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Symptomatic Human Hantavirus in the Americas

To the Editor: In a recent letter (1), dos Santos et al. described 3 cases of hantavirus pulmonary syndrome (HPS) from Juquitiba and stated that "the first human cases of symptomatic infection by hantaviruses were reported from Brazil in 1993." However, we described 8 cases of symptomatic hemorrhagic fever with renal syndrome (HFRS) in Recife, Brazil, 5 months before the initial May 1993 report of Sin Nombre virus (SNV)–induced HPS in the United States (2). Our report was therefore the first published account of symptomatic hantavirus infections, not just in Brazil but anywhere in the Americas (3).

Serum samples from our Brazilian HFRS cases, collected in 1990, were screened by an immunofluorescence assay (IFA) and ELISA for immunoglobulin G, as were the current Brazilian HPS cases (1). Two of our patients had an increased immunoglobulin M titer by ELISA (2). Rat-transmitted Seoul virus (SEOV) was considered most likely because this was the only hantavirus strain showing clear positive results in IFA (2,3). All the Recife cases in 1990 had reported likely rat contacts and were initially diagnosed as leptospirosis with acute renal failure and thrombocytopenia, clinical hallmarks of both HFRS and leptospirosis (3). We also subsequently found evidence of SEOV infection in 31 (15%) of 201 leptospirosis-suspected acute renal failure cases from Belém, Brazil, confirmed in 1 case with highly specific neutralization tests (4). Moreover, as we predicted (3), some of the 133 (41%) of 326 urban cases of acute renal failure from Salvador, Brazil, which appeared nonconfirmed for leptospirosis (5), were later shown to be caused by SEOV (unpub. data). Finally, of 379 schoolchildren from Salvador at high risk for frequent rat exposure, 13.2% were IFA positive for the Korean prototype Hantaan virus (HTNV) but none for the American SNV (6). Because both HTNV and its rodent reservoir are absent from the American biotope, HTNV seroreactivity should be considered a cross-reaction to another related murine antigen; that is to say, the ratborne SEOV.

Wild rats (*Rattus rattus and R. norvegicus*) are the only Old World rodents ubiquitous in the New World and thus a potential source of SEOV infection in the Americas (3,7). Moreover, the first hantavirus characterized in South America was SEOV, isolated as long ago as 1984 from a rat caught in Belém (7). Furthermore, the first 3 clinical cases of hantavirus infection in the United States were SEOV-induced (Baltimore rat virus) HFRS cases and not HPS (8).

The clinical syndromes of HFRS and HPS can appear identical, with pulmonary edema, shock, and renal insufficiency with marked proteinuria and thrombocytopenia (9). Moreover, worldwide ELISA testing with a single antigen such as SNV or Puumala virus (PUUV) can result in misleading cross-reactions, since both viruses are genetically related. Although this SNV-PUUV cross-reactivity enabled the first recognition of HPS cases in the New World 14 years ago, this may now lead to the wrong clinical diagnosis and reinforces the need for specific tests such as neutralization tests or reverse transcription–PCR. Although not as lethal and probably not so frequent as HPS, SEOV-induced HFRS may still be greatly underestimated in the Americas, or misdiagnosed as leptospirosis.

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Echinococcosis Risk among Domestic Definitive Hosts, Japan

To the Editor: Echinococcosis is a serious parasitic zoonosis in the Northern Hemisphere. In Japan, it is characterized by alveolar, hepatic, and cerebral disorders in humans caused by the larval form (metacestode) of the tapeworm *Echinococcus multilocularis*. The life cycle of the parasite is maintained in the wild by gray-backed voles, *Clethrionomys rufocanus*, as intermediate hosts, and by red foxes, *Vulpes vulpes*, as definitive hosts. Humans are infected by ingestion of the parasite eggs, mainly through water contaminated with the feces of wild red foxes, which have an estimated infection prevalence of 54%–56% (*1*).

The echinococcosis-endemic area in Japan is restricted to the northern island of Hokkaido, although sporadic human cases have been reported on other islands (*2*), and infected pigs have been documented on the main island of Honshu (*3*). While the threat of echinococcosis spreading into Honshu had raised fears, an emergent concern is the possible role of domestic dogs in dispersing the disease from disease-endemic areas during reloca-tion of residences by owners or when accompanying owners during domestic travel.

In September 2005, a stray dog in Saitama prefecture in mainland Honshu was found to be positive for *E. multilocularis* infection by PCR (mitochondria 12S RNA gene) (Y. Morishima, pers. comm.). The sequence was identical to the Hokkaido isolate (GenBank accession no. AB244598). This raised an alarm because the area in which the infection was found is adjacent to the Tokyo metropolis, the most populous zone in Japan. Reports also claimed that 2 of 69 dogs moved from Hokkaido to Honshu were positive for *E. multilocularis* by coproantigen examination (*4*).

Nearly 10,000 pet dogs were estimated to have been transported in 1 year to and from Honshu and Hokkaido by planes and ferries; this presumably included up to 30 *E. multilocularis*–infected pet dogs per year (*5*). Even so, no compulsory quarantine or *Echinococcus* examination is enforced for dogs transported within Japan. A compulsory requirement of a certificate from a veterinarian stating that the animal has been treated with praziquantel 3–4 days before traveling would be a helpful preventive measure. As part of an amendment to the Infectious Disease Law in Japan, *E. multilocularis* infection was included among the 4th Category Diseases (*6*). Thus, since October 2004, it has been mandatory for veterinarians who have diagnosed echinococcosis in dogs to report each case to health authorities, the first national reporting system of its kind worldwide.

Our laboratory established the Forum on Environment and Animals (FEA) to meet the demand for accurate and rapid diagnosis of echinococcosis in domestic dogs. FEA is a hub for veterinary practitioners around the country for confirmation of *E. multilocularis* infection in definitive hosts, especially dogs but also cats. Feces submitted are from dogs and cats that are suspected to be infected and that wander or walk in parks and woodlands and likely prey on wild rodents. Examinations are performed weekly, and results are immediately forwarded to the submitting veterinarians. Before examination, fecal samples are sterilized by heating for 12 hours at 70°C. Fecal egg examination is conducted by using centrifugal flotation (*7*) with sucrose solution with a specific gravity of 1.27. Sandwich ELISA using a monoclonal antibody EmA9 (*8*) is used for *E. multilocularis* coproantigen detection. Egg- and ELISA-positive fecal samples from dogs are subjected to PCR amplification (mitochondria 12S RNA gene) (*9*).

The Table presents data of samples from both dogs and cats examined by FEA from April 2004 through August 2005. A total of 1,460 domestic dogs were examined, and 4 (0.27%) were confirmed positive to echinococcosis by PCR, all from Hokkaido. Test results from eggs detected in cat feces suggested these animals were infected with *Taenia taeniaeformis*, a cat tapeworm, rather than *E. multilocularis*, because coproantigen ELISA results were negative and an ELISA-positive sample did not contain eggs.

To our knowledge, this survey registered the greatest number of domestic dogs examined recently in Japan

Table. Prevalence of echinococcosis in definitive hosts subjected to fecal egg examination, ELISA coproantigen test, and PCR copro-DNA detection, Japan

Species	No. samples	Positive samples (%)		
		Egg examination	ELISA	PCR
Dogs	1,460	3 (0.20)	6 (0.41)	4 (0.27)
Cats	128	4 (3.12)	1 (0.78)	ND*
Total	1,588	7 (0.44)	7 (0.44)	–

*ND, not done.