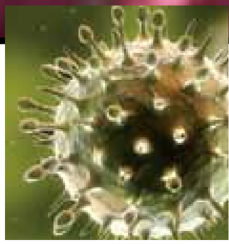

Primary Influenza Prevention and Control Measures in Pig Farms

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History of pandemic A/H1N1 influenza (2009-2010)

On March 18, 2009, the Mexican government announced 59 deaths and 854 people ill from influenza-related pneumonia (2). On August 10, 2010, the World Health Organization (WHO) declared that the A/H1N1 influenza pandemic had ended, and attributed the deaths of at least 12,220 people to it (3). During this period, massive amounts of human, material, financial, and informational resources were mobilized to respond to the crisis (4). Sequencing the A/H1N1 virus revealed that it was a mosaic of genes from human, swine, and avian influenza viruses, resulting from multiple genome reassortments over a period of more than 10 years (5). Because the first cases of human infection with the A/H1N1 influenza virus probably emerged from the swine industry in Mexico, the disease was named *swine influenza* by the WHO. However, organizations with the official mission of promoting and protecting animal production markets, such as the World Organization for Animal Health (OIE) and the UN Food and Agriculture Organization (FAO), collaborated with the WHO to rename the disease *pandemic A/H1N1 2009 influenza.* This new name helped to avoid an import ban on live pigs and on pork products, as well as helping to avoid the destruction of entire pig populations that would have had no positive impact on either public health or animal health (6, 7). The attitudes and behaviours of the population and various stakeholders during the crisis often evolved according to their perceptions and not necessarily to the known facts or the authorities' recommendations (8, 9). This review[1] of the evidence is intended to provide a summary of the known facts and key issues concerning the prevention of primary influenza and the control measures in pig farms, for the purpose of shedding some light on policies, programs, and practices.

Development

Canada is one of the world's primary swine producers and exporters. Accordingly, the Canadian Food Inspection Agency (CFIA) works in collaboration with industry and with various federal, provincial, and territorial agencies, to improve biosecurity programs in order to reduce the risk of infectious diseases for environmental, economic, and public health reasons (10). In general, biosecurity is divided into two fields. The objective of *bioexclusion* measures (external biosecurity) is to avoid the introduction of a pathogen

1 It is important to note that the first draft of this review was written in 2011. All information and data were accurate and current to that time. The authors and editors note that there may be newer information that is not included here.

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knowledge that's contagious!
Des saviors qui se transmettent!

and the contamination of a herd or a farm. The objective of *bioconfinement* measures (internal biosecurity) is to avoid the propagation of the disease to other animals in the herd or outside the contaminated farm.

Biosecurity is based on the epidemiology of a disease: the pathogenicity of the infectious agent, its survival in the environment, and the routes of contamination. Certain biosecurity principles can be applied to all types of swine production and all infectious agents, but the majority of preventive and control actions must be adapted to the target pathogen. It is therefore important to consider the proposed measures in light of the socioeconomic aspects, as they will have an impact on the effectiveness and feasibility of their application (11).

In pigs, detection of influenza viruses (including A/H1N1) does not require formal reporting of the disease, especially since the prevention and control strategies are not systematic in Canada or in other countries as well as with the OIE (12, 13). However, the CFIA supports some basic principles for ensuring biosecurity in the swine industry: pig isolation, sanitation system, traffic control, and pig health monitoring (14).

