



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

H5N1 AVIAN INFLUENZA IN CATS

ABCD guidelines on prevention and management

Etienne Thiry, Diane Addie, Sándor Belák, Corine Boucraut-Baralon, Herman Egberink, Tadeusz Frymus, Tim Gruffydd-Jones, Katrin Hartmann, Margaret J Hosie, Albert Lloret, Hans Lutz, Fulvio Marsilio, Maria Grazia Pennisi, Alan D Radford, Uwe Truyen and Marian C Horzinek



Infection of cats

Felids can be naturally and experimentally infected with H5N1 avian influenza virus. The first experimental evidence of its pathogenicity in the domestic cat was obtained in 2004, when infection of household cats was reported from Thailand.^{1,2} Two outbreaks of fatal disease in tigers and leopards in Thailand have subsequently been reported.³ The fatal outcome of these cases contrasts with earlier observations of subclinical infections in cats after experimental exposure to human H3N2 virus.⁴

In late February/early March 2006, three cats were found dead on the island of Rügen, Germany, and infection with H5N1 virus was established by laboratory tests. Also in March of that year, three healthy cats were found to be infected in an animal shelter in Graz, Austria.⁵⁻⁷

... and other mammals, including humans

The H5N1 subtype of avian influenza virus type A, a member of the *Orthomyxoviridae* family, occurs primarily in birds. Transmission to mammals happens sporadically, and the infection may cause high morbidity and mortality. Humans, primates, rodents, rabbits, ferrets, dogs and cats may be infected and may succumb to the disease (Fig 1).⁸

A statement from the World Health Organization, dated 28 February 2006, reads: 'There is no present evidence that domestic cats play a role in the transmission cycle of H5N1 viruses. To date, no human case has been linked to exposure to a diseased cat. No outbreaks in domestic cats have been reported*.

Unlike the case in domestic and wild birds, there is no evidence that domestic cats are a reservoir of the virus. All available evidence indicates that cat infections occur in association with H5N1 outbreaks in domestic or wild birds.'

(*Sporadic cases were observed in cats in Europe in 2006.)

Overview Avian influenza is a disease of birds, caused by a type A influenza virus. The subtype H5N1 avian influenza occurs primarily in birds and infection varies from mild disease with little or no mortality to a highly fatal, rapidly spreading epidemic (highly pathogenic avian influenza). It is extremely rare for cats to be infected and there are only very few confirmed reports of the disease in cats in Europe.

Infection Cats can be infected via the respiratory and oral routes (eg, by eating infected birds). The key precondition for infection is that the cat lives in an area where H5N1 virus infection has been confirmed in birds. Additionally, the cat should have had outdoor access to an environment where waterfowl is present, or contact with poultry or uncooked poultry meat, or close contact with an H5N1-infected, sick cat during the first week of infection.

Clinical suspicion Clinical signs in cats may include fever, lethargy, dyspnoea, conjunctivitis and rapid death. Neurological signs (circling, ataxia) have also been recorded.

Diagnosis The veterinary authorities should be notified. Oropharyngeal, nasal and/or rectal swabs or faecal samples of suspected cases should be submitted for PCR and/or virus isolation. Post-mortem samples of lung and mediastinal lymph nodes should be obtained. Particular care should be taken when handling the cat and/or samples.

Disease management The virus is sensitive to all standard medical disinfectants.

Cats with suspected H5N1 infection should be kept in strict isolation. Owners should be advised to confine the cat to a separate room prior to bringing it to the veterinary clinic.

Vaccination and disease prevention

No H5N1 vaccines are commercially available for cats. In the event of confirmed cases of H5N1 avian influenza in birds in the area, owners should keep their cats indoors until further information is available, and follow official regulations.

European Advisory Board on Cat Diseases

The European Advisory Board on Cat Diseases (ABCD) is a body of experts in immunology, vaccinology and clinical feline medicine that issues guidelines on prevention and management of feline infectious diseases in Europe, for the benefit of the health and welfare of cats. The guidelines are based on current scientific knowledge of the diseases and available vaccines concerned.

