

GUEST OPINION:

Bird flu virus H5N1 – a deadly risk for humans?

The recent spate of international conferences convened by scientists, UN agencies and the donor community on epizootic aspects of avian influenza (AI), referred to in the media as «bird flu», and on the possibility that it could develop into a human influenza pandemic, shows that AI is slowly being taken increasingly seriously around the world. International organizations especially are warning that the virus could leap species and spread to humans; some scientists, on the other hand are more sceptical as to whether there is any immediate danger of this happening.

Professor Dr Karl-Hans Zessin
Free University of Berlin
Faculty of Veterinary Medicine,
International Animal Health
Berlin, Germany
Zessin@vetmed.fu-berlin.de

The significance of avian influenza (AI) as an epizootic disease is clear and undisputed: since late 2003, starting in Southeast Asia, the highly pathogenic avian influenza virus (Asian lineage HPAI) of subtype H5N1 has been spreading worldwide. H5 is one of 16 subtypes of the HA virus (H1-H16) within the influenza A group among wild birds. Wild birds represent a natural reservoir of influenza A virus subtypes and are assumed to be the source of this group of viruses among other birds. The highly infectious avian influenza subtypes H5 and H7 produce the most severe forms of the disease. Chickens, turkeys and waterfowl are the most susceptible to the H5 form that is currently rampant. At 3 May 2007, H5N1 avian influenza in animals had been reported in 58 countries to the World Organisation for Animal Health (OIE) and more than several hundreds of millions of chickens had had to be slaughtered in an effort to control the disease. There is therefore no doubt about the fact that H5N1 warrants the utmost attention as the causative agent behind the current epizootic. It is also undisputed that H5N1 could theoretically lead to a human pandemic. It is doubtful whether such a pandemic is likely, despite

the horror scenarios forecasted by international organizations, for example.

Doubts regarding a human H5N1 pandemic

Is it really only a matter of time before an avian influenza virus – most probably H5N1 – acquires the capability of human-to-human transmission, which would lead to the outbreak of a human influenza pandemic? This was the view of Dr Lee Jong-wook, Director General of the World Health Organization (WHO) who unfortunately passed away in May 2006, as publicized in November 2005 (USA Today, November 7, 2005). Is it really plausible that a pandemic caused by AI would lead to the deaths of between 5 and 150 million people, as suggested in September 2005 by David Nabarro, Senior UN System Coordinator for Avian and Human Influenza (Press Conference, United Nations, 2005)? A small but illustrious number of scientists have been voicing their scepticism. They do not question the fact that another influenza pandemic is to be expected; they are not convinced, however, about whether it will be the predicted H5N1 pandemic. There is also scepticism about how



Photo: Mondry

One way to prevent a further spread of the disease among the birds is vaccination. This is also a safeguard measure for the villagers.

soon such a pandemic is to be expected, and about whether the death toll will be as high as has been suggested.

A closer look at the scientific data reveals other potential scenarios: first of all, every one of the six pandemics that have occurred since the late 18th century was caused by one of the three other – likewise recurring – subtypes of the virus, H2, H3 and H1, but not by H5. The three worldwide pandemics of the 20th century, often used as a reference point, were caused by H1 (1918: «Spanish flu»), H2 (1957: «Asian flu») and H3 (1968: «Hong Kong flu»). In the case of the current outbreaks of bird flu around the world, a few humans have contracted the H5 virus directly from birds. Those infected, however, had all been in very close contact with infected poultry, and they had been exposed to large amounts of the virus from infected or dead birds.

Up to 11 April 2007, 291 cases of the disease had been confirmed in humans in Azerbaijan, Cambodia, China, Djibouti, Egypt, Indonesia, Iraq, Lao PDR, Nigeria, Thailand, Turkey and Vietnam, resulting in 172 fatalities (WHO, 2007). This high mortality rate of more than 50 percent has raised doubts, however. It is plausible that the confirmed cases tended to be the ones where the patients had been so severely ill that they could not have escaped the notice of the health authorities. More recent data from Vietnam actually show that HPAI is occurring far more frequently in humans than is commonly assumed, especially in cases where there has been contact with poultry. Where illness arises as a result of infection with the virus, the symptoms are usually mild; in other words, it does not usually result in death and is therefore not continually recorded in the public health systems (Thorson et al., Arch Intern Med 166, 2006). For this reason, Paul Ewald, evolutionary biologist at the University of Louisville, Kentucky, is firmly convinced that even if H5N1 did develop the ability to cross the species barrier to humans, the infection would probably tend to be mild (Science 310, November 2005). Another argument that has been advanced is based on the fact that the three exclusive virus subtypes H2, H3 and H1 occurred at regular intervals for around 68 years.

Paul Offit, immunologist and virologist at the University of Pennsylvania School of Medicine (Science 310, November 2005) explains the hypothesis postulated by Maurice Hillemann. He considers that these intervals are explained because the population that was previously exposed to a pandemic and developed antibodies to it dies out after around 68 years, and the population that succeeds it is then completely vulnerable to a new pandem-



Photo: IBERI

ic. According to this theory, Offit says, another pandemic could occur around 2025, due to an H2 virus.

Consequences of mutation of the H5 virus

If infection of humans with the «original» H5 virus by chickens is thus the exception and, moreover, the ability of the virus to cross over to mammals is slight, the only basis for a pandemic would be the emergence of a new H5 virus capable of infecting humans more easily and with enhanced ability to spread infection among humans. This could take place by means of mutation (antigenic drift) of the H5 virus itself, or by recombination of the H5 virus with a human influenza virus (reassortment). The longer and further afield the virus circulates among birds, the greater the likelihood of mutations occurring; the avian virus transforms itself into a human virus by genetic reassortment. Paul Offit and microbiologist Peter Palese of the Mount Sinai School of Medicine in New York (Science 310, November 2005) point out, however, that since the highly publicized outbreak of bird flu in Hong Kong in 1997, H5N1 has shown no signs of

Prerequisites for infection with the H5 virus: close contact with poultry and exposure to large quantities of the virus.

any enhanced ability to cross the species barrier from chickens to humans, or to spread more quickly among humans. In fact, H5N1 has not just been around since the Hong Kong outbreak, but for a lot longer. The disease was first identified in 1959 in two chicken flocks in Scotland. Therefore, the virus has had not eight but 47 years to mutate or reassort, but has done neither; no pandemic has arisen.

Is this debate merely theoretical and academic? Certainly not; there would be nothing worse than if public vigilance were to flag and preparations to deal with a pandemic, including development and stockpiling of improved vaccines and medications, were to falter due to the forecasted H5 pandemic not taking place. No-one disputes that a pandemic is indeed to be expected and that every effort should be made to prepare for it. The scientific basis for predicting whether or not it will be the result of the H5N1 strain, however, seems less sound than is often suggested.