Published in final edited form as:
Lancet Infect Dis. 2014 February ; 14(2): 169–172. doi:10.1016/S1473-3099(13)70227-5.

A possible outbreak of swine influenza, 1892

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Abstract

Influenza A viruses are globally enzootic in swine populations. Swine influenza has been recognised only since 1918, but an anecdotal report suggests that a swine-influenza epizootic might have occurred in England in 1892, at the same time as an explosive epidemic (or pandemic recurrence) of human influenza. This outbreak suggests that the ecobiological association between human and swine influenza could extend to before 1918. By contrast with the recent documentation of swine influenza, influenza in horses has been well documented for hundreds of years, and was often linked temporally and geographically to epidemics of human influenza. Both decreased contact between people and horses, and the concomitant increase in swine production over the past century, might have altered the character and dynamics of influenza host-switch events between people and domestic mammals.

Background

Both the 2009 pandemic of H1N1 influenza, and 2012–13 reports of swine-to-human transmission of H3N2 variant influenza at US state fairs,[1,2] drew attention to the complex relation between swine and human influenza A viruses. No evidence has previously been identified for pigs having influenza before 1918,[3–5] when the new influenza pandemic was epidemiologically linked to outbreaks of a clinically similar and ostensibly new disease in pigs.[5] The prevailing view was, and remains, that in 1918 the pandemic H1N1 virus was transmitted from people to pigs, adapted to pigs, and has persisted ever since as the classic swine lineage of H1N1 influenza. In 1931 and 1933, H1N1 influenza viruses from pigs and from people, respectively, were isolated and found to be closely related to each other.[6,7]

However, in the past 95 years, swine-influenza haemagglutinin 1 (H1) has changed via accumulating mutations more slowly in pigs than in people, resulting in widening of the antigenic distance between the two H1N1 viruses.[1] This distance increased to such a degree

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Both authors contributed equally to the literature search, data interpretation, and the writing of this Personal View.

Conflicts of interest
We declare that we have no conflicts of interest.

that, in or before 2009, a swine virus with 1918-like H1 donated its H1 to create a new reassortant H1N1 virus that then became pandemic.[1,8] Pandemic spread of this virus was possible because people born after about 1930–50 were not fully immune to it. During their lifetimes, they had only been exposed to human seasonal H1N1, with an H1 that had drifted significantly from the H1 of the original influenza virus from 1918. By contrast, people born before about 1930–50 were largely immune to the 2009 pandemic virus, because of previous exposures to early post-1918 H1N1.[9–11]

Influenza epizootics

Little evidence consistent with influenza occurring in pigs before 1918 exists. Fleming[3,4] documented hundreds of historical epizootics in pigs and other domestic animals, spanning millennia, none of which seem to be consistent with influenza. We examined hundreds of centuries-old reports of outbreaks of human and animal influenza,[5] without identifying a single epizootic that suggested swine influenza. Accounts of influenza epidemics, particularly from the 18th and early 19th centuries, occasionally note concomitant outbreaks in farm animals (sometimes including pigs), but these reports are usually either clinically and epizootiologically inconsistent with influenza, or are mentioned off handedly with few or no characteristics to distinguish them from other animal diseases.

By contrast with these vague reports of epizootics in pigs and other animals, from the 1600s equine-influenza epizootics were extensively documented, with re cognisable clinical and epizootiological details. These epizootics were often associated with outbreaks in human beings, and sometimes coincided with outbreaks of influenza-like disease in dogs (usually acquired from ill horses), cats (often associated with ill people), and, less frequently since the late 1700s or earlier, chickens and domestic poultry.[5,12] Several avian epizootics in 1789 in northern Italy,[13] and a US national epizootic in chickens associated with the 1872 western hemispheric panzootic of equine influenza,[14] are suggestive of highly pathogenic avian influenza. That numerous global reports of apparent influenza in other domestic animals were documented over a 300–400 year period, without similar disease documentation in pigs, is consistent with the belief that swine influenza did not occur before 1918.

Influenza in pigs

We recently became aware of an obscure report of an influenza-like outbreak in English pigs during an explosive recurrence of the 1889 influenza pandemic in 1892.[15] At the time of this swine epizootic, epidemic influenza was widespread throughout England, in temporal and geographical association with multiple epizootics and case reports of influenza-like illnesses in horses, dogs, and cats. The 1892 report was submitted by the physician Sir Peter Eade (1825–1915) to the influenza epidemiologist and historian Richard Sisley (1856–1904), who maintained an interest in influenza of domestic animals. It was read by Sisley at the Feb 17, 1892, meeting of the London Epidemiological Society.[15]

> *"It may interest you to learn that a large pig-farmer* [ie, a farmer with a large pig-breeding operation]… *was sure that many of his hogs had recently had the influenza. Those affected were seized with fever, panting, and distressing cough, and then in two to four days the illness appeared to pass off, and they were well,*

except for a little cough, which often remained a few days longer. One or two of them died."

