are sent to the MPI Animal Health Laboratory for confirmatory testing;

Biosecurity NZ is also working with DOC on any suspected exotic diseases in wild bird populations, including native birds:

- DOC staff in the sub-Antarctic islands and Antarctic New Zealand staff at Scott Base, Antarctica have been issued sampling kits and instructions. Sample-handling systems for this Antarctic and Sub-Antarctic pathway have been validated. DOC staff and

researchers in the sub-Antarctic islands and Chatham Islands have collected samples from seabirds for baseline health monitoring in the 2023/24 summer season. Any detection of Avian Influenza viruses will be reported to Biosecurity NZ.
- A collaboration with the University of Otago, ESR and others to understand the transmission of avian viruses between migratory and sedentary birds in NZ and to develop rapid, in-field, testing.
- DOC is also working on a HPAI vaccine trial, beginning with five native species.

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