Animal influenza research needs: protecting humans, animals, food, and economies

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Influenza A viruses infect a wide range of animals including poultry, wild birds, pigs, horses, dogs, and marine mammals. Influenza in animals threatens animal health and welfare, agricultural productivity, public health, food security, and the livelihoods of farmers across the globe. The recent H1N1 pandemic of 2009, continuous reporting of zoonotic infections with highly pathogenic avian influenza (HPAI) H5N1 and other avian and swine influenza viruses, such as H3N2v, raise ongoing concerns regarding the emergence of zoonotic viruses with pandemic potential.¹

Different strains of influenza A virus show host specificity and are often defined by the species in which they are initially found to be circulating. However, over time the situation becomes more complicated as the viruses continuously evolve, through mutation and reassortment, and in some cases are transmitted from species to species. The next major pandemic is likely to be caused by a strain of influenza virus that is new to that generation; a virus to which the human population has little or no immunity. Almost certainly such a strain would contain genes from influenza viruses that have been circulating in animals.

A better understanding of the mechanisms responsible for interspecies transmission, and information on host adaptation and pathogenicity are needed to allow more informed assessment as to when and where the next pandemic may arise. Timely identification of viruses with pandemic potential could ultimately reduce the impact of a new pandemic. With current levels of knowledge and surveillance, it is not possible to accurately assess geographic location of all animal influenza viruses, the production systems in which they circulate, and which of these viruses may be transmitted to and adapt in the human population. This makes predictions about which strains of influenza virus to select for vaccines for pandemic preparedness a challenging task.

With mortality rates reaching up to 100% in affected populations, HPAI viruses continue to have a devastating impact in poultry populations. Low-pathogenic avian influenza (LPAI) viruses also have a significant and variable

impact on poultry production, depending on the strain and health status of the birds, and may evolve into HPAI viruses, for example, the recent HPAI H7N3 outbreak in Jalisco, Mexico.^{2,8} These impacts together with consequential cost of control and trade measures, aimed at preventing further spread, lead to huge economic costs. There is often a greater impact on countries with a lower Gross Domestic Product (GDP), who rely on agriculture for economic development and for sustenance.

Early detection of HPAI and H5 and H7 LPAI virus infections in poultry is essential for an effective response which relies on a combination of classic control measures (culling infected flocks and high risk contacts, disinfection, biosecurity, and trade measures) and, where appropriate, vaccination.³ Delays in detection lead to spiraling costs to keep epidemics under control and make the disease more difficult to eradicate. In the case of H5N1 HPAI, effective control in the animal source is needed to reduce the public health risk. Developing countries do not always have the resources to maintain the infrastructure and technical capacities needed for rapid and accurate diagnostic testing and characterization of viral strains. These countries rely on international reference laboratories to test their specimens and characterize the viruses. Research is needed to develop accurate, cheap, and robust diagnostic tests to ensure that the disease is detected early, with sufficient confidence, to allow timely initiation of effective response measures. For initial disease confirmation, both sensitivity and specificity of tests are essential because the implications of false-negative and false-positive results can be considerable.

Animal influenza is not only a constraint for agriculture and food production. Equine influenza is an ongoing problem for companion and competition horses and has a huge impact on the horse racing industry. The 2007 equine influenza outbreak in Australia is estimated to have cost the horse racing and gambling industries 3.6 billion Australian dollars in lost revenue.⁴ Research, accompanied by increased global surveillance, is needed to ensure that the equine sector

is able to access effective up-to-date vaccines so that many can continue to benefit from the enjoyment and financial gains that horse sports offer.

Some suggest that historic accounts showing a temporal relationship between respiratory disease in horses and humans may implicate influenza viruses.⁵ However, these accounts date back to a time before influenza viruses had been isolated, and a clear link to influenza as we know it would be difficult to prove. Influenza viruses of subtype H3N8 currently circulating in the horse population have also crossed the species barrier and become established in dogs. However, this subtype and other strains of equine influenza viruses do not appear to be a significant zoonosis despite intense exposure of owners to their horses and dogs, and vice versa. An understanding of the underlying reasons for this may help to explain why other influenza viruses are zoonotic.

Effective and cost-effective control require targeting resources for optimal impact. Research is needed to gain an understanding of how control measures can be better targeted. More rapid control in the animal population will limit impacts on animal health and public health when the influenza virus is zoonotic and will minimize costs in terms of production losses and access to international markets. Currently, vaccination does not always prevent infection of birds nor does it prevent infected vaccinated birds from shedding virus. If vaccines are not adequately matched antigenically to circulating field viruses and at least 60–80% of the susceptible populations are immunized, vaccination as a program will not be effective. Further research is needed to improve the effectiveness of the control measures themselves, such as vaccination, and to provide improved access to resources needed for control.