On April 24, 2009, in light of the global A/H1N1 influenza situation, the CFIA began actively collaborating with its partners in various agencies to improve surveillance and safety measures in swine production facilities (12). Although Canada had not reported a single case of infection with the influenza A/H1N1 virus in pigs before April 27, 2009, compared to six clinical cases in humans, the Canadian Pork Council (CPC) and the Canadian Swine Health Board (CSHB) recommended that producers revise and reinforce their biosecurity measures in order to avoid contamination of Canadian pig farms. The recommendations issued were intended to protect both workers and animals. This summary notice made mention, among others, of guidelines governing the sanitary conditions for entry onto pig farms, the operation of ventilation systems, the role of veterinarians, and the use of vaccination in both humans and swine (15). It is indeed strongly recommended not to have visitors inside hog barns regardless of their clinical status, and personnel who visited a region affected by the pandemic as well as workers exhibiting flu symptoms (fever, cough, aching muscles, vomiting, diarrhea, etc.) were to be kept apart for at least seven days. Clothing changes and hand washing were to be intensified and the use of gloves and N95 masks encouraged (15). Ventilation was to be adjusted to minimize air recirculation within buildings (16). There exists a technical guide on air filtration systems for swine facilities, created by the *Centre de Développement du Porc du Québec Inc.* (CDPQ)(17).

In the United States, the Centers for Disease Control and Prevention (CDC) recognized the key preventive role of workers by publishing the *Interim Guidance for Workers who are Employed at Commercial Swine Farms: Preventing the Spread of Influenza A Viruses, Including the 2009 H1N1 Virus*. The recommendations of the CDC were much more scientifically sound, for example concerning the need for training, than those issued by the CPC/CSHB, although covering the same issues in sanitation systems, vaccinations, and the role of veterinarians. This is partially explained by highly specific references to the regulatory and institutional framework currently in place (18).

The *Working Document on Surveillance and Control Measures for the Pandemic (H1N1) 2009 Influenza Virus in Pigs* of the European Commission on Health and Welfare proposes measures for its member states on various epidemiological scenarios. Their recommendations are based on the principles of vigilance, proportionality, and flexibility. Preventive and control actions are established according to two hypotheses. The first is the *status quo*, corresponding to the current situation/knowledge of the moderate effects of the virus in the pig population and the absence of the virus in Europe at the time the text was written. The second anticipates a significant increase in the virulence of the A/H1N1 virus in terms of transmission, mortality, and morbidity (13).

Although these reference documents do not completely coincide, they agree in their response to the principle of external biosecurity. In other words: how do we protect pigs from people? This question arises because it has been recognized that in most cases, the infection of swine with the A/H1N1 virus was by human transmission, particularly in Alberta, Manitoba, Argentina, Australia, Ireland, Norway, and Thailand (19-25). Such contamination between humans and swine (anthropozoonosis) is most likely to occur when both species are living in close proximity (26, 27). Since swine influenza virus is common in pig populations worldwide, people with regular exposure to pigs are thus at higher risk of contracting swine flu infection (26). The routes of transmission can be either direct contamination from coughing or sneezing, or indirect contamination through contact with surfaces recently contaminated by the virus, as the influenza virus has a short lifespan outside the host.

Contamination by water, feed, and manure is therefore considered an insignificant transmission source. Moreover, the transmission potential of influenza A/H1N1 is affected by temperature, as the cold lengthens the life of the virus while exposure to sunlight or low humidity tends to have the reverse effect. It is therefore possible to observe seasonal infection models, which can be taken into consideration when developing biosecurity rules (11, 28, 29). Still, industrial production such as the factory farming in North America implicitly contributes to protecting swine from humans because the ratio of swine to humans is much higher than in more rudimentary production (30).

Pandemic influenza A/H1N1/09 (A/H1N1) transmission between human and pigs was found in 49 cases globally during 2009–2011 (31), supporting the need for a vaccine against this influenza strain. It is also for this reason that vaccination of all workers in contact with pigs was strongly recommended in the United States. Moreover, many studies showed evidences of increased risk of zoonotic influenza virus infection for swine workers (26, 27, 32). Therefore, the CDC maintained that workers in the swine industry should receive the seasonal flu vaccine, although it does not protect against the A/H1N1 strain, in order to avoid simultaneous infection by the seasonal strain and the pandemic A/H1N1 strain (18). This is of major interest, because reassortment of the genetic material from these two viruses could result, leading to the development of a more pathogenic viral strain in spite of phylogenetic studies showing that the pandemic A/H1N1 strain is relatively stable (33-35). The CDC did not formally ask swine producers to receive the new A/H1N1 vaccine; the priority groups for receiving the first doses of the A/H1N1 vaccine were health care workers and persons at risk (pregnant women, children less than six months old, etc.) (36). This recommendation therefore agreed with that of the CPC/CSHB in that it was the responsibility of workers in the swine industry to discuss with their doctors the possibility of receiving the new A/H1N1 vaccine (15). This prioritization was partly a corollary to the low availability of the vaccines at the start of the national vaccination programs such as the one in Canada (37).

