Highly Pathogenic Avian Influenza (HPAI, Fowl Plague, „Bird Flu“)
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Disease and causative agent

What is fowl plague and “bird flu”?
Classical fowl plague is a fatal disease of birds particularly affecting chicken and turkeys. Bird species such as ducks and geese in general show a lower susceptibility. The disease is caused by highly pathogenic (strongly disease inducing, HP) avian influenza viruses (AIV) of the subtypes H5 and H7.

Highly pathogenic AIV evolve by mutation from low pathogenic influenzaviruses, i.e. variants, which induce only mild symptoms of disease. Only infections with HP-AIV variants induce dramatic courses of disease with mortality rates of up to 100 % which may spread rapidly and are therefore named fowl plague.

“Bird flu” is the term used by the general public for infections of farmed poultry with avian influenzaviruses since the occurrence of highly pathogenic H5N1 virus from Asia.

Why are some influenzaviruses particularly pathogenic for birds, while others cause no or only mild symptoms of disease?
Avian influenzaviruses belong to the group of influenza A viruses. They have two surface proteins, hemagglutinin (H) and neuraminidase (N), which are important for interaction with cells and thus for their infection. These proteins may occur in different variants (subtypes). In avian influenzaviruses 16 hemagglutinin subtypes (H1-16) and nine neuraminidase subtypes (N1-N9) have been described. The subtypes of the virus are named based on the structure of H and N, e.g. H5N1, H5N8, H7N3, or H7N7.

Both surface proteins are subject to continuous change. This leads to novel variants which are not recognized by the host’s immune defense, sometimes infect new hosts and thus ensure their spread. In the environment, only subtypes H5 and H7 can spontaneously mutate from low pathogenic (LPAIV) into highly pathogenic variants. While LPAIV replicate only locally in the respiratory and intestinal tract of birds, HPAIV spread throughout the organism and cause death within 2 to 3 days. The mutations involved in this process consist in a modification of a hemagglutinin section which is important for activation of proteolysis.

What is the difference between highly pathogenic influenzaviruses of the subtypes H5N8 and H5N5?
The two causative agents of fowl plague mainly differ in one of their surface proteins, neuraminidase, abbreviated with N. First analyses of the HPAIV of the subtype H5N5 detected in Germany indicate that it might be a novel “mixed virus” (reassortant) based on the original H5N8 virus.

How do such “mixed viruses” (reassortants) evolve?
Mixed viruses of avian influenzaviruses, so-called reassortants, evolve when one animal is infected simultaneously with several virus subtypes and the virus subtypes exchange genetic material during replication. This exchange of genetic information is typical for influenzaviruses and contributes to their high variability.

What are the consequences of the occurrence of H5N5?
The occurrence of reassortant avian influenzaviruses of the type H5N5 is not surprising and has no impact on the risk assessment of the FLI on fowl plague or on the recommendations for measures to be taken (see information of the FLI).
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Distribution

Where does the fowl plague virus H5N8 come from?
Highly pathogenic avian influenza virus of the type H5N8 (HPAIV H5N8) was first detected in early 2014 in South Korea. Approx. 12 million animals had to be culled to control the infection. Outbreaks were also reported from China and Japan. In late 2014 H5N8 occurred in different European countries, among them Germany, the Netherlands, and the United Kingdom. The virus also spread to North America in late 2014. There H5N8 reassorted with other American influenza viruses resulting in the highly pathogenic subtype H5N2 which infected about 150 poultry holdings before the epidemics could be stopped in summer 2015.

In summer 2016, highly pathogenic H5N8 viruses were detected in wild birds in Southern Siberia and since the end of October again also in European wild birds. The currently detected viruses are very closely related with those from Southern Siberia, but differ genetically from the previously detected HPAIV H5N8. It has not been clarified yet whether the biological characteristics of these viruses also changed. In contrast to 2014 a larger number and other species of wild birds seem to be infected. The clinical symptoms observed so far are also more severe. This is in particular shown by the increased mortality rate in tufted ducks.