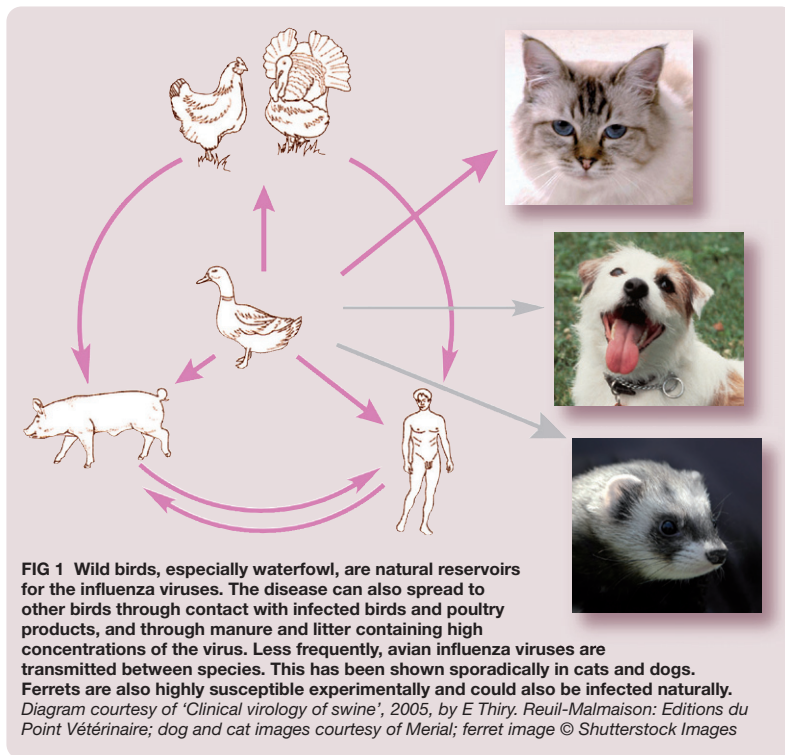
An extended version of the guidelines on H5N1 avian influenza in cats presented in this article is available at www.abcd-vets.org



European Advisory Board on Cat Diseases
www.abcd-vets.org

Corresponding author: Etienne Thiry
Email: Etienne.thiry@ulg.ac.be





What do we know?

The following facts and figures have been obtained from experimental infections and observations from field cases.^{5,9-11} They summarise and reflect the current state of knowledge, and will have to be revised and expanded as additional information becomes available:

- ❖ Cats can be infected via the intratracheal and oral routes (eg, by eating infected chickens);
- ❖ Infection can occur upon contact with infected birds (Fig 2);
- ❖ Virus might be indirectly transmitted through infected bird faeces (eg, on a cat's fur);
- ❖ Infected cats can transmit the virus to in-contact cats;
- ❖ Moderate amounts of virus are sufficient to infect a cat;
- ❖ The virus is shed in nasal secretions and faeces; nasal excretion starts 3 days after infection and continues for 4 days or more;
- ❖ The incubation period in experimental infections is about 2 days;
- ❖ Clinical signs may include fever, lethargy / depression, dyspnoea, serosanguineous nasal discharge and



FIG 2 All available evidence indicates that feline infections occur in association with H5N1 avian influenza outbreaks in domestic or wild birds. © Shutterstock Images

conjunctivitis, protrusion of the nictitating membrane, neurological signs (convulsions, ataxia) and icterus. When clinical signs occur, death normally ensues within 1 week, and occasionally within 2 days.

- ❖ At necropsy, multifocal lung lesions and petechial haemorrhages in the tonsils, mandibular and retropharyngeal lymph nodes and the liver are seen;
- ❖ On histology, inflammatory and necrotic lesions are found in the lungs, heart, brain, kidneys, liver and adrenal glands. Lesions in the small intestine (ganglioneuritis of the intestinal plexus) have been observed in cats that had been fed infected chickens, as was a non-suppurative encephalitis. Subclinical infections occur, mainly at low infectious doses and when the lower respiratory tract is unaffected;
- ❖ So far, there is no evidence of cat-to-cat transmission in areas where primary H5N1 cases have been found in birds and cats.⁷
- ❖ Some efforts to develop H5N1 vaccines for cats have been reported.^{12,13}

When should H5N1 virus infection be suspected in an ill cat?

Before the veterinary practitioner expresses a suspicion, the potential risk must be evaluated according to the case history and circumstances (see box on page 617). If these conditions are fulfilled, a risk is assumed when a clinical assessment reveals fever, lethargy / depression, dyspnoea, conjunctivitis; neurological signs may also be seen. Rapid progression and death are important indicators.

