ORIGINAL ARTICLES AAEM

Ann Agric Environ Med 2009, 16, 79–85

# THE FIRST ESTABLISHED FOCUS OF HANTAVIRUS INFECTION IN POLAND, 2007

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Nowakowska A, Heyman P, Knap JP, Burzyński W, Witas M: The first established focus of hantavirus infection in Poland, 2007. *Ann Agric Environ Med* 2009, **16**, 79–85.

**Abstract:** The first hantavirus infection outbreak in Poland (with different seroetiology) was identified between August–December 2007. Thirteen cases were reported in south-east Poland: 12 cases in the Carpathians bordering with northeast Slovakia, mainly in the forested areas of the Bieszczady mountains, and one case approximately 100–120 kilometres north from the others, in the adjacent Sub-Carpathian region. Four additional cases of past infection were identified retrospectively, based on the presence of the hantavirus specific IgG antibodies. Thus, the total number of infections identified in this area amounts to 17. Most probably, this number does not constitute the real hantavirus participation in the infections in this area. Considerable evidence for the probable participation of Dobrava virus (10 cases out of 17) and Puumala virus (3 cases out of 17) in the hantavirus diseases has been revealed. There were no fatal infections. However, out of 13 symptomatic cases, major HFRS clinical manifestations were observed in 10 cases and a typical nephropathia epidemica in the next 3 cases. Haemorrhagic diathesis was observed in 9 patients. Five patients underwent haemodialysis treatment due to acute renal failure. One, a female patient, haemodialysed in 10$^{th}$ week of gravidity, managed to maintain pregnancy and remains under interdisciplinary care.

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**Key words: Haemorrhagic Fever with Renal Syndrome (HFRS), Nephropathia Epidemica (NE), Hantavirus Cardio-Pulmonary Syndrome (HCPS), hantavirus diseases (HVD), Dobrava virus (DOBV), Puumala virus (PUUV), rodent-borne viral zoonoses.**

## INTRODUCTION

Human infections caused by a number of RNA-hantavirus serotypes (family *Bunyaviridae*, genus *Hantavirus*) occur on all inhabited continents (except Australia). They pose an increasing global problem and meet the requirements of "emerging infectious diseases". Clinical presentation and disease course severity of these zoonoses are determined mainly by their serotypes [5, 14, 22]. Two polar forms of the disease have been distinguished: 1) severe Haemorrhagic Fever with Renal Syndrome (HFRS), caused by Hantaan virus (HTNV), Dobrava virus (DOBV) and Seoul virus (SEOV), with the mortality rate amounting up to 20%, and 2) considerably milder Nephropathia Epidemica (NE), caused mainly by Puumala virus (PUUV) [4, 21, 23]. Very severe Hantavirus Cardio-Pulmonary Syndrome (HCPS), caused mainly by Sin Nombre virus (SNV) and Andes virus (ANDV), occurs only on the American continent [14, 30].

Rodents are the natural reservoir of the virus; they are also its vectors. The territories inhabited by rodents define the areas of particular infection occurrence. The rodents transmitting hantaviruses are the direct cause of the presence of these viruses in the area they inhabit [5, 30]. These

Received: 8 July 2008
Accepted: 28 May 2009

rodents represent 3 families: *Muridae* – responsible for transmitting Hantaan (HTNV) [2], Seoul (SEOV), Dobrava (DOBV), Saaremaa (SAAV) and other viruses; *Arvicolinae* – responsible for transmitting Puumala (PUUV), Tula (TULV) [3] and other viruses; *Sigmodontinae* – responsible for transmitting Andes (ANDV), Sin Nombre (SNV) and other New World hantaviruses. Hantavirus disease (HVD) is known in most European countries [7]. Research on this disease in Poland started very late, despite the detection of a severe HFRS case as early as 1973 [25] in a man working in a rat infested environment. The first serologically documented HFRS case was diagnosed in 2005 [20] in a submontane region of southeast Poland.