What is the role of migratory birds in the spread of highly pathogenic H5N8?
It has been proven scientifically that wild birds are a natural reservoir for avian influenza viruses (AlV) and spread them. The spread of the 2014 virus by migratory birds was among others investigated and described by an international research consortium of virologists, epidemiologists and ornithologists (Lee et al. 2015, J. Virol. 89, 6521-6524; Kuiken et al.: Role for migratory wild birds in the global spread of avian influenza H5N8; Science 14 Oct 2016: Vol. 354, Issue 6309, pp. 213-217, doi: 10.1126/science.aaf8852). The spread of AIv by wild birds is a plausible explanation for many outbreaks within and outside Europe.

Can infected wild birds travel over longer distances?
It is unknown how far infected wild birds are able to fly. However it is not necessary that an infected bird travels over long distances. It is essential to maintain a chain of infection, so that the virus is passed from one resting place to another. Thus, a gradual spread of the pathogen from Asia is entirely possible as breeding areas and migration routes overlap.

A number of factors may be involved in the introduction of avian influenza viruses into domestic poultry holdings. In outdoor holdings direct contact of poultry with infected wild birds is possible. Also in seemingly closed indoor holdings introduction of the virus by indirect contact is possible: among others addition of new animals, human and vehicular traffic, goods, food and water represent risks for introduction. Indirect introduction by possibly contaminated food, water, equipment or litter must be considered. Even invisible traces of feces or nasal secretions of wild birds are sufficient for transmission.

Which routes of introduction exist?
Clear routes of introduction of the HPAIV H5N8 currently circulating in Europe have not been identified yet. Based on detailed analyses of the viruses from 2014 and from the current outbreak indicate a presumable involvement of migratory birds.
Diagnostics and outbreak investigations

How can the pathogen be detected in wild birds and domestic poultry?
To confirm the disease, determination of the subtype (H5 or H7) and of the pathogenicity (low or highly pathogenic) is required in addition to virus detection. For further information please refer to the Official Method Collection (Amtliche Methodensammlung, in German language, in particular item 2: sample material): https://openagrar.bmel-forschung.de/receive/openagrar_mods_00005454.
This link provides detailed information on the test kits used and an overview of the test procedure. As a rule, clarification of a suspect case at the FLI takes about half a day.

Is it possible to determine whether a carrion-eating wild bird has acquired H5N8 infection or has only ingested contaminated carrion?
Yes, this is possible. An infected carrion-eating wild bird has a high virus load in the respiratory tract (not in the digestive tract). This clearly indicates infection with H5N8.

Does the FLI also investigate the spread of fowl plague virus via transportation routes of the international poultry industry?
Yes, in case of an outbreak all possible introduction routes are investigated, also access of poultry and possibly contaminated goods or objects to the affected holding. Furthermore, the import of and intra-Community trade with birds and animal products are observed using TRACES, a reporting system of the EU.

Import of poultry and poultry products from HPAI-affected areas is prohibited; however, illegal import is possible and represents a risk which should not be neglected. In case of an exposure of poultry this would lead to an outbreak of fowl plague with high mortality rates among the infected animals at least in gallinaceous birds. This would not remain unnoticed.

In the frame of epidemiological investigations it is of utmost importance to ensure that biosafety measures within the poultry holdings are assessed and improved so that the number of further outbreaks is reduced.

Is there a risk that an unnoticed infection might occur in a domestic poultry holding, e.g. during the incubation period, when animals do not show any clinical symptoms yet?
Monitoring results from domestic poultry do not indicate that there is a latent, unnoticed HPAI infection in German poultry holdings.