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As for the American Association of Swine Veterinarians (AASV) and the Minnesota Pork Board, they recommended that all workers in the swine industry have priority when vaccinating for any new influenza strain, for their own personal protection and to reduce viral transmission to pigs (38, 39). This reasoning is in addition to the fact that the predictors of intention to vaccinate are consequences of the perceptions of certain groups of individuals concerning the relative risk of the new strain compared to the seasonal flu as well as vaccine safety, efficacy, and side effects (40, 41). Educating target populations for vaccination is thus important. The most common adverse events reported to seasonal vaccination in adults are mild. They included injection-site reactions, pain, fever, myalgia, and headache. Only one percent of the seasonal flu shots in adults were classified to lead to adverse events and from those 14% were classified as serious adverse events (42). Also, employee vaccination is more common in the largest swine facilities, as the program is encouraged and facilitated by their organizational structure as well as their higher level of financial support (38).

The objective of vaccinating swine is to reduce the clinical impact of the influenza virus in the pigs, to reduce contagion within the pig facility, and to reduce the risk of worker infection (43). Those effects are part of internal biosecurity within barns. The AASV proposed continuing the use of seasonal swine vaccines to control the clinical picture, and using approved vaccines specific to the A/H1N1 pandemic strain (38), a proposal with which the CDC agreed (18). According to the European Commission on Animal Health and Welfare, vaccination of the pig population, whether mandatory or voluntary, should be considered even though it is not to be considered sufficient for eradicating the virus. In addition, emergency vaccination of uncontaminated pigs in infected swine facilities is not recommended, because the speed at which the virus propagates is faster than the development of the immune response to the vaccine (13). Various vaccines have been tested without complete success in their efficacy against the pandemic A/H1N1 strain, including an attenuated vaccine (44), an autogenous vaccine (21), and two inactivated vaccines (45, 46). Thus, the OIE considers swine vaccination to be an inconclusive preventive measure (11). Despite various candidate influenza vaccine types for swine, it seems there needs to be an emphasis on more research, better sharing of intellectual property rights, and the creation of monitoring infrastructures, in order to develop and introduce vaccines as safe and effective as those for the human market (47). Moreover, current swine influenza vaccines lack cross protection against other virus strains of different subtypes (48). The CFIA suggested that the decision to vaccinate pig herds with existing vaccines should be made by consulting the veterinarian on a case-by-case basis (12). In Canada, vaccination is therefore less common than in the United States. This is partially explained by the influenza virus tending to be present in larger numbers and persisting longer in large production facilities and those with a high population density (30, 49). Canadian swine population densities are relatively small in spite of the significant size of the industry. As a result, Canadian veterinarians are generally less inclined to vaccinate against swine influenza. Ultimately, however, it is a decision based on economic viability, which takes into account the severity of the clinical picture of the A/H1N1 pandemic and the anticipated effectiveness of the vaccine.

In its *Updated Interim Recommendations for the Use of Antiviral Medications in the Treatment and Prevention of Influenza for 2009-2010 Season,* the CDC also recommended for human treatment the use of antiviral treatments and chemoprophylactic measures for the pandemic A/H1N1 influenza. Chemoprophylaxis can be used by workers during and for some time after working directly with pigs diagnosed with influenza. Both oseltamivir and zanamivir antivirals are suggested, while amantadine and rimantadine are not recommended by the CDC because of resistance (18). However, more than 265 cases of oseltamivir resistance have been reported (4).

