A Newly Discovered Variant of a Hantavirus in *Apodemus peninsulae*, Far Eastern Russia

To the Editor: Hemorrhagic fever with renal syndrome (HFRS) is caused by *Hantaan virus* (HTN) or *Seoul virus* (SEO) in Asia and *Puumala virus* (PUU) or *Dobrava virus* (DOB) in Europe (1). Each of these hantaviruses is predominantly associated with a single rodent species as its primary natural reservoir: HTN with the striped field mouse *Apodemus agrarius*, SEO with *Rattus norvegicus*, PUU with the bank vole *Clethrionomys glareolus*, and DOB with the yellow-necked mouse *Apodemus flavicollis.* An additional rodent reservoir of DOB, *A. agrarius*, was reported recently (2).

The first HFRS cases (then called "hemorrhagic nephroso-nephritis") were clinically described in the Amur River basin during the 1920s by Russian scientists (3). Serologic studies suggest that numerous hantaviruses are present in humans and rodents in the far east of Asian Russia (4-5). Serologic evidence of hantavirus infection in *A. agrarius, A. peninsulae* (Korean field mouse), *R. norvegicus, Cl. rufocanus*, *Cl. rutilus,* and *Microtus fortis* has been reported (5). Only *Khabarovsk virus* (KBR), isolated from *M. fortis,* has been characterized in detail, and no association with human disease was established (6).

To genetically characterize hantaviruses in *A. peninsulae*, we studied samples from rodents captured in July and August 1998 in the same forest near Khabarovsk. Lung-tissue samples were screened by enzyme-linked immunosorbent assay for HTN/SEO/PUU-related antigen. Samples from four hantavirus-positive rodents were tested by reverse transcription and nested polymerase chain reaction (PCR). Four M-segment PCR products (nt 2639-3000) and two S-segment PCR products (nt 592-945) were produced and directly sequenced (GenBank accession numbers AF332569-AF332573). All sequences were closely related to each other, with nucleotide diversity between strains not exceeding 0.6% for M segments and 1.3% for S segments. Comparative analysis of the M segments showed that hantaviral nucleotide sequences from *A. peninsulae* were very similar to those we identified earlier in HFRS patients (diverging 3.1% to 6.6%), which we term the Amur genotype of HTN (7). The S-segment sequences of the AMR genotype from human patients were not available for comparison. The nucleotide sequence (the M and S segments, respectively) of the hantavirus detected in *A. peninsulae* diverged substantially from those of other hantaviruses (15% to 19% for HTN, 21% to 28% for SEO, 22% to 29% for DOB, 38% to 39% for PUU, and 36% to 37% for KBR).

Neighbor-joining phylogenetic analysis based on partial sequences of the S segment indicated that the hantaviral sequences from *A. peninsulae* form a separate lineage on the phylogenetic tree, and together with HTN virus strain 76-118, which originates from *A. agrarius,* constitute a well-supported group. A phylogenetic tree based on partial M segment sequences placed all hantavirus strains originating from *A. peninsulae* or from HFRS patients apart from all HTN sequences recovered from *A. agrarius* (strain 76-118) and HFRS patients from Korea (strains HoJo, Lee). The taxonomic placement of this hantavirus (Amur genotype) as a distinct hantavirus or a distinct genetic lineage of HTN remains to be determined. In addition, the finding of distinct DOB genetic lineages in *A. flavicollis* and *A. agrarius* raises the same question of whether the two DOB variants represent distinct hantaviruses (2).

A. peninsulae is widely distributed throughout eastern Asia, from Altai and south Siberia to the Russian far east, northeastern and eastern parts of China, and Korea. A survey of hantavirus antigens in rodent populations in the far east of Russia demonstrated the presence of HTN-like antigen in 8% to 16% of *A. peninsulae* (5). Whether pathogenic AMR genotype of virus exists in *A. peninsulae* throughout far eastern Asia, from Russia to China and Korea, requires further study. Comparing hantaviral genome sequences available from GenBank shows that the M segment nucleotide sequence recovered from an HFRS patient from China (strain H8205, GenBank accession number AB030232) was very similar to the AMR genotype from *A. peninsulae* (94% to

96% identity), suggesting that this hantavirus is also present in *A. peninsulae* in China.

In earlier studies, we found that sera from patients infected by the AMR genotype of hantavirus showed extensive cross-reactivity with HTN and SEO antigens in immunofluorescent antibody tests (7). Consequently, many HFRS cases previously thought to have been caused by HTN or SEO may instead have been caused by infection with the hantavirus described here.

Our data represent the first genetic evidence for the AMR genotype of HTN in *A. peninsulae* and suggest that this rodent species may be a natural reservoir for this pathogenic hantavirus.

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