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Human hantavirus disease due to infection by Dobrava-Belgrade virus in Northern Germany – the first comprehensive study.

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We present comprehensive serological and molecular evidence of Dobrava-Belgrade virus (DOBV) as human health threat in Northern Germany. Sixteen patients from the federal states Schleswig-Holstein and Mecklenburg-West Pomerania found within the last 3 years were specifically investigated. Patients suffered from typical clinical symptoms of hantavirus disease, as high fever and renal impairment.

From 3 patients virus sequences were amplified and characterized. Molecular phylogenetic analysis revealed their belonging to the genetic lineage DOBV-Aa (associated with Apodemus agrarius as reservoir host) with the highest similarity to the DOBV-Aa strain "Greifswald", very recently isolated from an infected mouse in Northern Germany.

Acute serum samples were obtained from 15/16 patients between day 2 and 16 (mean, day 5) and from 1 patient 110 days after onset of symptoms. Their investigation revealed positive IgM and IgG titers in an EIA using recombinant DOBV nucleocapsid protein as antigen. EIA cross reactivity with Puumalavirus nucleocapsid protein was seen in 7/15 sera, however, with clearly higher titers against DOBV. The virus neutralization assay (cFRNT) confirmed infections by DOBV in all 16 patients. To address the question whether the cFRNT can distinguish between antibody responses to different DOBV lineages, we determined the neutralization levels of virus strains from all 3 virus lineages (DOBV-Aa, isolates Slovakia and Greifswald; DOBV-Af, isolate Bel-1; DOBV-Ap, isolate Sochi-1) by acute and convalescent sera of the 16 patients. As expected, a reliable differentiation between the DOBV lineages was not possible by cFRNT but requires the analysis of viral nucleic acid.