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*Phil. Trans. R. Soc. Lond. B* 1980 **288**, 433-437  
doi: 10.1098/rstb.1980.0020

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## Animals in the influenza world

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In the history of influenza there are many references, notes and comments about influenza epizootics occurring among various non-human animals, sometimes coinciding with epidemics of influenza in human beings. That the first influenza viruses were recovered from non-human animals is not so surprising, given the current knowledge of the distribution of influenza among animals. Influenza viruses are found in a wide variety of mammalian and avian species. In some species the disease that occurs as a result of the infection mimics the influenza disease of human beings, in other species there are no signs of disease, and in others there is disease specific to a species. It is clear that influenza viruses have a significant impact on the health of several animal species. In recent times it has also become clear that many species of animals are inextricably entwined in the puzzle of influenza viruses and human influenza. Our knowledge in animals has provided both questions and answers about the influenza viruses and their diseases. Certainly our understanding of human influenza has been advanced because of the animals in the influenza world.

## INTRODUCTION

The term influenza has been used to describe various kinds of acute respiratory and generalized diseases of several animal species, especially horses, probably for as long as the term has been used for describing disease in human beings. In some cases, reference is made to the animal 'influenza' coinciding with episodes of 'influenza' in human beings. Given the current knowledge of the distribution of influenza virus infections among animals, it is not unreasonable to believe that some of the diseases were in fact caused by influenza viruses. However, it was not until the late Richard E. Shope demonstrated the viral nature of swine influenza (Hsw1N1) in 1930 that the viral cause of any influenza was known.

Three years later the first influenza virus of human origin was isolated with the use of an animal 'substrate', the ferret. Then more than two decades were to pass before influenza viruses were identified in species other than human beings and pigs. The influenza world expanded considerably in 1955–6 with the identification of influenza viruses from horses and ducks and the revelation that the fowl plague virus contained the type A influenza virus type-specific ribonucleoprotein (RNP).

Over the next two decades, 1955–75, animals became more conspicuous in the influenza world. For example, a second antigenically distinct virus was found in horses, and the H3N2 (Hong Kong) viruses were found in pigs, cattle, chickens, dogs and other species throughout the world. The most remarkable proliferation of animals in the influenza world was among the avian species. Since 1956, uncounted viruses, possibly hundreds in all, have been found in more than 50 species of birds. Although the number of viruses and species reported continues to increase, not all members of the animal kingdom are affected by influenza virus infections.

[ 145 ]

31-2

It is my purpose to consider here first those best known, common influenza virus infections of domestic species, provide an overview of the other various mammalian and avian influenza virus infections, and to examine the significance of influenza virus infections among animals.

#### SWINE INFLUENZA

From time to time since 1918, when the disease was first described, swine and influenza of swine have received considerable attention. The disease, apparently unchanged, has remained common among swine throughout north central United States where it was described as a new disease by those who first worked with it. While the infection and the disease may have existed among swine populations before that time, it is unlikely that a disease with such distinctive characteristics would have gone unnoticed and unreported. The disease received its name because of the remarkable similarity of the signs of the disease in the pig to those that were being observed in human beings during the 1918 pandemic.

What does this infection mean to a herd of pigs and to the owner of those pigs? In north central United States, swine influenza is an acute, febrile, respiratory disease of pigs of all ages. It is characterized by sudden onset, coughing, fever, a high morbidity rate, a low mortality rate and a rapid recovery. Virus is present in the nasal secretions, most commonly during the febrile period. Generally, the lesions are those of rhinitis, pharyngitis and focal viral pneumonia. Occasional severe viral pneumonia may cause death. The overall death rate is believed to be less than 1%. Higher death rates occur in very young pigs. Based on a serological study in the mid-1960s in Wisconsin and a more recent nationwide surveillance programme conducted by Webster & Hinshaw in Tennessee and by Easterday and Gundersen in Wisconsin, it has been estimated that at least 25% of all pigs in the United States that go to slaughter have been infected with the swine influenza virus. The infectivity rate is slightly higher among those animals that have been used for breeding purposes and which are sent to slaughter when they are 2 or more years old.

