

was our opinion that this patient qualified for rabies PEP.

Several studies of the safety of rabies PEP for pregnant patients demonstrated no association between treatment and adverse outcomes (3–6). In 1 study, tissue culture-derived vaccines and human immune globulin did not lead to an increased risk for congenital anomalies; no effects were observed on intrauterine or infant growth or development with a follow-up period of 1 year postpartum (6). Although these studies are not comprehensive in their assessment of all reproductive outcomes, they do suggest that PEP is generally safe.

On the basis of the exposure and our literature review, we recommended that the patient receive rabies PEP. After discussing options with her husband, the patient chose not to receive treatment, citing continued concern about the effect of rabies PEP on the fetus. There must be a greater public health effort to educate clinicians and the public about proper response to bat exposures, particularly undetectable bite exposures such as this case. Had public health authorities been contacted to collect and test the captured bat for rabies, there would have been no ambiguity as to the appropriate course of action.

This research was supported by University of Michigan Medical Scientist Training Program Grant No. GM0786.

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#### Letters

Letters commenting on recent articles as well as letters reporting cases, outbreaks, or original research are welcome. Letters commenting on articles should contain no more than 300 words and 5 references; they are more likely to be published if submitted within 4 weeks of the original article's publication. Letters reporting cases, outbreaks, or original research should contain no more than 800 words and 10 references. They may have one Figure or Table and should not be divided into sections. All letters should contain material not previously published and include a word count.

## Novel Orthoreovirus from Diseased Crow, Finland

**To the Editor:** Corvids, especially American crows (*Corvus brachyrhynchos*), are reported to be highly susceptible to lineage 1 of West Nile virus (WNV), which causes them to show symptoms of encephalitis. They are regarded as indicator species in the surveillance of WNV in the United States (1). In parts of Europe, WNV is endemic and studies are ongoing to detect WNV in wild birds. Thus far, no evidence of WNV in birds has been found in northern Europe.

In August 2002, in southern Finland, a diseased wild hooded crow (*Corvus corone cornix*) was found flying abnormally with coordination problems, abnormal postures, cramps, and paralysis. Because WNV infection was suspected, virologic tests were performed, which resulted in the isolation of a novel orthoreovirus, which was likely the causative agent of the disease.

Avian orthoreoviruses (ARVs) belong to the family *Reoviridae*, genus *Orthoreovirus*. They infect wild and farm-raised birds and are important fowl pathogens associated with various disease conditions such as gastrointestinal malabsorption syndrome, tenosynovitis (arthritis), growth retardation, and sudden death. They have also been isolated from asymptomatic birds. The reovirus virion is icosahedral, nonenveloped, and has a double-capsid structure that shelters the segmented double-stranded RNA genome (2).

Heart, lung, liver, kidney, and brain tissues of the diseased crow tested negative for WNV RNA. Virus isolation from brain homogenate was carried out in BHK (baby hamster kidney)–21 cells. On day 2 after infection, a strong cytopathic effect was observed, including syncytium formation. Spherical, spiked virus particles,

consistent with those of members of the family *Reoviridae*, were observed by electron microscopy. The diameter of the particles was slightly smaller ( $\approx 70$  nm) than that reported for ARV (85 nm) (3). Members of the genus *Orthoreovirus* differ in their host reservoir and capability of syncytium formation; most avian orthoreoviruses are fusogenic and fail to agglutinate erythrocytes, unlike the mammalian reoviruses (4). The isolate, designated as Tvärminne avian virus (TVAV), failed to hemagglutinate chicken, goose, or human O erythrocytes.

Members of the genus *Orthoreovirus* have a genome consisting of 10 dsRNA segments in 3 size classes, large (L1–3), medium (M1–3), and small (S1–4). The RNA was extracted from TVAV-infected BHK-21 cells with TriPure isolation reagent (Roche Diagnostics, GmbH, Mannheim, Germany). Ten double-stranded RNA genome segments were separated by electrophoresis, showing a pattern typical of ARV with the S1 segment migrating between S- and M-segment classes (5). The S1 segment encodes the orthoreovirus type-specific antigen,  $\sigma$ C protein, which is the minor outer-capsid protein, a spiked structure mediating cell attachment.

For phylogenetic analyses, the partial  $\sigma$ C gene was amplified by reverse transcription-PCR with avian reovirus-specific primers (6). The obtained sequence (GenBank accession no. DQ470139) was aligned with 25 published orthoreovirus sequences. The phylogenetic tree was constructed by using the maximum likelihood method, with general-time reversible model of substitution determined by Modeltest using PAUP\* (7). The analyses showed that TVAV did not group with avian or mammalian orthoreoviruses but formed a separate clade (Figure). In further analysis, no evidence for recombination events was found. The nucleotide sequence homology of the  $\sigma$ C gene was  $<50\%$ , and amino acid homology was  $<40\%$ , when

compared with previously described orthoreovirus strains. Additionally, a partial M3 segment was sequenced (GenBank accession no. EU053426) that also showed low ( $<40\%$ ) amino acid homology and genetic relation to other orthoreoviruses, which supports the result obtained from the  $\sigma$ C gene.