## MATERIALS AND METHODS

Despite the lack of a common EU case-definition of Hantavirus disease, we considered the following criteria (compatible with Heyman *et al.*, [13] and the Koch Institute definition [11]): detection of IgM specific antibodies and evidence of seroconversion in a follow-up sample. Additionally, in all 17 cases, serologic diagnosis of leptospirosis (MAT – microscopic agglutination test with 16 *Leptospira* serovars) was performed. All of the 17 cases also fulfilled the epidemiological risk factors criteria, according to Crowcroft *et al.* [8]: "cases were more likely to live less than 50 meters from a forest and have seen rodents in or around their home, to have been digging, to have spent long periods in forests and been in contact with wood or disturbed earth or dust."

The research was conducted in 2 groups of patients: the first one, admitted to hospital, included 13 cases with clinical symptoms (based on the above-mentioned HVD diagnostic criteria) [19, 24], i.e. cases with a sudden, acute onset of the disease (with influenza-like symptoms), high fever, increased parameters of hepatocellular failure (A1AT, AspAT), thrombocytopenia and renal failure selected out 33 clinically suspected persons. The second group included 28 persons from the immediate vicinity of the patients. This group was subject to laboratory investigation since all case-patients had direct contact with rodents in – or in the immediate vicinity of – their houses; consequently, it was supposed that asymptomatic or oligosymptomatic infection could be present in that environment.

The screening included both immunoblotting and enzyme linked immuno assays (ELISA). IgM and IgG specific antibodies against HTNV, SEOV, DOBV and PUUV serotypes were searched for using the immunoblotting method [14, 31]. Recombinant N protein antigens of the above-listed serotypes (recomLine Bunyavirus IgG/IgM – Strip-Immunoassay, MIKROGEN GmbH, Neuried, Germany) were used for the reactions with antibodies of the patients. The sera of both groups of cases were also tested with ELISA method, with the use of a monospecific test for detecting IgM and IgG antibodies to PUUV and HTNV serotypes (Hantavirus (Puumala) IgG/IgM ELISA and Hantavirus (Hantaan) IgG/IgM ELISA, PROGEN Biotechnik GmbH, Heidelberg, Germany). Consistent results of ELISA antibodies detection in different laboratories (Brussels – Belgium; Rzeszów, Warsaw, Wrocław – Poland) meet the requirements of quality control measures for the serologic diagnosis of hantavirus infections [6, 13]. Leptospiric infection and coexistence was excluded in 16 cases by microscopic agglutination test (MAT) with 16 *Leptospira interrogans* serovars: Icterohaemorrhagiae, Javanica, Canicola, Ballum, Celledoni, Sejroe, Autumnalis, Australis, Grippotyphosa, Bataviae, Cynopteri, Hebdomadis, Tarassovi, Pomona, Mini, Pyrogenes.

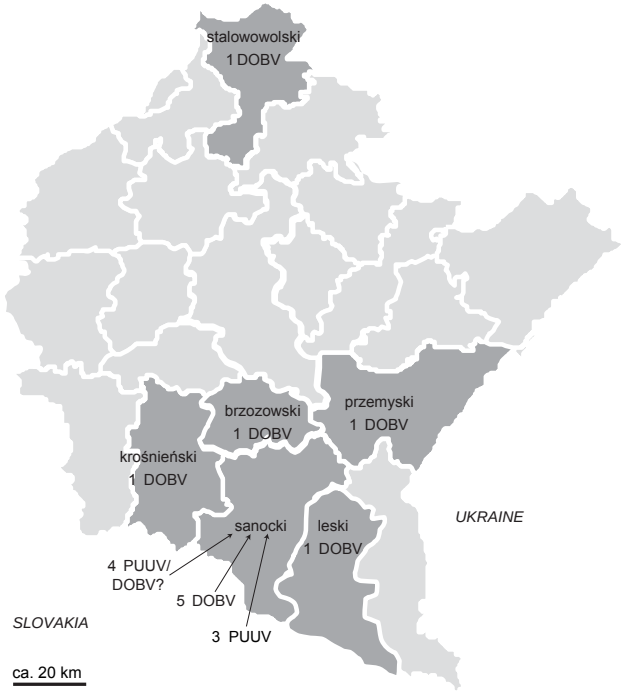


**Figure 1.** The area of hantavirus infection occurrence in the Sub-Carpathian region. DOBV, PUUV/DOBV?, PUUV – probable causal serotype.