Despite unprecedented levels of international investment to support avian influenza surveillance between 2004 and 2009, global surveillance for influenza viruses in animals is woefully inadequate, with too little being undertaken without adequate coordination. Improvements in surveillance are required to provide early warning for effective control and to inform much needed research.⁶ As well as surveillance in domestic animals (poultry, horses and pigs), surveillance in wildlife is important; it is now evident that wild birds also play a role in the primary introduction of avian influenza in previously disease-free areas.⁷

Today, we are not able to fully manage the threats and impacts from animal influenza. In one form or another, influenza A viruses are circulating in every country on the planet. Our understanding of the mechanisms responsible for interspecies transmission, adaptation, and pathogenicity is incomplete, and the methods for risk assessment and disease control are rudimentary. Challenges to reduce threats from animal influenzas are considerable and will only be improved through extensive research and innovation.

Continued reports of notifiable avian influenza⁸ and animal influenza associated human infections highlight the need to monitor influenza viruses in all animal species to better understand their role in causing pandemics and severe zoonotic infections, and in reducing agricultural productivity.

OFFLU is the World Organisation for Animal Health (OIE) – Food and Agricultural Organization of the United Nations (FAO) global network of expertise on animal influenza, established in 2005 to address the animal and public health threats from H5N1 HPAI. Since then, its mandate has been extended to cover all animal influenza viruses. OFFLU is unique in that its participation comprises a global representation of leading experts in animal influenza including researchers, diagnosticians, policy makers, economists, and epidemiologists. One of OFFLU's core objectives is to advocate for more research, to highlight specific influenza research objectives, promote their development, and to ensure coordination. OFFLU works closely with WHO on all influenza issues at the human–animal interface, including identifying commonly agreed research priorities.

Following the OFFLU annual technical meeting in 2010 attended by avian, swine, equine, and public health experts, it was decided that there was an urgent need to develop a Research Agenda to highlight and coordinate research priorities for the animal influenza sector. The Research Agenda highlighted needs in different animal species and at the human–animal interface. It is designed to help policy makers, researchers, and donors ensure that their efforts and resources are targeted to areas where there is an identified need. The agenda should also be used to leverage funds for animal influenza research. In today's world where there is a huge volume of information of variable quality, the OFFLU Research Agenda has been designed to be concise and digestible; it comprises only 11 pages.

The animal and human influenza networks share the common goal of reducing public health threats from animal influenza viruses. OFFLU has been working closely with its parent organizations, the OIE and the FAO, and its partner the World Health Organization (WHO) to ensure that its efforts are complementary and well coordinated. In 2008 and 2010, the OIE-WHO-FAO tripartite held joint technical consultations on avian influenza at the human–animal interface in Verona, Italy and discussed other technical interface topics of common interest. The experts identified that more research is needed on modes of transmission, behaviors associated with increased risks of transmission, virologic and ecologic aspects, and viral persistence in the environment to address the human exposure risks to H5N1 infection.⁹

Importantly in practical terms, OFFLU contributes animal influenza data to the biannual WHO influenza vaccine composition meetings. This information is critical in allowing selection of the most appropriate strains of virus for vaccines to protect against potential zoonotic pandemic

influenza, including H5N1 and H9N2 avian influenza.¹⁰ Where zoonotic strains of influenza are undergoing antigenic drift in animal populations, the situation is being monitored in real time to allow selection of relevant influenza virus seed strains and antigens for vaccines for public health preparedness. OFFLU and WHO experts are working together to better understand which animal influenza viruses may pose a risk to human health. This ongoing risk assessment is supported by OFFLU's drive to improve and better collate data from avian, swine, and equine influenza surveillance programs world-wide.

Animal influenza research is suffering from donor fatigue, and it is a continuing challenge to ensure that sufficient resources can be secured to address the priorities that have been identified, ultimately to improve health and economies. It is considered possible to prevent a human influenza pandemic by identifying influenza viruses with pandemic potential in animal species; this will only be achieved through further influenza research studies in animals. A large body of animal influenza data has been generated in recent years, presenting a real opportunity to increase our understanding of how to identify risk and better control the adverse effects of influenza in animals and at the human–animal interface. Many questions still remain to be answered. Structured and coordinated research toward prioritized goals and objectives will greatly facilitate this.

The 'OFFLU Research Agenda' is a first for the animal health sector and will help to steer animal influenza research toward the identified objectives, providing maximum benefits for public and animal health. The influenza research priorities focus on several topics including control and education, diagnostics, epidemiology, immunology and immune responses, pathogenesis, transmission, vaccines and vaccination and virus characteristics and evolution in poultry, wild birds, swine and equine.

The full OFFLU research agenda can be viewed at http://www.offlu.net/fileadmin/home/en/publications/pdf/OFFLU_Research_Priorities_photo.pdf.

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Conflict of interest

The authors have no potential conflicts of interest to declare.

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