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Avian H5N1 Influenza in Cats

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The relationship between avian influenza A virus and its hosts has changed dramatically in recent years, with important consequences for human health (*1*). The most recent example is the 2003-2004 avian influenza A (H5N1) virus outbreak in Asia, which not only caused vast mortality in poultry, but also resulted in 34 officially reported cases of direct bird-to-human transmission, of which 23 were fatal (*2*). During this outbreak there were also anecdotal reports of fatal H5N1 virus infection of domestic cats and zoo felids after feeding on virus-infected chickens (*3*). This is extraordinary, because domestic cats are generally considered to be resistant to disease from influenza A virus infection (*4*). To determine the pathogenicity of this virus for domestic cats, we experimentally infected 4- to 6-month-old European shorthair cats with H5N1 virus by different routes and examined them by virological and pathological techniques. Each group of cats was placed in a separate negatively pressurized glove box.

First, we intra-tracheally inoculated three cats with 2.5×10^4 median tissue culture infectious dose ($TCID_{50}$) of a H5N1 virus isolated from a fatal human case in Vietnam (A/Vietnam/ 1194/04). They showed clinical signs, including significantly raised body temperature from 1 day post infection (dpi) onwards ($P < 0.05$, one-way ANOVA; fig. S1), and decreased activity, protrusion of the third eyelid, conjunctivitis, and labored breathing, by 2 dpi. One cat died unexpectedly at 6 dpi. The cats excreted virus by 3 dpi at relatively low titers (Fig. 1A), likely because the infection predominantly involved the lower respiratory tract. On necropsy at 7 dpi, they had multiple to coalescing foci of pulmonary consolidation (Fig. 1B), which consisted histologically of diffuse alveolar damage, resembling that from H5N1 virus infection in humans and non-human primates (Fig. 1C; Ref. *5*). H5N1 virus infection was confirmed as the cause of these lesions by virus isolation and immunohistochemistry (Fig. 1D). In contrast, three cats inoculated with an influenza A (H3N2) virus isolate from a human case in the Netherlands (A/Netherlands/ 18/94)—the most prevalent subtype of influenza A virus in humans—showed no evidence of virus infection or disease. These results show that this H5N1 virus can productively infect domestic cats, cause diffuse alveolar damage, and result in clinical disease or death.

Second, we tested whether cats could be infected with H5N1 virus by horizontal transmission by placing two sentinel cats in contact with the intra-tracheally inoculated cats above at 2 dpi. Third, we determined whether cats could by infected with H5N1 virus by feeding on virus-infected birds. To test this, we inoculated one-day-old chicks intra-tracheally with 2.5×10^4 $TCID_{50}$ of H5N1 virus and, after euthanasia at 1 dpi, fed one chick to each of three cats. In both the sentinel cats and the cats fed on chicks, virus excretion (Fig. 1A), clinical signs (fig. S1), and pulmonary changes were similar to those of intra-tracheally inoculated cats. In contrast, two cats fed on chicks inoculated with phosphate-buffered saline solution showed no evidence of virus infection or disease (Fig. 1, A to D, fig. 1S). These results show that cats can be infected with H5N1 virus both by horizontal transmission and by feeding on virus-infected birds.

The implications of the above findings are first that, during H5N1 virus outbreaks, domestic cats are at risk of disease or death from H5N1 virus infection, either due to feeding on infected poultry or wild birds (*6*), or due to contact with infected cats. Second, the role of cats in the spread of H5N1 virus between poultry farms, and from poultry to humans, needs to be re-assessed. Third, cats may form an opportunity for this avian virus to adapt to mammals, thereby increasing the risk of a human influenza pandemic.

References and Notes

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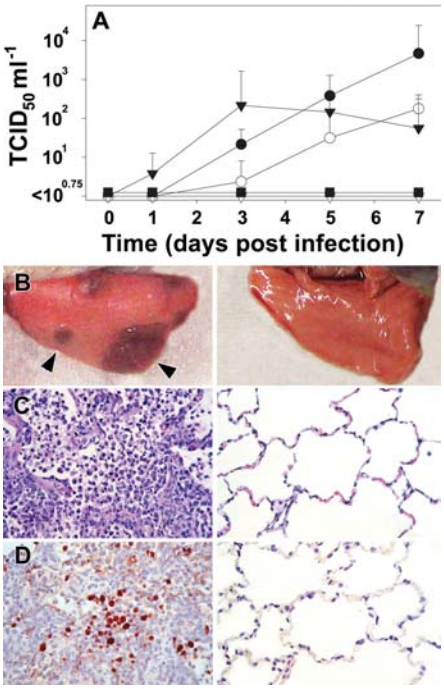
Fig. 1. Virus excretion and pulmonary lesions in cats infected with influenza A (H5N1) virus. (A) Pharyngeal virus excretion (mean and s.d.) in cats inoculated: intra-tracheally with H5N1 virus (●), by contact with H5N1-virus-inoculated cats (○), by feeding on chicks inoculated with H5N1 virus (▼) or with phosphate-buffered saline (PBS) solution (▽), and intra-tracheally with H3N2 virus (■). Lung of a cat fed with a H5N1-virus-inoculated chick (left side of panels) has (B) multiple foci (arrowheads) of consolidation consisting (C) histologically of diffuse alveolar damage, with (D) expression of influenza virus antigen in inflamed tissue by immunohistochemistry. Lung of a cat fed with a PBS-inoculated chick (right side of panels) as a control.


A
10^4
10^3
10^2
10^1
$<10^{0.75}$
$TCID_{50}\ ml^{-1}$
0 1 2 3 4 5 6 7
Time (days post infection)
B
C
D