## RESULTS

Between August–December 2007 in the Sub-Carpathian region, among 33 clinically suspected persons, 13 cases of acute diseases with hantavirus etiology (39,4%) were identified based on serological investigation: 6 women and 7 men, aged between 17 and 52 (average – 34.7 yrs). Among the 16 Polish regions, the Sub-Carpathian region (area – 17,926 km$^2$, population in 2005 – 2,126,000) is the most southeasterly. It is bordered by Slovakia to the south and the Ukraine to the southeast (Fig. 1).

Twelve cases were identified in the southeast part of the region, in the mountainous region of the Carpathians, near the Polish-Slovak border. One case was identified in the northern part of the region, approximately 100–120 kilometres from the other cases, near vast forest complexes (Puszcza Solska, Lasy Janowskie). In all of the 13

**Table 1.** Serological tests results list in hantavirus disease patients (No. 1–13) and in cases of past infection (No. 14–17), according to the method of hantavirus specific antibodies typing.

| No. | Age/ name | Sex | Altitude of home (metres) | Sample No. | Antibodies typing with immunoblot method (qualitative testing)[a] | | | Antibodies typing with ELISA method (qualitative testing)[b] for a monospecific antigen | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | HTNV | | PUUV | | Probable causal serotype |
| | | | | | IgM | IgG | Antibodies presence for serotype group | ratio: OD sample/OD reference serum | | | | |
| | | | | | | | | IgM | IgG | IgM | IgG | |
| 1 | 32 LCC | F | 440 | 232, hosp[c] | + | + | DOBV/HTNV/SEOV | 2.48[pos] | 2.48[pos] | 0.88[neg] | 0.85[neg] | DOBV |
| 2 | 18 BR | M | 340 | 234, hosp[c] | + | + | DOBV/HTNV/SEOV | 2.53[pos] | 2.37[pos] | 0.64[neg] | 1.00[pos] | DOBV |
| 3 | 37 KI | F | 520 | 236, hosp[c] | + | + | DOBV/HTNV/SEOV | 2.52[pos] | 2.43[pos] | 0.84[neg] | 0.46[neg] | DOBV |
| 4 | 25 LT | M | 560 | 237, hosp[c] | + | + | PUUV | 1.59[pos] | 1.06[pos] | 5.07[pos] | 1.81[pos] | PUUV |
| 5 | 30 LW | M | ca. 600 | 238, hosp[c] | + | + | DOBV/HTNV/SEOV | 2.53[pos] | 2.31[pos] | 1.84[pos] | 0.48[neg] | DOBV |
| 6 | 47 WA | M | 320 | 241, hosp[c] | + | + | DOBV/HTNV/SEOV | 2.49[pos] | 2.45[pos] | 0.54[neg] | 1.07[pos] | DOBV |
| 7 | 30 NS | F | 560 | 268, hosp[c] | + | + | PUUV | 0.98[neg] | 0.73[neg] | 4.57[pos] | 1.78[pos] | PUUV |
| 8 | 52 BA | M | 580 | 282 | + | + | DOBV/HTNV/SEOV | 3.80[pos] | 2.40[pos] | 0.52[neg] | 1.32[pos] | DOBV |
| 9 | 34 MK | F | 540 | 320, hosp[c] | + | + | PUUV | 4.09[pos] | 0.62[neg] | 4.60[pos] | 1.02[pos] | PUUV |
| 10 | 40 ZD | M | 157 | 338, hosp[c] | + | + | DOBV/HTNV/SEOV | 4.04[pos] | 2.58[pos] | 1.14[pos] | 1.04[pos] | DOBV |
| 11 | 50 HI | F | 420 | 341, hosp[c] | + | + | DOBV/HTNV/SEOV | 2.9[pos] | 2.57[pos] | 1.29[pos] | 1.79[pos] | DOBV |
| 12 | 17 BE | F | ca. 600 | 343, hosp[c] | + | + | DOBV/HTNV/SEOV | 4.06[pos] | 2.50[pos] | 2.83[pos] | 1.34[pos] | DOBV |
| 13 | 39 ML | M | 500 | 281, hosp[c] | – | + | PUUV[e] | 3.63[pos] | 1.39[pos] | 4.32[pos] | 1.74[pos] | PUUV/ DOBV?* |
| 14 | 69 GA | M | ca. 600 | 374, hosp[c, f] | – | + | PUUV | 0.42[neg] | 1.78[pos] | 0.44[neg] | 1.82[pos] | PUUV/ DOBV?* |
| 15 | 27 LA | F | ca. 600 | 305, fam[d 238] | – | + | PUUV | 0.78[neg] | 1.55[pos] | 0.98[neg] | 1.37[pos] | PUUV/ DOBV?* |
| 16 | 65 GA | F | ca. 600 | 307, fam[d 238] | – | + | PUUV | 0.73[neg] | 1.09[pos] | 0.89[neg] | 0.96[neg] | PUUV/ DOBV?* |
| 17 | 50 HJ | M | 420 | 377, fam[d 341] | – | + | DOBV/HTNV/SEOV | 0.41[neg] | 1.55[pos] | 0.64[neg] | 1.09[pos] | DOBV |