Due to the highly pathogenic characteristics of the virus H5N8 infection in a poultry holding will be noticed very rapidly based on the increasing number of dead animals. In infected chicken and turkeys the usual incubation period, e.g. the time from infection to the occurrence of clinical symptoms or death of the animal, is 1 to 3 days at the most. During the asymptomatic incubation period no or only little virus is excreted. Only after virus replication in the infected animal, which is accompanied by the development of severe clinical symptoms, increased virus excretion and infection of other animals or contamination of the environment occur. Prior to slaughtering animals are investigated clinically and symptoms of the disease will be observed. The chance that asymptomatic poultry will be slaughtered at exactly this stage of infection is extremely low. Gallinaceous birds are extremely susceptible to fowl plague, they transmit the pathogen by eye or nasal discharge and can excrete it with their feces. If this happens, the H5N8 infection will spread at an explosive rate throughout the holding and will cause an extremely high mortality rate within 1 to 2 days. Infected eggs also die off very quickly, so that the embryo will not hatch.
Poultry holders are obliged by law to report even a slightly increased mortality rate and have their holding investigated for fowl plague.

In waterfowl (ducks and geese) kept in captivity infection may be less obvious. However, the currently circulating fowl plague virus H5N8 also induces clear symptoms in waterfowl which will help identify infected holdings. Random investigation of waterfowl kept in captivity and analyses in association with the current outbreak have not indicated an unnoticed presence of HPAIV H5N8 in domestic poultry in Germany.

**Measures**

**What will happen when cases of fowl plague occur in domestic poultry in Germany?**

EU-wide and national regulations are in force for the control of fowl plague. In principle, poultry in infected holdings will be culled and disposed of securely. In addition, the responsible authorities will define protection and surveillance zones where poultry holdings are observed very closely to avoid a further spread of the pathogen. Further information can be found in the „Verordnung zum Schutz gegen die Geflügelpest“ (in German language).

**What happens to contaminated feces, litter etc. from infected holdings?**

In case of an outbreak the responsible local veterinary authority will also impose mandatory disinfection of feces, litter and liquid manure from infected holdings (section 19, paragraph 1 number 3a of the Geflügelpest-Verordnung). These potential sources of infection will thus be rendered harmless and eliminated.

**Vaccination**

**Would prophylactic vaccination of domestic poultry be a possibility?**

Vaccination is not permitted in the EU. Due to the high variability of the viruses vaccination against influenza often does not provide sufficient protection. Furthermore, prophylactic vaccination in poultry holdings increases the risk that an outbreak of fowl plague will be masked, as no reliable differentiation between infected and vaccinated animals is possible. Even clinical protection, i.e. animals do not show symptoms of disease after infection, does not protect animals reliably from infection and excretion. The infection might spread unnoticed and lead to continuous outbreaks. This can be seen in countries like Egypt and China.

There is a possibility to vaccinate in exceptional cases and under certain conditions, e.g. in zoo birds or rare species.

This requires permission of the EU Commission which is associated with strict obligations with regard to the continuous surveillance of the holding. Details must be discussed with the local veterinary authorities.

**Human health risk**

**Do fowl plague viruses represent a health risk for humans?**

So far, no human infections with HPAI H5N8 or H5N5 have been detected worldwide. As for all fowl plague viruses increased protective measures recommended for handling potentially infected poultry and wild birds must be observed.

For further information please refer to the website of the Robert Koch-Institute under: http://www.rki.de/aviaere-influenza.
Do poultry products represent a health risk for consumers?
Theoretically, there is a possibility that the pathogen (H5N8) might be transmitted by infected food products. However, this is highly unlikely.

Information can be found on the website of the Federal Institute for Risk Assessment (BfR): [www.bfr.bund.de](http://www.bfr.bund.de).

Is there a possibility that the bird flu virus might spread via drinking water?
The German Federal Environmental Agency commented on this already in 2006 and stated that “in Germany no human disease caused by the so-called bird flu (...) can be induced by drinking water (...) distributed via the water supply network. (...) The viruses potentially present in the raw water are filtered during processing or inactivated by disinfection measures.” The complete report (in German language) can be found under: [http://www.umweltbundesamt.de/sites/default/files/medien/publikation/long/3553.pdf](http://www.umweltbundesamt.de/sites/default/files/medien/publikation/long/3553.pdf)