

# AN OUTBREAK CAUSED BY HANTAVIRUS IN THE BLACK SEA REGION OF TURKEY, JANUARY – MAY 2009

M Ertek on behalf of the Refik Saydam National Public Health Agency ([mustafa.ertek@saglik.gov.tr](mailto:mustafa.ertek@saglik.gov.tr))<sup>1</sup>, T Buzgan on behalf of the Ministry of Health<sup>2</sup>

1. Refik Saydam National Public Health Agency, Ankara, Turkey  
2. Ministry of Health, Ankara, Turkey

We present a preliminary report of 12 laboratory-confirmed cases of haemorrhagic fever with renal syndrome (HFRS) in Turkey, diagnosed between January and May 2009 according to the clinical symptoms and serological confirmation. Studies are still ongoing to better understand the dynamics of the reservoir population as well as the epidemiological characteristics and risk factors among humans.

### Background

Since the first hantavirus, Hantaan virus (HTNV), was isolated in 1976, many other hantaviruses have been identified, and at least 22 of them are pathogenic to humans. Hantaviruses are rodent-borne, enveloped RNA viruses with a diameter of 120 nm, belonging to the family Bunyaviridae. Each hantavirus is carried by a specific rodent species (subfamilies: *Murinae*, *Arvicolinae*, *Sigmodontinae*) or insectivore species and transmission to other species including humans is a “dead end” for the virus [1-4]. Transmission of hantavirus is believed to occur mainly through aerosols from infected animal excreta, i.e. saliva, urine and faeces. Although this is undoubtedly the most common route of transmission among rodents and from animals to humans, virus transmission by bite may also occur and result in both animal and human infection [1,4-6]. Hantaviruses have the potential to cause two different types of diseases in humans: haemorrhagic fever with renal syndrome (HFRS) and hantavirus pulmonary syndrome (HPS).

### Outbreak investigation

In January 2009, the Ministry of Health in Turkey (MoH) was informed by the public health authorities of provinces Zonguldak (A) and Bartın (B) about a cluster of three suspected cases of HFRS with clinical symptoms. Both provinces share a common border and have similar natural vegetation and animal diversity (Figure 1).

A blood sample was taken from only one of the three first reported cases and the laboratory investigation confirmed an infection caused by hantavirus. This was the first laboratory-confirmed case of hantavirus infection in Turkey. Therefore, an epidemiological investigation was initiated to facilitate case-finding in the affected area.

For investigation purposes, the following case definitions were adopted:

- A suspected case of HFRS was defined as a patient:
  - without any previously known blood or kidney disease;

- who has been in a location with suspected or confirmed cases of HFRS within the last two months before onset of illness;
- with an acute illness characterised by abrupt onset with at least two of the following criteria: fever, diarrhoea, nausea, myalgia, weakness, abdominal pain, chill, thrombocytopenia, impaired renal function.

A confirmed case was defined as a patient with IgM positive test result by using immunoblot technique in the serum sample.

In February 2009, all physicians and the local authorities in the two provinces affected were informed by the MoH about an increased risk of hantavirus infection. A case management flow chart was drawn and distributed to all healthcare facilities. It was requested that patients who meet the case definition criteria for suspected case of HFRS should be referred to the Zonguldak Karaelmas University Hospital and serum and urine samples should be sent to the Refik Saydam National Public Health Agency in Ankara.

Indirect immunofluorescence assay (IFA) (hantavirus mosaic-1 (Euroimmun, Germany)) was used as diagnostic test and performed according to the manufacturers' instructions. Result at a dilution  $\geq 1:100$  was considered positive. All of the IgM IFA-positive cases were confirmed by immunoblot (Euroimmun, Germany). In addition, molecular analysis by generic hantavirus RT-PCR method was performed on samples (serum/plasma and/or urine) taken from 14 patients.

### Preliminary findings

Between 22 January and 1 May 2009, a total of 25 suspected cases of HFRS were reported. Blood samples were taken from 23 patients and tested for hantaviruses. The remaining two patients had died before sampling, so they are considered as suspected cases. We confirmed that 12 out of 23 samples (52.2%) were positive for hantavirus in IFA and immunoblot. However, no positive result was found in the plasma/serum (n=14) and/or urine samples (n=6) by RT-PCR method.

The epidemic curve is shown in Figure 2. The mean age of laboratory-confirmed patients was 56 years (range 22-78), the male to female ratio was 6:1. All 25 suspected cases were admitted to hospital. The fatality rate among these hospitalised patients was 8%.