* – PUUV/DOBV? – probable causal serotype based on comparison between the results of immunoblotting and ELISA tests; [a] Hantavirus specific antibodies typing was conducted in the Laboratory for Microbiology, Serology and Parasitology, Voivodeship Sanitary-Epidemiological Station, Rzeszów, Poland. The interpretation criteria: positive – the presence of band for monospecific serotype; negative – the absence of band for monospecific serotype; [b] Hantavirus specific antibodies typing was conducted in Research Laboratory for Vector-Borne Diseases, National Reference Centre for Hantavirus Infections, Queen Astrid Military Hospital, Brussels, Belgium. The interpretation criteria: [pos] – positive for IgM – above 1.00, [neg] – negative for IgM – below 1.00, [pos] – positive for IgG – above 1.00, [neg] – negative for IgG – below 1.00; [c] patient hospitalized; [d] person from patient's family No.; [e] the presence of Leptospira interrogans serovar Australis antibodies in 400 titre; [f] patient with unconfirmed hantavirus disease; + Antibodies presence for hantaviruses in the given antibodies class was detected; – Antibodies presence for hantaviruses in the given antibodies class was not detected.

hospitalized cases with acute HVD symptoms, IgM and IgG specific antibodies against hantavirus serotypes were detected. In one person (Table 1., No. 14), hospitalized due to high fever, IgG antibodies were also detected, but the further course of the disease excluded acute HVD phase. In the second group (28 persons), consisting of members of the patients' households, Hantavirus IgG specific antibodies were detected only in 3 persons (10.7%), who did not present any symptoms of the disease. Together, one patient with unconfirmed HVD and 3 seropositive family members were defined as 4 cases of past infection. Thus, the total number of infections identified in the study area amounted to 17. The results of the serological tests are presented in Table 1.

