

newsletter

Avian influenza (bird flu)

On 9 September 2004 the Ministry of Public Health in Thailand confirmed another fatal case of infection with H5N1 avian influenza. The victim, an 18-year-old, had come into contact with infected poultry.

Introduction

Influenza viruses are responsible for numerous highly contagious and potentially fatal diseases in humans (clinical influenza) and in different species of mammals and birds (avian influenza). In Germany alone, seasonal influenza epidemics claim some 5,000 – 8,000 lives each year and force a further million or so workers to take short-term sick leave. The type of avian influenza that affects bird populations has a mortality approaching 100%.

H5N1 influenza virus

Type A influenza viruses are arranged into subtypes according to specific surface antigens (H and N). Up to now, scientists have managed to isolate 15 H subtypes and 9 N subtypes. These normally infect specific hosts only. However, by swapping or "reassorting" genetic material, they can mutate to form a novel subtype different from other influenza viruses. The virus responsible for the seasonal influenza epidemic in 2003/2004 was given the name H3N2/Fujian. H5N1/Hong Kong, the type responsible for bird flu, was not transmitted to humans until 1997. To date, 39 cases of illness and 28 human deaths through infection with the H5N1 avian influenza virus have been reported in Thailand and Vietnam.

It was not until 1997 that the H5N1 avian influenza virus, having previously affected only birds, succeeded in crossing species, leading to considerable albeit localised financial losses involving stocks of farm animals.

Current situation

Despite the culling of millions of birds, hens and chickens, the virus broke out again in south-east Asia at the end of 2003 and has so far (September 2004) reached China, Indonesia, Japan, Cambodia, Laos, South Korea, Thailand and Vietnam. In August 2004, it became apparent that the same subtype had been found in pigs in China in 2003. In the same month, Malaysia confirmed its first cases of infection in poultry. Other subtypes were evidently responsible for outbreaks in the USA, Canada, Pakistan and Taiwan. The virus found in south-east Asia is an influenza virus of the H5N1 strain, one that has undergone a series of genetic mutations since first appearing in 1997 (Nature 2004; 430: 209-213). Today, this virus is found not only in hens and chickens, but also in domestic ducks. Despite the renewed slaughter of the entire poultry stocks of infected farms, experts now fear that the virus has become endemic and that an avian influenza epidemic in south-east Asia is now inevitable, especially since the virus can be transmitted also by birds living in the wild. Farms in China, Indonesia, Thailand and Vietnam are affected. Cases of human infection are currently being reported only from Thailand and Vietnam. The World Health Organisation (WHO) has since confirmed that the four people who died between

2 August and 9 September 2004 had been infected with H5N1 influenza.

Risk Pandemics

Influenza viruses are highly adaptable, and experts fear that there will be a pandemic if the H5N1 virus genetically mutates to such a degree that it becomes readily transmissible from person to person – something which has not, however, been observed so far. The few cases of transmission from birds to humans observed (67 cases out of millions of infected birds) points to a relatively low risk of transmission.

However, reports from China that the aggressive and highly pathogenic H5N1 strain had been discovered in otherwise healthy pigs were grounds for serious concern. This is all the more worrying since pigs can be infected by the H3N2 human influenza virus, too. Were these animals to be co-infected, the two strains would be able to swap genetic material in the organism of the pig and produce a new subtype as highly contagious as the human strain and as lethal as the avian. A virus of this nature would be readily transmissible from person to person and would very likely trigger a pandemic on the scale of the Spanish influenza virus of 1918/19 which resulted in an estimated 40 - 50 million deaths and 500 million people becoming sick. A genetic mix of this nature would be conceivable also if a person infected with avian flu were to become infected with the human form of the flu virus. In genetic terms, this represents a relatively small step for the influenza viruses.

Inoculation, Treatment with drugs

Annual inoculation of humans with vaccines effective against currently circulating human influenza strains can help avoid major epidemics. Vaccination in areas where avian influenza is endemic can reduce the likelihood of co-infection of humans with avian and influenza strains, and thus reduce the risk that genes will be exchanged. The WHO advises workers on south-east Asian poultry farms to keep a supply of antiviral drugs available so that treatment can be started at the first sign of symptoms and the spread of the virus can be checked as far as possible.

Furthermore, the WHO has set up a global influenza network with 112 surveillance centres across the continents in order to be able to respond quickly to outbreaks. The WHO is keeping a particular eye on bird flu so that early warning of an emerging pandemic can be given.

The emergence of a pandemic H5N1 virus with the ability to move from person to person would result in a huge demand for the appropriate vaccine. However, such vaccines cannot be produced until the new strain is known, and since production capacity has to be geared to current demand due to the specific production techniques, manufacturing drugs in significant quantities takes time. For this reason, the R&D departments of several drug companies are turning their attention to the development and accreditation of new manufacturing processes and on the creation of additional capacity by purchasing and expanding vaccine factories (eg in Austria and the Czech Republic). One multinational is planning to step up production to 100 million doses a year, and two other leading players claim to be able to satisfy world demand for any new vaccine within 4-6 months in an emergency. Research carried out by the New York Times suggests that various governments are considering stockpiling the antiviral drug Oseltamivir. In Europe and the USA, plans are afoot to establish large stocks. China is apparently conducting negotiations with a manufacturer, Taiwan already has stocks, and Japan is planning its own domestic production.

Only one company in Europe currently produces Oseltamivir and, by its own admission, is not in a position to increase production at short notice. Other drugs for the prevention and treatment of influenza infections include Zanamivir, Amantadin and Rimantadin. However, the latest research suggests that both Amantadine and Rimantadine may already be ineffective against the current H5N1 virus, which has now mutated into a new antigenic variant.

**Information for
the underwriter**

1.2 % of the recognised cases of vaccine-related injury that occurred in Germany between 1972 and 1999 involved the human influenza virus. In the USA, 1 % of such injuries is caused by the flu vaccine. Around 80 % of these cases were not regarded as serious, but 20 % resulted in death, disability, hospitalisation or chronic illness. This corresponds to around 2,200 cases of serious impairment from 530 million influenza vaccinations (figures from the USA over a 10-year period).

In 1976, a number of soldiers in the USA began to show the symptoms of a swine flu infection. In order to prevent a major epidemic, the government initiated a mass inoculation programme in the course of which some 45 million people were treated with a hastily prepared emergency vaccine. Of the 1.7 million soldiers who received the vaccine, 500 developed what is known as Guillain Barré Syndrome (GBS) or "acute ascending polyneuritis", a disorder in which a person's immune system attacks the myelin sheaths that surround the axons of many peripheral nerves. Although the disease normally disappears after a few weeks, it can become chronic and in rare cases cause death due to paralysis of the respiratory muscles. The case demonstrates how mass inoculation with emergency preparations may well lead to cases of bodily injury and health impairment among recipients, even if the numbers are negligible compared with the number of people who would most certainly in a pandemic without any inoculation programme.

Although the drugs used produce side-effects, too, these are not considered to be serious. With mass usage, however, one would have to reckon with increased incidence of illness.

Ultimately, the scale of a potential pandemic involving a highly contagious strain of avian influenza will depend largely on the mobility of the population in question and on the ability of the authorities to instigate adequate countermeasures in good time.

Generally speaking, we can assume an increased liability risk in connection with influenza vaccines due to short development and production cycles, and large number of single treatments.

Contact

AssTech GmbH
Postfach 1211
85766 Unterföhring bei München
Telephone + 49 89 3844-1585
Telefax + 49 89 3844-1586
info@asstech.com
www.asstech.com