According to the OIE, the role of the veterinarian, or more generally the veterinary services, was to monitor swine populations effectively in order to detect clinical signs of A/H1N1 influenza (fever, loss of appetite, weight loss, cough, respiratory distress, reduced fertility, abortion, etc.). The veterinarian was also to use appropriate tools to confirm the diagnosis and then report the case to the authorities, including the OIE (50). This was clearly conveyed as part of a monitoring program orchestrated by the *Ministère de l'Agriculture, des Pêcheries et de l'Alimentation du Québec* (MAPAQ) which encouraged the submission of samples and covered the analysis expenses. Between April 28, 2009 and March 31, 2010, MAPAQ received 526 submissions from more than 40 practitioners. Working in collaboration with the diagnostic services of the Université de Montréal Faculty of Veterinary Medicine, MAPAQ detected the pandemic strain of the A/H1N1 influenza virus in four cases (51). In addition, according to Alberta Pork, the veterinarians were to collaborate with swine producers to develop strategies appropriate to their conditions, in order to limit the incidence and propagation of the virus (52). However, according to the Minnesota Pork Board, the monitoring procedures in the United States were more comprehensive relative to the various local, regional, national, and international agencies and their respective responsibilities when it came to identify a case (53).

The approach of the CFIA to case management was further refined based on research and observations during the A/H1N1 influenza pandemic (10). They came to align with the OIE recommendations stating that there was no danger from consuming pork products. It was concluded that there was no significant evidence that animals played any role in propagating the virus in the general population, and that the pandemic A/H1N1 virus does not behave differently than other influenza viruses in pigs. Based on this information, for public health protection the CFIA recommended monitoring the infected swine populations to verify complete remission of the impacted pigs, not quarantining them. Also according to the CFIA, the Canadian swine production system made sufficient routine inspections based on clinical signs and carcass examination to ensure that only healthy pigs reached the end of the chain. Control measures were also in effect to ensure the healthy condition of pigs involved in the import and export processes. In parallel, the American system put into operation a very similar system for managing swine cases of A/H1N1 influenza (53).

In retrospect, considering that the pandemic A/H1N1 influenza is not severe in pigs, one should question the appropriateness of the Canadian reaction during the first outbreak on a farm in Alberta in May 2009, which resulted in the destruction of a large number of pigs (20). The management by a long quarantine would have been adequate. One should remember, however, that this was a global first in a situation, which attracted a lot of attention because of the feared potential for virulence of the virus. Members of the CFIA and the Public Health Agency of Canada (PHAC) met several times with various stakeholders and specialists in order to react in a carefully considered and coordinated manner, while still deciding to destroy the pig herd for financial, population, and market access reasons. In fact, the name "swine flu" was influencing public opinion, all the more so as this was a new situation, leading many countries to ban the import of pigs or to destroy them in large numbers, although this was without benefit to public health or animal health, or to the producers (7). With such an unstable situation, the confusion and questions of stakeholders and the dismay of producers also needed to be considered. Would it have been possible to act more quickly and euthanize the pigs on site rather than at the slaughterhouse? As preliminary information indicated that slaughterhouse workers were primarily in an age group having a high mortality rate from the influenza pandemic, it was politically difficult to carry out this action. The approach was prudent and avoided the loss of control seen in Egypt, where tens of thousands of pigs were destroyed in haste, leading to a public health problem because the pigs were feeding on trash and were part of the trash management (54).

Canada then faced new cases of pigs with pandemic A/H1N1 influenza in various facilities in Manitoba (21). Based on its experience, the authorities handled these cases by applying the new CFIA measures complementing those of the OIE. Other countries also had to confront problematic situations; Norway had insufficient staff, which led to non-compliance with certain health measures such as an employee working with pigs although he had the flu (24).