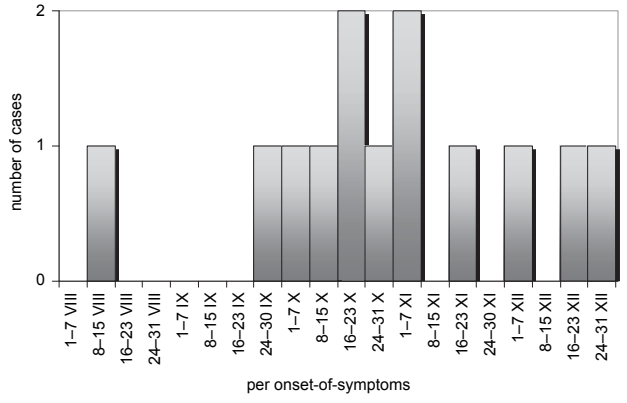


**Figure 2.** Course of the epidemic hantavirus infection in the Sub-Carpathian region, 2007.

The course of the epidemic is presented in Figure 2. The highest number of cases (5) was identified in October. During the epidemic, the temperatures were higher than usual, atypical for mountain regions. Eight cases presented near the Polish-Slovak border which runs on a Carpathian ridge. Twelve cases were identified in the mountainous Sanok Poviat (area – 1,186 km$^2$, population – 55,338), which borders with Slovakia. The incidence for the Sub-Carpathian region amounted to 0.56/100,000, for the Sanok Powiat – 14.5/100,000, whereas the cases were epidemically focused in the fourth quarter of 2007.

The clinical courses in our cases were mostly severe (Tab. 2). Acute onset with fever occurred in all patients, diarrhoea – in at least 10 cases, signs of acute renal failure in 10 out of 13 patients (haemodialysis was necessary in 5 cases), hepatic injury in at least 10. Thrombocytopenia and/or haemorrhagic diathesis were detected in 9 cases. Table 2, Case No. 1, a 32-year-old woman who became ill in the 10$^{th}$ week of gravidity, who managed to keep her baby despite a very severe course of the disease, with explicit haemorrhagic diathesis and acute renal failure with the need for a series of haemodialyses.

## DISCUSSION

The first cases of HFRS focus in the Sub-Carpathian region were reported in October 2007, when the Voivodeship Sanitary-Epidemiological Station in Rzeszów started a routine HFRS diagnostic procedure in the region. Thus, determining the real beginning of the epidemic is quite difficult; consequently, precise epidemiologic analysis of the epidemic focus should be conducted cautiously. Despite the uncertainty concerning the beginning of the epidemic,

**Table 2.** Clinical characteristics of cases of hantavirus disease diagnosed in the Sub-Carpathian region, 2007.

| Course of a disease[a] | The cases in order of serologic identification | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 232 LC case 1 | 234 BR case 2 | 236 KI case 3 | 237 LT case 4 | 238 LW case 5 | 241 WA case 6 | 268 NS case 7 | 282 BA case 8 | 320 MK case 9 | 338 ZD case 10 | 341 HI case 11 | 343 BE case 12 | 281 ML case 13 |
| Acute onset with influenza-like symptoms | 25 IX 2007 + | 4 X 2007 + | 18 X 2007 + | 11 X 2007 + | 20 X 2007 + | 27 X 2007 + | 4 XI 2007 + | 9 VIII 2007 + | 1 XII 2007 + | 22 XI 2007 + | 18 XII 2007 + | 27 XII 2007 + | 2 XI 2007 + |
| Diarrhoea | + | + | – | + | + | nd | + | + | + | + | + | + | nd |
| AlAT, AspAT increase in serum | nd | nd | + | + | + | + | + | + | + | – | + | + | + |
| Thrombocytopenia | + | nd | + | – | + | nd | + | + | + | – | + | + | – |
| Haemorrhagic diathesis symptoms | +[b] | +[c] | + | nd | + | nd | + | +[d] | + | nd | + | + | nd |
| Cough | [e] | – | + | + | [e] | – | + | – | – | – | – | – | + |
| Proteinuria | + | – | + | + | + | + | – | + | + | + | – | + | + |
| Haematuria | + | – | + | – | + | + | – | + | – | – | – | – | + |
| Creatinine increase in serum | + | + | + | + | + | + | – | + | – | + | – | – | + |
| Electrolyte balance disorders | + | – | + | + | + | + | – | + | – | – | – | – | + |
| Oliguria | + | – | + | – | + | + | – | + | – | – | – | + | + |
| Haemodialysis | + | – | – | – | – | + | – | + | – | + | – | – | + |
| Probable causal serotype[f] | DOBV | DOBV | DOBV | PUUV | DOBV | DOBV | PUUV | DOBV | PUUV | DOBV | DOBV | DOBV | PUUV/ DOBV? |
| Clinical severity | severe | moderate | severe | moderate | severe | severe | mild | severe | mild | severe | moderate | moderate | severe |