Whether Eade's swine outbreak was actually influenza, or some other disease, cannot be known with certainty. However, occurrence of an outbreak of influenza-like clinical features in pigs at a time of widespread pandemic and epizootic influenza, reported by a notable and careful observer such as Eade (a prominent consulting physician at the Norfolk and Norwich Hospital, and an expert in clinical influenza), is suggestive. Other epizootic diseases of pigs such as swine fever (also known as hog cholera) had been sufficiently well characterised by 1892 that confusion with influenza is unlikely.

This outbreak happened more than 25 years before the description of influenza as a distinct disease in pigs, and if it was influenza it places the epizootic in temporal association with the then-new 1889 pandemic influenza virus. On serological and epidemiological grounds, the 1889 pandemic virus probably did not have H1, and the 1892 swine epizootic was unlikely to have been caused by H1 influenza virus, if it was in fact related to the 1889 pandemic virus. Available evidence suggests that the 1889 pandemic was caused by H3 influenza,[16] although other interpretations suggest that H2 influenza was responsible.[17] In the modern era, both human influenza viruses H1N1 and H3N2 circulate in pigs.[18] H3 viruses became enzootic in pigs only after the 1968 pandemic of H3N2 influenza; H2 viruses are far less common in pigs today, and none seem to be descendants of viruses that caused the 1957 pandemic of H2N2 influenza. Swine H2N3 viruses isolated in the USA in 2006 seem not to have become established in pigs.[19]

Changing associations between people and animals

If an outbreak of swine influenza happened in 1892, and if the virus was derived from a circulating pandemic or epidemic strain, why did it not (apparently, since additional swine outbreaks are not known) become established in pigs at the time, as did equine influenza in earlier years? The relative geographical isolation of England, and the lack of large-scale movement of pigs between England and continental Europe, might have prevented the spread of swine influenza virus from England, but no evidence suggests that the swine disease noted by Eade spread even locally, let alone abroad. The ubiquity and population structures of domestic animals such as pigs and horses, and their relation with people, should be noted. Between 1647 and 1918, episodic equine influenza, which sometimes appeared in roughly 4 year cycles, was commonly associated temporally and geographically with human influenza, whereas swine influenza was rarely (if ever) detected;[5,12] since 1918, enzootic swine influenza has become more prominent than equine influenza. As horses have become less ubiquitous in urban settings, equine influenza has tended to predominate in developing countries and in the stabled horse populations of developed countries, where it remains a notable enzootic problem causing periodic explosive outbreaks.[20,21]

An important difference between these pre-1918 and post-1918 enzootic periods could be the extent and degree of human proximity to the animals in question. The last large-scale nationwide epizootic of equine influenza in the USA was in the winter of 1915–16,[5] when horses were being rapidly replaced by automobiles in urban areas and by gasoline-powered farm machines in rural areas. Similar changes were occurring in Europe and the rest of the

developed world. A trend towards high-intensity pig farming seems to have been well underway by 1892. England's National Pig Breeder's Association, established in 1884, was already energetically fostering the growth of so-called factory-style systems for pig breeding,[22] a forerunner of modern intensive methods for pig farming (figure).

We speculate that coadaptation of human influenza A viruses to domestic mammals in close proximity to each other and to people was an important determinant of these epizootiological patterns; inversely, people were probably exposed to influenza A viruses adapted to domestic mammals under conditions of frequent or intense animal–host exposure. In the modern era, human-to-swine and swine-to-human transmission of influenza viruses is relatively common, creating a complex and dynamic ecosystem of enzootic and endemic influenza viruses with bidirectional flow of viral genes. Horses might have had an analogous role in the 17th to 19th centuries, the period of most frequent epizootics of equine influenza. At this time, almost all people in Europe and North America, whether in urban or rural areas, lived and worked in close proximity to horses. Horses were typically stabled together in environments that probably precipitated and sustained horse-to-horse transmission, and often travelled over large areas.

