

**Vector-Borne Diseases: Impact of Climate Change on Vectors and Rodent Reservoirs**  
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**Network „Rodent-borne pathogens“ in Germany: Longitudinal studies on the geographical distribution and prevalence of hantavirus infections**

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Human hantavirus infections have been reported in Germany since the 1980s. These infections can cause haemorrhagic fever with renal syndrome (HFRS), usually representing with renal failure. *Puumala virus* (PUUV) causes the majority of HFRS cases in Germany which are characterized by mild to moderate courses. The geographical distribution and frequency of hantavirus infections in humans is well documented by large seroprevalence studies and recording of clinically apparent infections according to the “Infektionsschutzgesetz”. Endemic regions have been known for long time in Baden-Wuerttemberg (Suebian Alb) and Bavaria (Lower Franconia). Whereas in 2001-2004 and 2006 about 70-240 human cases were recorded annually in Germany, in 2005 and 2007 a large increase in the number of cases was observed, reaching 448 and 1339 cases, respectively (Robert Koch-Institut: SurvStat, <http://www3.rki.de/SurvStat>, Data from 19.09. 2007). The majority of cases was recorded in Bavaria (2004, 2007), Lower Saxony, North Rhine Westphalia (2005) and Baden-Wuerttemberg (2007).

Potential reservoirs for hantaviruses in Germany are bank vole (*Myodes glareolus*, formerly *Clethrionomys glareolus*), common vole (*Microtus arvalis*) and striped field mouse and yellow-necked mouse (*Apodemus agrarius* and *A. flavicollis*). PUUV and *Tula virus* (TULV) were indeed detected in bank voles and common voles, respectively. However, the reservoir for *Dobrava-Belgrade virus* (DOBV) in Germany remains obscure. The similarity of a patient DOBV sequence to other *A. agrarius*-derived DOBV sequences suggested an *A. agrarius* origin of the infection. Other rodents, e.g. Norway rat (*Rattus norvegicus*) and house mouse (*Mus musculus*), as well as shrews might represent reservoirs for other hantaviruses as well.

In contrast to the well-documented distribution of human hantavirus cases the geographical distribution and prevalence of hantavirus infections in rodent reservoirs is poorly studied. Moreover, there is little known about oscillations of the prevalence and sequence variation of the hantaviruses and the underlying molecular processes driven by rodent population dynamics as well as by transmission and migration processes. The influence of climate change on these processes is also unknown. Therefore, the network "Rodent-borne pathogens" was initiated representing a platform for an interdisciplinary collaboration of research groups dealing with rodent reservoirs themselves, i.e. their biology, population genetics, distribution and population dynamics, and studies dealing with pathogens of different nature (i.e. viruses, bacteria, parasites).

The investigations in the first "descriptive" phase of the network were focussed on the following objectives: (i) establishment of a monitoring program of hantaviruses and other rodent-associated pathogens, (ii) identification of causative hantaviruses in outbreak regions during 2004, 2005 and 2007, (iii) promotion of population dynamics studies including potential influences of climate conditions and (iv) search for novel rodent viruses which may represent model viruses for human pathogens.

In a pilot study in Brandenburg, a serological and RT-PCR screening of about 1,700 rodents trapped during 1994 - 2005 demonstrated for the first time a continuous presence of TULV in common vole (*Microtus arvalis*) and field vole (*M. agrestis*) populations at certain trapping sites throughout the study period. A serological screening of 341 bank voles, common voles and field voles trapped during 2004-2007 in Brandenburg, Saxony-Anhalt, Saxony and Mecklenburg-Western-Pomerania was performed by ELISA using recombinant nucleocapsid proteins of PUUV and TULV. These investigations revealed a low number of samples with specific antibodies against PUUV and TULV from Brandenburg (1/66), Mecklenburg-Western-Pomerania (2/39) and Saxony-Anhalt (3/150).

During hantavirus outbreaks, investigations were focused on rodents from different parts of Bavaria (Lower Bavaria 2004, Lower Franconia 2007), North Rhine Westphalia (city of Cologne, 2005, and rural region close to Muenster, 2007), Lower Saxony (a rural region close to Osnabrück, 2005) and different regions in Baden-Wuerttemberg (2007). In all investigated regions a high PUUV prevalence of 10-90% was observed in bank voles. RT-PCR amplification and subsequent phylogenetic analysis of S and M genome sequences demonstrated significant differences between PUUV strains originating from the different regions. Initial longitudinal studies in rural regions of Lower Bavaria and close to Osnabrueck as well as in the city of Cologne demonstrated a continuing presence of PUUV in the local bank vole populations.

The distribution and prevalence of rodent-associated diseases is mainly driven by oscillations in demographic structure and density of rodent populations but also by habitat properties. A study about the fluctuations in population density of common voles was initiated. Time-series of population abundance of 12-125 years duration were obtained from >20 locations in Germany. Initial analyses suggest that there was no change in outbreak frequency since the late 1800s. There seems to be no consistent pattern in changes in amplitudes of peak densities of common voles across Germany. However, reports from West Germany and Central Spain suggest that common vole outbreaks recently occurred in historically unaffected regions. Time series data will be used to develop spatially-explicit pattern-oriented models that link population dynamics to environmental parameters. These parameters will include climate variables to identify potential effects of climate change on the population dynamics of common voles. This work will be extended in the network "Rodent-borne pathogens" to include interactions of rodent population dynamics, epidemiology and

evolution of viral and bacterial diseases in the rodent host, and prevalence of zoonoses in humans.

In conclusion, the network will enable synergistic effects by a close collaboration of zoologists, veterinarians, physicians, epidemiologists, virologists, geneticists, microbiologists, parasitologists and evolutionary biologists. The centralized facility for rodent necropsy, sample storage and documentation and a standard scheme for necropsy will allow a coordinated study on rodent biology and rodent-associated viral and bacterial pathogens. A network database will be established to help to identify potential interactions of the various pathogens in rodents and to link these aspects to population genetic markers. The longitudinal studies will allow conclusions about the evolution of rodent-borne pathogens and changes in their distribution which might result in a risk assessment for human infections. This may become very important in order to evaluate changes in the epidemiology of rodent-borne pathogens in the light of expected global climate changes in the future.

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