### Seroprevalence study

From 18 to 20 March 2009, a seropositivity study for hantaviruses among the healthy population was carried out in province B. The aim of the study was to show the presence of hantavirus in the area and to identify the possible risk factors of infection. In the study, convenience sampling method was used, the study population consisted of six groups: four of these were at known risk for hantavirus infection (hunters, foresters, villagers involved in forestry, miners), subjects of the fifth group originated from the three villages where confirmed/suspected cases were living, and the last group was from an urban area of province B. A total of 306 sera were collected. A questionnaire was filled in for each person including demographic data, clinical symptoms (if any) and the date of onset of symptoms, diagnostic tests and treatment, and epidemiological data on housing conditions, travel history and animal exposure in the past two months.

The final results of this study are not yet available. To date, the laboratory testing has been completed but the statistical analysis is still being performed by the epidemiology unit. Preliminary results indicate that the overall seroprevalence was 5.2%.

### Conclusion

We confirmed 12 cases of HFRS reported in Turkey in 2009 using IFA and immunoblotting techniques. Our results were serologically positive for Puumala subtype, but it should be considered that among the subtypes of hantavirus, cross-reactivity is frequently seen serologically. In addition, the generic hantavirus RT-PCR was not positive; hence, sequence analyses have not been performed.

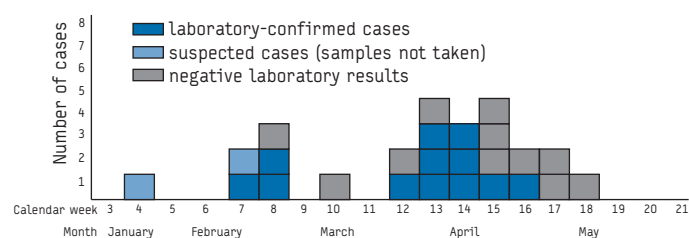
FIGURE 1

Map of Turkey indicating the area where human cases of hantavirus infection were reported in January - May 2009



FIGURE 2

Distribution of suspected cases of hantavirus infection reported in Turkey, from January to May 2009, by week of notification



The reason for this might be that viraemia is very short in hantavirus infections. Another limitation of the study was that neutralisation tests have not been performed.

We found a 5.2% seroprevalence of hantavirus antibodies amongst the healthy but at-risk population of one of the affected provinces. These preliminary data show that the virus is circulating in the area. Until now, asymptomatic or mild infections with non-specific symptoms may have been the cause for the underestimation of the real number of hantavirus infections. It is necessary to finalise the statistical analysis of the seroepidemiological study to plan further studies and surveys in Turkey. The plan is to inventorise the local rodent species, identify circulating hantavirus serotypes in rodents, perform molecular characterisation of strains isolated from rodents and humans and compare them with strains circulating in the neighbouring countries, and investigate transmission mechanisms and the time and space-distribution of human hantavirus infections.

Hantavirus causes a significant number of human illnesses, making it a global public health threat [7]. The presence of the virus in Turkey is not surprising because it is circulating in the neighbouring countries [1,4,7]. In the affected area, a comprehensive preventive strategy against hantavirus infection, including health education and promotion activities, rodent control and surveillance, has been implemented. For example, guidelines were distributed for public on rodent proofing and trapping in and around homes, and the careful disposal of dead rodents.

### Acknowledgements

We thank all members of the Hantavirus study group in Turkey.

### References

1. Zhenqiang B, Pierre BH Formenty, Roth CE. Hantavirus infection: a review and global update. *J Infect Developing Countries*. 2008;2(1):3-23.
2. Schmaljohn CS, Hasty SE, Dalrymple JM, LeDuc JW, von Bonsdorff CH, Brummer-Korvenkontio M, et al. Antigenic and genetic properties of viruses linked to hemorrhagic fever with renal syndrome. *Science*. 1985;227(4690):1041-4.
3. Goldsmith CS, Elliott LH, Peters CJ, Zaki SR. Ultrastructural characteristics of Sin Nombre virus, causative agent of hantavirus pulmonary syndrome. *Arch Virol*. 1995;140(12): 2107-22.
4. Vapalahti O, Mustonen J, Lundkvist A, Henttonen H, Plyusnin A, Vaheri A. Hantavirus infections in Europe. *Lancet Infect Dis*. 2003;3(12): 653-61.
5. Lednicky JA. Hantavirus: a short review. *Arch Pathol Lab Med*.2003;127(1):30-5.
6. Hart CA, Bennett M. Hantavirus infections: epidemiology and pathogenesis. *Microbes and Infections*. 1999; 1(14):1229-37.
7. Heyman P, Vaheri A, the ENVID members. Situation of hantavirus infections and haemorrhagic fever with renal syndrome in European countries as of December 2006. *Euro Surveill*. 2008;13(28):pii=18925. Available from: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=18925>

This article was published on 21 May 2009.

Citation style for this article: M Ertek on behalf of the Refik Saydam National Public Health Agency, T Buzgan on behalf of the Ministry of Health. An outbreak caused by hantavirus in the Black Sea region of Turkey, January - May 2009. *Euro Surveill*. 2009;14(20):pii=19214. Available online: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19214>