Epizootics of equine influenza tended to precede human epidemics by several weeks,[5] suggesting that epidemic and endemic influenza viruses could have arisen from equine reservoirs. At the very least, the circulation and evolution of human-adapted and mammalian-adapted influenza viruses in this era could have been distinctly different from that observed today.

Whether equine influenza viruses of the 19th century and earlier moved bidirectionally between people and horses with the same ease that they do today between people and pigs is unknown. The horse–human species barrier might be fundamentally different from the swine–human species barrier, or transmission barriers could result from properties of individual viral subtypes rather than animal species differences. Although people have been infected experimentally with equine H3N8 viruses, human outbreaks of H3N8 influenza have not been recognised in the modern era. Of uncertain significance, the equine H7N7 influenza virus (which is probably extinct) was once tenuously linked to human cases.[23] Between 1647 and 1917, horse-to-human and horse-to-dog transmission of influenza was widely reported to occur in many but not all equine epizootics, and equine epizootics and human epidemics were repeatedly linked in place and time.[5,12] Thus, the epizootic behaviour of equine influenza might be quite different today from what it was, and expectations about the species barrier imposed by equine and other mammalian viruses might be coloured by the mammalian viruses that currently prevail.

A shifting disease landscape

Swine influenza today might be similar to equine influenza in previous centuries, with pigs acting as a principal reservoir (or at least an amplifying host or cohost) of enzootic influenza viruses, available to seed human outbreaks or even pandemics. More than one mammalian reservoir for influenza could exist at a time, and the pattern of equine-influenza epizootics of earlier centuries probably would still prevail had the population structures of horses not

changed in the modern industrial era. Moreover, additional risks of influenza pandemics and epizootics might now derive from frequent introductions of avian influenza viruses to mammals such as pigs, horses, and dogs, and from increasing human-to-pig, pig-to-human, and horse-to-dog transmission, with pigs supporting the replication, reassortment, evolution, and movement of avian, swine, and human influenza viruses.[24–26]

As intensive farming and breeding of domestic mammals expands worldwide, the risk of viral emergence of influenza into human populations continues, as for other viral pathogens (eg, Nipah and Hendra viruses).[26] Study of the circulation of influenza viruses between people and domestic animals (including bidirectional cross-species transmission between people and pigs, horses, dogs, birds, and perhaps other domestic species[27]), and examination of the determinants and viral evolutionary outcomes of such transmissions (including mutations and reassortments) should be a high-priority subject for influenza research. Other important topics include study of viral genetics and epidemiology of early host-switching events (eg, the avian-derived H1N1 virus in European pigs, the avian-descended H3N8 virus in horses, and movement of the classic equine-descended H3N8 and avian-descended H3N2 viruses into dogs); study of avian viruses that sometimes infect people or pigs, such as highly pathogenic avian H5N1 and low-pathogenicity H7N9 and H9N2; and the role of environmental determinants, such as intensive pig production, live poultry markets, and dog sheltering, in the epizootic behaviour and evolution of these increasingly dynamic viruses.

Acknowledgments

This work was supported by the Intramural Research Program of NIAID, and is work of the US Government.

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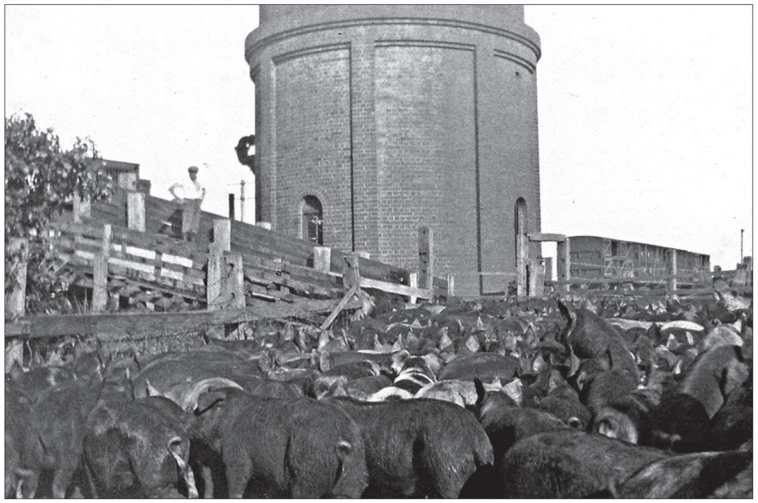

Figure.

Intensive pig farming seems to have become common beginning in the late 19th century
Undated photograph, probably late 1800s or early 1900s, New South Wales, Australia.