For many years it was believed that the disease and infection with the virus occurred only in the late autumn and early winter. Shope offered the hypothesis that the virus was maintained during the inter-epidemic period in an 'occult' or latent state in lungworm larvae, in earthworms, or in adult lungworms in the pig. He could not offer any other explanation for the maintenance of the virus from one epidemic season to another. However, during the same period Scott reported that swine influenza was present at all times of the year, albeit more common in the autumn and early winter. It is now quite clear, on the basis of observations made over a long period of time and extensive serological and virological surveys, that the infection and disease occur at all times of the year. Thus, it is not necessary to propose a complicated multiple host system for the maintenance of the swine influenza virus.

It is not likely that the swine husbandry practices were sufficiently different during the 1930s to be responsible for a different natural history of swine influenza. From all accounts it would appear that the natural history of swine influenza has not changed in a significant way in north central U.S.A. over the past 50 years. That situation seems to be unique in the world because there are no other areas where swine influenza has been reported to be maintained in such an unchanging way for such a long period of time.

Another aspect of the same question is the disappearance of swine influenza from Czechoslovakia. During the 1950s, influenza was reported there to be a disease similar to that reported

in the U.S.A. Through the 1960s the disease, along with its causative virus, disappeared. In that country it is quite clear that there were marked changes in swine husbandry practices.

Why be concerned about swine influenza? Because as is well known, any disease condition contributes to the cost of production. It thus remains to quantify the economic impact of this disease on the production of pork. How does it increase the cost of production if the mortality rate is very low? Assume that 25% (20 million) of the pigs in the United States are infected with swine influenza each year. Then assume that the effect of infection and disease is to delay the pig's reaching market by 2 weeks. That means that the pig must be cared for, fed, housed, etc., by the owner for an additional 14 days. The 1978 agricultural statistics indicate that it costs \$0.50 to \$0.60 per day to produce a pig to 100 kg in 180 days. Thus, that additional 2 weeks requires an additional \$7.00 that the owner must invest in those pigs. That \$7.00 for each of 20 million pigs is a \$140 million burden on the industry and ultimately the consumer. That loss does not include dead pigs, reduced breeding efficiency, etc. It is reasonable to ask whether those losses can be reduced. Studies on a small scale indicate that pigs can be protected against disease by vaccination. It remains to determine whether the cost : benefit ratio would justify some type of vaccination programme for swine.

Another aspect of swine influenza that remains to be defined is the occupational hazard of infection of caretakers. All speculation as to whether human beings could be infected by pigs came to an end in 1976 when the virus was recovered from sick pigs and their sick caretakers on two farms in Wisconsin (U.S.A.). However, the frequency of such occurrences remains to be determined.

#### EQUINE INFLUENZA

More than a quarter of a century passed after the swine influenza virus was isolated before an influenza virus was to be isolated from another non-human mammalian species. Tumova and her colleagues reported the isolation of a type A influenza virus (Heq1Neq1) from horses in Czechoslovakia in 1956 after a report by Swedish workers of the presence of type A influenza antibody in horses in that country in 1955. Subsequently, another type A influenza virus (Heq2Neq2) was recovered from horses in the United States in 1963. The disease in the horse is similar to the disease in pigs and human beings in that it is an acute febrile, respiratory disease characterized by sudden onset, high fever, cough, shedding of virus for several days and a rapid and uneventful recovery, assuming that the animals are allowed to rest after the acute stages of the disease. The infection and the disease of horses are associated with the movement of horses and epidemics tend to follow from one horse show to another, from one race course to another and from one stable to another. There have been considerable economic losses associated with this disease in horses, especially as it relates to race horses. When a horse is ill it is unable to race, when it is unable to race it does not earn money for its owner and it does not bring revenue into the public coffers by the pari mutuel betting system. The use of the vaccines has been effective in the control of this disease, provided they are properly administered. In contrast to swine influenza, equine influenza seems to be quite uniformly spread throughout the world and the characteristics of the infection and disease are similar in all places.