To our knowledge, no sequences of ARV isolates have been previously available from northern Europe. The TVAV isolate described differs clearly from other known ARV strains and could be considered a candidate for a new species in the genus *Orthoreovirus*. ARVs are not generally associated with encephalitic disease, in contrast to reoviruses that infect mice, baboons, and snakes (8,9). Systemic infection with ARV could cause viremia also in the brain, but since other tissues were

not studied, whether they were infected remains unclear. In Finland, a bird-pathogenic orthoreovirus was isolated in the same geographic region 6 years earlier from the bursa of Fabricius from common eider (*Somateria mollissima*) carcasses and was suspected to be the cause of their death (10). The eider reovirus induced syncytium formation, lacked hemagglutination activity, and had an RNA genome segment migration pattern similar to that of TVAV. However, instead of showing symptoms that appeared to affect the central nervous system, experimentally infected mallards (*Anas platyrhynchos*) showed hemorrhages in liver, spleen, and bursa of Fabricius tissues. Unfortunately, no sequence data are available from the eider virus isolate that can be compared with TVAV. Be-

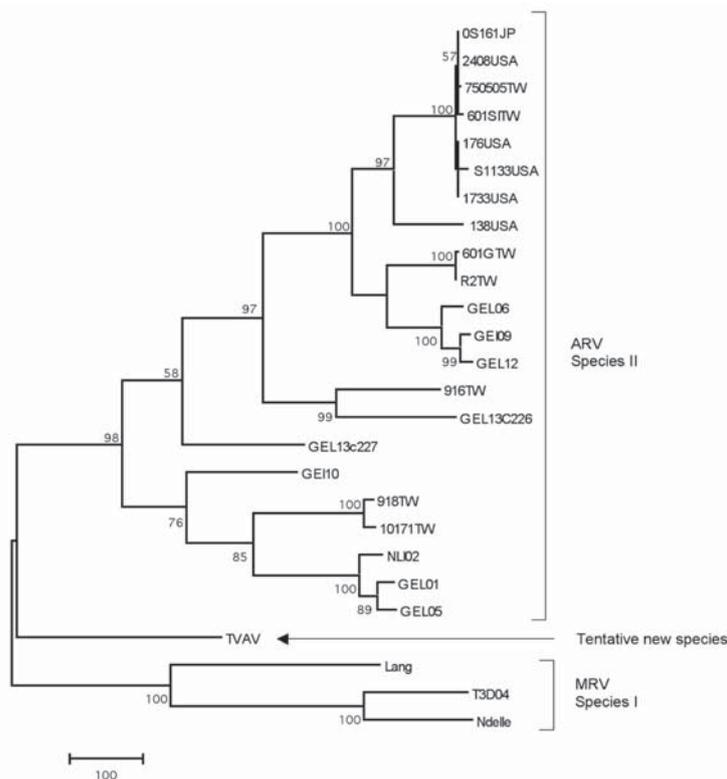


Figure. Maximum parsimony tree based on a 916-bp nucleotide sequence of the  $\sigma$ C gene. The scale bar indicates a branch length corresponding to 100 character-state changes. Bootstrap support values  $<50$  are not shown. The tentative species is shown together with the closest relatives within the *Orthoreovirus* genus; avian orthoreovirus (ARV), mammalian orthoreovirus (MRV). GenBank accession nos.: AF204946, AF204945, AF204950, AF204947, AF18358, L39002, AF004857, AF218359, AF297217, AF297213, AF354224, AF354220, AF354225, AF297214, AF354226, AF354227, AF354219, AF297215, AF297216, AF354229, AF354221, AF354223, DQ470139, M10260, AY785910, AF368035.

cause many ARVs are poultry pathogens of economic importance, more studies are needed to determine the taxonomic classification of the TVAV isolate and its pathogenicity for avian hosts. In addition, the recognition of potential avian pathogens in wild birds is important due to the possible threat for farm-raised birds and also for the surveillance of zoonotic viruses transmissible to humans.

### Acknowledgments

We thank Henrikki Brummer-Korvenkontio for assistance, Christine Ek-Kommonen for providing reagents for the hemagglutination test, and Irja Luoto for excellent technical assistance in electron microscopy.

The study was supported by grants from Hospital District of Helsinki and Uusimaa (TYH4211, 6215) and The Finnish Agency for Technology and Innovation.

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## Detecting Human-to-Human Transmission of Avian Influenza A (H5N1)

**To the Editor:** This letter is in response to a recently published article about statistical modeling to assess human-to-human transmission of avian influenza A (H5N1) viruses in 2 case clusters (1). Sporadic cases and clusters

of human infection with highly pathogenic avian influenza A (H5N1) viruses have occurred after direct contact with diseased or dead poultry (2,3). Limited, nonsustained human-to-human transmission of avian influenza (H5N1) viruses is believed to have occurred in some clusters (4). Every human infection with a novel influenza A virus should be investigated, and suspected clusters should be investigated immediately to assess exposures and transmission patterns.

Yang et al. applied a statistical model to evaluate publicly available data from 2 case clusters of human infection with avian influenza A (H5N1) viruses (1). These clusters were investigated in detail during 2006 by field epidemiologic investigation teams. Yang et al. suggest that statistical methods can prove or confirm human-to-human transmission, but this suggestion is misleading. Modeling approaches can suggest transmission modalities to account for case patterns, but determination of human-to-human transmission requires detailed field epidemiologic investigations in which human, animal, and environmental exposures as well as clinical and laboratory data are assessed and interpreted.

Indication that a novel influenza A virus has acquired the ability to spread among humans could be reflected by a change in the epidemiology of clusters, such as increases in 1) size and frequency of clusters, 2) cases among nonrelated persons, and 3) clinically mild cases. This ability could also be reflected in accompanying changes in viruses isolated from case-patients. When facing emerging infectious disease threats such as those posed by highly pathogenic avian influenza A (H5N1) viruses, surveillance should rapidly detect human cases and case clusters and facilitate accurate identification of the agent. Field epidemiologic investigations, initiation of evidence-based clinical management of case-patients, and epidemiologic disease-control methods (including ap-