To date, no human case has been linked to exposure to a diseased cat.



If H5N1 virus infection is suspected, minimise all physical contact with the cat, avoid scratching and biting, and wear gloves, a mask and protective eyewear when handling the cat.



The differential diagnosis should exclude other infections leading to similar systemic and respiratory signs, such as those caused by feline herpesvirus, calicivirus, coronavirus (feline infectious peritonitis), bacteria (*Bordetella bronchiseptica*, *Chlamydomphila felis*) or *Mycoplasma* species.

Finally, remember that clinical signs can only result in a clinical suspicion, which must be confirmed by laboratory testing.

How should samples for laboratory diagnosis be handled?

The authorities should be notified according to the national regulations, and an appropriate diagnostic laboratory contacted for detailed instructions. However, some general rules apply when collecting oropharyngeal, nasal and rectal swabs or faecal samples:

- ❖ Label plastic sample tubes using an

alcohol-proof ink marker;

- ❖ Transfer the samples to the tubes, and close tightly;
- ❖ Wipe the outside of the tubes with alcohol to reduce the risk of infection to laboratory staff;
- ❖ Ship the sample tube safely enclosed in plastic bags to the national reference laboratory.

Post-mortem samples of lung and mediastinal lymph nodes should be obtained and shipped in 10% formol saline. (Note that the handling of potential H5N1 post-mortem samples is forbidden in some countries.)

The use of in-house influenza detection tests is discouraged.

What measures should a veterinary practitioner take if H5N1 infection is suspected in a cat?

For personal protection

- ❖ Minimise all physical contact with the cat, to avoid scratching and biting;
- ❖ Avoid contact with saliva, respiratory secretions, faeces and urine;
- ❖ Wear gloves, a mask and protective eyewear when handling the cat;
- ❖ Sedation of the cat is recommended before collecting samples;
- ❖ Use a standard medical disinfectant for surface decontamination.

For protection of practice staff and other animals

- ❖ The suspected cat should be kept in isolation in a cage at the veterinary clinic.

For protection of owner and family

- ❖ At the owner's house, the cat should be confined to a separate room prior to presentation at the practice;
- ❖ Physical contact with the cat should be minimised, and scratching and biting avoided;
- ❖ Litter trays, bowls, baskets and other potentially contaminated objects should be disinfected using a hypochlorite solution (household bleach);
- ❖ Rooms to which the cat had access before the visit to the veterinary clinic should be thoroughly cleaned using a household detergent.

Risk considerations

How can cats become infected?

If the cat lives in a region where H5N1 virus-infected birds have been identified by laboratory tests, the following must be considered as being risk factors:

- ❖ The cat lives in an environment where waterfowl are present;
- ❖ The cat has access to outdoors;
- ❖ The cat has contact with free-range or indoor poultry;
- ❖ The cat has been fed uncooked poultry meat;
- ❖ The cat has been in close contact with an H5N1 virus-infected cat.

Can a cat be infected by another cat?

During the first 7 days after infection, a sick cat can transmit H5N1 virus to another cat in close contact. The infection is inapparent for a short incubation period, but persistent infections have not been reported in mammals.

How might a cat transmit the infection to a person?

To date, no virus transmission from cat to person has been reported. However:

- ❖ An H5N1 virus that has infected a cat is already adapted to a mammalian species. Viruses isolated from humans have exhibited increased virulence for mammals;¹⁴
- ❖ The virus is excreted via the oral and respiratory route (saliva, nasal secretions), and in the urine and faeces;
- ❖ Enough virus is shed to allow in-contact cats to become infected;
- ❖ In view of the habitual close contacts between cats and their owners, a shedding cat could probably infect a human;
- ❖ The risk of infection and disease for humans is unknown at present.

What can owners do to minimise the risk of H5N1 infection in their cats?

- ❖ The development of the epidemiological situation should be followed in the national and local media;
- ❖ Feeding of uncooked poultry meat to cats should be avoided;
- ❖ If many deaths occur among wild birds, cats should be kept indoors until further information about the cause is available.