## AVIAN INFLUENZA

In reality, the viral aetiology of influenza was established in 1900 when fowl plague was shown to be caused by a 'filterable agent'. However, it was not until 1955 that Shafer determined that the fowl plague virus was an influenza virus as demonstrated by the presence of the type A RNP. Classical fowl plague was one of those devastating diseases of chickens reported in many parts of the world for many years. It caused very high mortality and spread rapidly among domestic chickens. It was a generalized disease of short duration and high mortality. It was one of the diseases for which the United States developed eradication and control measures to protect the poultry industry. Fowl plague, as such, today appears to be rare and seldom described, though it has been one of the limiting factors in poultry production in many parts of the world.

A different kind of avian influenza era began in 1956 with the isolation of type A influenza viruses from ducks in Czechoslovakia and England. Subsequently, it was shown that type A influenza viruses other than fowl plague had been isolated in 1949 from chickens in Germany and in 1952 from ducks in Manitoba. After 1956 there was a brief lull until a type A influenza virus was isolated from chickens in Scotland in 1959; there was another lull until 1961 when another virus was isolated from terns in South Africa. In both of those the viruses involved were virulent and caused a high mortality in the affected species. During the 1930s, many influenza viruses were recovered from avian species, both domestic and wild, throughout the world. Such recoveries continued through the 1970s to the present and influenza viruses with a very wide range of antigenic characteristics were detected. In fact, most of the known antigenic surface determinants have been identified among viruses isolated from birds. Since infection is widespread and produces little disease of birds, it is likely that there has been a very long and adaptive relation between at least some of the avian species and many of the influenza viruses.

In recent years, and especially during the months before this symposium (October 1978–January 1979), there have been extensive losses among turkeys in northern Wisconsin and Minnesota in the U.S.A., due to these influenza viruses. The economic loss associated with those infections has not been determined. However, it was estimated that the losses in Minnesota in late 1978 were in excess of \$4.0 M.

## OTHER SPECIES

There are no novel influenza virus antigens that have been identified first in any mammalian species other than swine, horses and human beings. However, it is clear that influenza viruses have been isolated infrequently from other mammalian species, e.g. the H3N2 viruses from cattle and dogs. Why is it that populations of domestic ruminants such as cattle, sheep, and goats have not entered the influenza world along with swine and horses?

There are many more interesting questions that could be asked about animal influenzas and animals, animals in the influenza world or influenza in the animal world. What is so unique about the United States with regard to swine influenza? Swine influenza similar to that in the U.S.A. has been reported in Italy. Why is it that the chicken populations of the United States have remained so free from influenza virus infections when they have been so commonly infected in some other parts of the world? It seems especially strange in view of the widespread infections among turkeys and migratory waterfowl in the United States. Why is it that these viruses are so widespread in birds? Will it eventually be found, if not already, that all of the

antigenic and genetic characteristics of influenza viruses occur among influenza viruses isolated from birds? Why is it that ruminants have remained so free of these infections, considering the ubiquity of some of the influenza viruses and the association that those animals have with human beings? What is the impact of these infections on these various domestic and wild animal populations?

#### PUBLIC HEALTH

One of the major reasons for concern about influenza in animals is not for the animals themselves but rather for the public health significance of infected animals.

There has been long continued and extensive speculation on the role of animals in the natural history of influenza and the relations between animal and human influenza. One prevailing hypothesis is that novel pandemic strains are the result of a recombinational event in an animal to man infected with two influenza viruses. Furthermore, for about 20 years, from 1957 to 1976, many have looked for an incident that would put an end to speculation about whether influenza viruses transfer from animals to man. That event occurred in Wisconsin in November and December of 1976, on farms, when the same virus (Hsw1N1) was recovered from sick pigs and a sick man who had cared for the pigs.

Speculation continues, and further hypotheses have been offered, about the animal origin of strains of influenza viruses that are pandemic for human beings. If we continue to entertain these as major hypotheses for the origin of pandemic strains of influenza viruses, then there should be a much greater commitment to the support and study of the ecology of influenza viruses and to the role of animals in the influenza world.

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