[a] all the diseased confirmed contact with rodents; [b] purpura on lower limbs; [c] profuse epistaxis; [d] coffee-grounds vomiting; [e] fluid in pleural cavity; [f] hantavirus serotype based on comparison between the results of immunoblotting and ELISA tests, indicating the possible virus participation in the infection; [+] presence of this symptom; – absence of symptom; nd – no data; PUUV/DOBV? – probable causal serotype based on comparison between the results of immunoblotting and ELISA tests.

**Table 3.** Mast years preceding the years of hantavirus infection increase, based on the fructification of beech, one of the basic ingredients of small rodents' diet.

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Beech mast years in the Sub Carpathian region [a, c, d] | 1992 | | | 1995 | | | 1998 | | 2000 | | | 2003 | | |
| Years of HVD increase in Europe [b] | | 1993 | | | 1996 | | | 1999 | | 2001 | | 2003 | | 2005 |

[a] data based on the information from the Forest Cultivation Division of the Krosno Regional State Forests Authority, Poland; [b] data based on the publication by Heyman *et al.*, [13]; [c] Eastern Slovakia (natural focus): the relative density of small mammal populations in the surveyed areas: 2001 – 120.6 exemplars per 100 tracks; 2003 – 32.9 exemplars per 100 tracks [35]; [d] The Slovak Republic – the number of HFRS infections in humans: 2003 – 2 (0.04/100,000), 2004 – 37 (0.69/100,000), 2005 – 10 (0.15/100,000).

we present the results of serologic and epidemiologic investigation of the first laboratory-confirmed hantavirus infection focus in Poland. An HFRS case with severe course and hepatorenal failure indicating the presence of DOBV [20] was diagnosed in 2005 in the Sub-Carpathian region, approximately 40 kilometres from the described focus, in similar physiographic and ecological conditions. Since then, routine serologic HFRS diagnostics were implemented, together with a large-scaled educational campaign regarding this disease among primary care physicians and doctors working in hospitals. It should be assumed that numerous diseases diagnosed in summer and autumn 2003 among forest officers from the described mountainous region, who presented with acute course, influenza-like clinical symptoms, proteinuria and hepatorenal syndrome, were in fact HFRS cases, similar to the etiologically unrecognized cases of acute inflammatory renal failure admitted to the regional wards of nephrology in the past. In this respect, we are planning a retrospective seroepidemiological investigation. In 2007, a seroepidemiological investigation was conducted among forest officers from the National Kampinoski Forest in central Poland. Puumala IgG antibodies were detected in only one forest officer, aged 47, who had been working in the Sub-Carpathian region for many years.