Acknowledgements

The European Advisory Board on Cat Diseases (ABCD) is indebted to Dr Karin de Lange for her judicious assistance in organising this special issue, her efforts at coordination, and her friendly deadline-keeping. The tireless editorial assistance of Christina Espert-Sanchez is gratefully acknowledged. The groundwork for this series of guidelines would not have been possible without financial support from Merial. The ABCD particularly appreciates the support of Dr Jean-Christophe Thibault, who respected the team's insistence on scientific independence.

KEY POINTS

- ❖ Avian influenza is a disease of birds, caused by a type A influenza virus.
- ❖ The subtype H5N1 avian influenza can evolve to highly pathogenic avian influenza.
- ❖ Transmission to mammals, including humans, happens sporadically.
- ❖ It is extremely rare for cats to be infected and there are only very few confirmed reports of the disease in cats in Europe.
- ❖ Cats can be infected via the respiratory and oral routes.
- ❖ There is no evidence that cats play a zoonotic role.
- ❖ Only when a risk assessment indicates a high potential risk (eg, local presence of confirmed cases in wild birds or poultry, outdoor access) should suspicion of infection in a cat be raised.
- ❖ In case of suspicion, the veterinary authorities should be notified.
- ❖ Keep cats with suspected infection in strict isolation with barrier nursing.
- ❖ No vaccines are commercially available for cats.



References

- 1 Kuiken T, Rimmelzwaan G, van Riel D, et al. Avian H5N1 influenza in cats. *Science* 2004; **306**: 241.
- 2 Keawcharoen J, Oraveerakul K, Kuiken T, et al. Avian influenza H5N1 in tigers and leopards. *Emerg Infect Dis* 2004; **10**: 2189–91.
- 3 Thanawongnuwech R, Amonsin A, Tantilertcharoen R, et al. Probable tiger-to-tiger transmission of avian influenza H5N1. *Emerg Infect Dis* 2005; **11**: 699–701.
- 4 Hinshaw VS, Webster RG, Easterday BC, Bean WJ Jr. Replication of avian influenza A viruses in mammals. *Infect Immun* 1981; **34**: 354–61.
- 5 Leschnik M, Weikel J, Möstl K, et al. Subclinical infection with avian influenza A (H5N1) virus in cats. *Emerg Infect Dis* 2007; **13**: 243–47.
- 6 Thiry E, Zicola A, Addie D, et al. Highly pathogenic avian influenza H5N1 virus in cats and other carnivores. *Vet Microbiol* 2007; **122**: 25–31.
- 7 Marschall J, Schulz B, Harder TC, et al. Prevalence of influenza A H5N1 virus in cats from areas with occurrence of highly pathogenic avian influenza in birds. *J Feline Med Surg* 2008; **10**: 355–58.
- 8 Songserm T, Amonsin A, Jam-On R, et al. Fatal avian influenza A H5N1 in a dog. *Emerg Infect Dis* 2006; **12**: 1744–47.
- 9 Rimmelzwaan GF, van Riel D, Baars M, et al. Influenza A virus (H5N1) infection in cats causes systemic disease with potential novel routes of virus spread within and between hosts. *Am J Pathol* 2006; **168**: 176–83.
- 10 Van Riel D, Munster VJ, de Wit E, et al. H5N1 virus attachment to lower respiratory tract. *Science* 2006; **312**: 399.
- 11 Klopfleisch R, Wolf PU, Uhl W, et al. Distribution of lesions and antigen of highly pathogenic avian influenza virus A/Swan/Germany/R65/06 (H5N1) in domestic cats after presumptive infection by wild birds. *Vet Pathol* 2007; **44**: 261–68.
- 12 Karaca K, Swayne DE, Grosenbaugh D, et al. Immunogenicity of fowlpox virus expressing the avian influenza virus H5 gene (TROVAC AIV-H5) in cats. *Clin Diagn Lab Immunol* 2005; **12**: 1340–42.
- 13 Vahlenkamp TW, Harder TC, Giese M, et al. Protection of cats against lethal influenza H5N1 challenge infection. *J Gen Virol* 2008; **89**: 968–74.
- 14 Maines TR, Lu XH, Erb SM, et al. Avian influenza (H5N1) viruses isolated from humans in Asia in 2004 exhibit increased virulence in mammals. *J Virol* 2005; **79**: 11788–800.

Available online at www.sciencedirect.com