In total, fewer than twenty countries declared cases of pandemic infections in their commercial swine production to the OIE. This small number of declaring countries could be a result of there being no requirement to notify the authorities of a case of pandemic influenza in swine, as long as the animals recover properly, particularly as there are potential negative economic repercussions to making such a disclosure (55). In addition, there were insufficient funds to ensure optimum surveillance (6). Good biosecurity strategies are based on proper characterization of the situation as well as a properly established communication network between the various bodies (11). For example, it would be essential to have a list of all the producers' e-mail addresses in order to reach them immediately and give them the information they need in case of a crisis (56).

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To this end, each link in the swine industry chain should have appropriate biosecurity protocols for its situation, and should plan for training tools. The biosecurity measures must be analyzed from different perspectives. Each measure must be evaluated based on: its potential impacts for the internal and external biosecurity aspects, and the persistence of these impacts; the time to implement the measure; its initial and recurring costs; the interruption of the production chain; and its social acceptability. In addition, this analysis must be adapted to the type of facility to which the measures are applied and also to the size and density of the swine population (11). Finally, the implementation of preventive and control measures requires adopting a specific behavior and attitude. The Canadian Swine Health Board (CSHB) is currently conducting a national survey in order to collect data on biosecurity practices in Canadian pig farms. This should enable evaluating the beneficial effects of current biosecurity programs and determining the areas where biosecurity needs to be reinforced (57).

Future Perspectives

As the A/H1N1 influenza pandemic demonstrated, the risk of infectious disease transmission is rising with the increase in market globalization and in the circulation of animals and people. As a result, biosecurity standards are essential at the international level. Although the WHO declared the pandemic to be ended in August 2010, the A/H1N1 virus continues to circulate endemically in pig and human populations (58, 59). Even so, the reaction when new cases are detected should be in proportion to the level of risk to animal health and public health, and therefore should be carefully considered (60). Previous studies have reported that the health status of up to 94% of the pigs infected with the pandemic A/H1N1 virus were not affected by Swine Influenza Virus (SIV) since they did not display any clinical signs; pigs were completely asymptomatic and displayed most of the time no organ lesions after slaughter (25). This, added to the fact that consumption of pork products from SIV-positive swine is safe and that the first notifications of positive cases of SIV caused considerable financial losses to porcine industry, reinforces the stance of the industry that the reporting of infections should not be required. In parallel, the high level of asymptomatic pigs demonstrates that the pandemic A/H1N1 virus may have escaped certain biosecurity policies and infrastructures, including syndromic surveillance based on clinical signs. Thus, in order to detect all positive cases of SIV, other diagnosis assays such as hemagglutination inhibition assay, ELISA, qRT-PCR, high throughput sequencing might be required and mandatory, and should be conducted on a regular basis.

As a result, improved surveillance particularly in the human/animal interface is a central issue in managing infection prevention and control in the swine industry. Establishing new surveillance measures requires reconciling various interests and therefore relies on cooperation (61). Sampling only animals expressing severe swine flu clinical signs is not enough because most animals infected by SIV are asymptomatic or have mild clinical signs. The cost of vaccination versus the low economical impact of SIV infection on the livestock performance does not encourage the swine industry to vaccinate their animals on a regular basis and to conduct routine SIV testing and viral genomic characterization. Punctual and random sampling (with whole viral genome sequencing) financed by the Canadian federal government might be a good surveillance of current and emerging SIV cases and could lead to a better prevention of a new possible epidemic. One must take public health and animal health into account as well as the economic impact, and must also apply economic compensatory measures as well as psychological monitoring with stakeholders if actions must be taken. The partnership must also be reinforced through communication and consultation with specialists, stakeholders, and producers, not only at the provincial level but also at the national and international level, in order to arrive at a consensus before any public communication is issued to ensure that words and deeds coincide. On the whole, the lessons drawn from this pandemic will have prepared the swine industry to reduce the risk of virus introduction and propagation for future, even more pathogenic agents.

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