The occurrence of HFRS epidemic focus in the Polish-Slovak frontier zone of the East Carpathian Mountain region was assessed for comparison with adjacent regions in both countries. It should be noted that the region is one of the unique areas in Poland from the geographical and natural points of view. The natural conditions of the region are especially favourable for the spread of zoonoses transmitted by small rodents (the so-called robo-viruses, rodent-borne viral zoonoses) and other mammals (e.g. *Echinococcus multilocularis* transmitted by the red fox [10], as well as vector-borne zoonoses (viral, rickettsial, bacterial, protozoan) transmitted by arthropods. These zoonoses form natural foci, which were precisely localized by Slovak researchers. The environmental conditions are also favourable for an exceptionally numerous and diversified population of small rodents [1]. The Carpathian forests are the most biologically diversified area in Poland, they are also the only region with the predominance of deciduous trees: oak (*Quercus robur*), beech (*Fagus sylvatica*), maple (*Acer pseudoplatanus*), ash (*Fraxinus excelsior*). They are a natural source of food (fruit, seeds) for animals, mainly small rodents, whose population density is an important factor in the infection transmissions to humans. The interrelation between, e.g. good mast years and the increased number of infections (Tab. 3) reflects the tendency for the hantavirus reservoir maintenance in this region.

The region is inhabited by rodents from *Arvicolinae* family, the primary PUUV and TULV vectors, and *Murinae* family – HTNV and DOBV vectors [16]. The main feature of mast years in this region is the abundance of beech mast [1, 13]. 95% of the forests in the region are under different forms of protection; the people living or working in and near the forests remain in close proximity to nature. All those infected had regular contact with rodents at work or home, and fulfilled the HFRS high risk criteria developed by Crowcroft *et al.* [8]. In the 4 cases where the acute HFRS phase was excluded, PUUV and DOBV/SEOV/HTNV IgG antibodies were detected, which proves that the patients had contact with the virus; moreover, it confirms the presence of HVD in the endemic area. One patient (ML, aged 39, Table 1, No. 13), suffering from acute febrile disease with hepatorenal failure, was diagnosed an HFRS – leptospirosis co-infection (reciprocal titer of 400 for *Leptospira interrogans* serovar Australis antibodies). Such co-infections were described, e.g. in Bosnia [9]. In another case (GA, aged 69, Table 1, No. 14 – a patient with acute febrile disease with multiple organ involvement and severe clinical course, who had PUUV anti-IgG antibodies) HVD – the etiology was not established.

The mountainous region where the 12 HVD cases were reported borders with Slovakia, which has the same physiographic and ecological conditions. The 4 cases identified in frontier villages are situated 20–25 kilometers "in a straight line" from the Slovak hantavirus natural focus (Ruska Poruba-Zavada). As early as between 1951–1955, the first 2 fatal cases of HFRS in humans in Slovakia were reported within this focus [27]. In the epidemic area, at least 16 species of small rodents, including both *Murinae* and *Arvicolinae* species, were identified. Between 1955–1956, in

the Ruska Poruba region, 1,189 specimens of small rodents were captured; the most numerous were *Microtus arvalis*, *Apodemus flavicollis*, *Apodemus agrarius*, *Mus musculus* and *Myodes glareolus*. In the following years, the presence of hantaviruses was detected in rodents captured within this focus (and other focuses identified in its vicinity) [12, 35]. Large-scale research [16, 17, 32] proved that DOBV, PUUV and TULV viruses are present in Slovakia, while DOBV is the most frequent and has 2 characteristic genetic lines, DOBV(A-a) and (A-f), depending on the vector [5, 15, 18, 36]. Despite the lack of Gold Standard confirmatory tests (such as focus or plaque reduction neutralization tests) directly confirming the role of Dobrava and Puumala viruses in the infections, these serotypes could be assumed to be present on the territory under research, according to positive results of serological investigation of IgM and IgG specific antibodies. The data presented indicate the possibility of PUUV and DOBV viruses co-circulation on the Polish-Slovak border in the mountainous Carpathian area and the possibility of DOBV virus dominance in this region. The results of Slovak research and the severity of the clinical course in the Polish cases are another argument confirming this possibility.

DOBV is the most pathogenic European *Hantavirus*. In the Balkans, HFRS caused by DOBV can attain a death rate amounting up to 12% [5]. Sibold *et al.* [33] investigated 19 patients from northeast Germany and Slovakia who suffered from HFRS caused by DOBV. The diagnosis was verified by neutralization tests. Typical signs and symptoms of HFRS (influenza-like symptoms with fever, thrombocytopenia, elevated serum creatinine and acute renal failure syndrome) were observed. There were no fatal cases. Two patients (10,5%) showed pulmonary symptoms. No manifestation of haemorrhagic diathesis, despite trombocytopenia, was detected. Haemodialysis was necessary in 4 patients. We saw many similarities in an elaboration of the clinical result of our research for described hantavirus infections in Europe, especially in central and southeastern Europe. We have written typical features of a phase course HFRS and mild features of NE. Although serology cannot definitely determine the causal hantavirus – for that a neutralisation test is needed – we observed a clear relation between the presence of antibodies to different serotype groups in immunoblotting and ELISA and the severity of the clinical course of the disease [5, 14, 22]. Among the 3 cases with PUUV monospecific response, the course of the disease was mild in 2 cases and moderate in 1 case, whereas among the 9 cases with DOBV/HTNV/SEOV response in immunoblotting, the disease had a severe course in 6 cases and a moderate course in 3 patients. The last hantavirus infection case that can be defined as PUUV/DOBV was severe.

In the centre of Poland, near Łódź, 2 strains of TULV virus have been isolated: Lodz-1 and Lodz-2 [34]. Molecular testing revealed their phylogenetic similarity to a TULV strain isolated from a severe HFRS case in Germany, near the border with Poland [16, 26, 33]. The HFRS cases that have been reported in Poland usually have a severe course [19, 20], which correlates with the antibodies dynamics and suggests the presence of DOBV and PUUV viruses in the country. Large-scale, interdisciplinary clinical tests and field research on isolating hantaviruses from small mammals are indispensable. Aerosol hantavirus transmission is currently considered the main route of infection, whereas the transmission of the disease by vectors (ticks) and direct contact between humans has not been considered probable, at least in Eurasia. However, a group of Slovak scientists made a thorough research on arthropods – ectoparasites of the rodents which are hantaviruses natural carriers; their potential role as these viruses vectors could not be disclaimed [12]. The detection of Puumala virus copy in the saliva, urine and milk of breastfeeding women of the Scandinavian HVD cases suggests a different view on the possibilities of hantaviruses infections in humans [28, 29].

## CONCLUSIONS

1. The presence of hantaviruses in symptomatic human infections in southeast Poland was proved based on the first HVD epidemic focus in indisputably endemic territory of the country.
2. The differentiation specific antibodies again serotype groups Dobrava and Puumala viruses was proved.
3. In 7 out of 13 cases, the course of the disease was severe, with thrombocytopenia, haemorrhagic diathesis, hypertransamination, oliguria and renal failure of different severity (haemodialysis due to acute renal failure was indispensable in 5 cases). One patient, haemodialized in 10$^{th}$ week of gravidity, managed to keep pregnancy. There were no fatal cases.
4. In 3 healthy persons (members of the patients' households) and 1 non-HFRS diseased person from the epidemic area, anti-*Hantavirus* IgG specific antibodies were identified, which proves the existence of infection in their close vicinity.
5. Virologic research on small rodents caught in the immediate vicinity of the described HVD focus cases is indispensable.

**Acknowledgements**

The author wish to thank Katarzyna Cioch, Laboratory for Microbiology, Serology and Parasitology, Voivodeship Sanitary-Epidemiological Station, Rzeszów, Poland; Urszula Litarska, Leptospires Laboratory, Voivodeship Sanitary-Epidemiological Station, Wrocław, Poland; Alicja Rączka, Medical Military Institute, Warsaw, Poland; Marek Marecki, Forest Cultivation Division, Krosno Regional State Forests Authority, Poland; Jan Lech, Provincial Sanitary-Epidemiological Station, Sanok, Poland. The Belgian research was conducted on Grant Dg-Vmg WB28 from the Belgian Ministry of Defense.

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