## DETECTION OF ANTIBODIES TO THE WESTERN AND THE EASTERN TYPE OF HAEMORRHAGIC FEVER WITH RENAL SYNDROME IN PATIENT'S SERA FROM SLOVAKIA

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Summary. — We present serological evidence of infection with western and eastern type of haemorrhagic fever with renal syndrome (HFRS) virus in patient's sera from Slovakia by indirect immunofluorescence. Treatment of sera with 2-mercaptoethanol decreased levels of haemagglutination-inhibition (HI) antibodies to the eastern type of HFRS suggesting primary infection of the patients by this virus.

Key words: haemorrhagic fever with renal syndrome (HFRS); eastern and western types of HFRS; Fojnica strain; serum antibodies

## Introduction.

In 1984 we detected the antigen of western haemorrhagic fever with renal syndrome (HFRS) in the lungs of small rodents in Eastern Slovakia (Grešíková et al., 1984). It was found by complement-fixation reaction that the antigens were closely related to the western type of HFRS Puumala (Karabatsos, 1985). Antibodies to the western type of HFRS were detected in the sera of Clethrionomys glareolus, Apodemus agrarius, Pitymys subterraneus collected in Eastern Slovakia and in the sera of Clethrionomys glareolus, Apodemus sylvaticus, Microtus arvalis and Microtus economus collected in western Slovakia (Grešíková et al., 1986). The western type of HFRS antigen was demonstrated in Clethrionomys glareolus and Microtus arvalis (Grešíková et al., 1984; Daneš et al., 1986). The eastern type of HFRS antigen Hantaan (Karabatsos, 1985) was found in Apodemus agrarius (Daneš et al., 1986; Grešíková et al., 1988).

The antigen for haemagglutination and for HI test was prepared from the brain of suckling mice infected with Fojnica virus (the eastern type of HFRS kindly supplied by Dr. A. Gligië, Institute of Immunology and Virology, "Torlak," Beograd, Yugoslavia) by sucrose-acetone extraction (Clarke and Casals, 1958). The immunofluorescence procedure for the sera of patients was made according to Tkachenko et al. (1981). The haemagglutination and the HI tests were

The name of patients	Clinical diagnosis	The date of sample collection	IFA titres with antigen	
			Hantaan	CG-1820
D.L.	HFRS	12. X. 87	16	64
D.L.	HFRS	23. X. 87	16	512
D.L.	HFRS	30. X. 87	16	512
D.L.	HFRS	1. XII. 87	16	512
R.M.	Nephritis	7. XII. 87	512	16
R.M.	Nephritis	18. XII. 87	512	16
T.L.	Nephritis	1. VI. 88	128	0
M.M.	Influenza	18. VIII. 88	128	2048
B.R.	HFRS	29. IX. 88	128	16
Z.J.	HFRS	3. VIII. 88	0	0

Table 1. Immunofluorescent antibody (IFA) titres to HFIS in patient's sera

HFRS = Haemorrhagic fever with renal syndrome CG-1820 = The western type of HFRS

performed as described by Clarke and Casals (1958). The sera were treated by 2-mercaptoethanol and then extracted by acetone and adsorbed on concentrated goose crythocytes.

During the years 1987 and 1988 sera were obtained from patients with clinical diagnosis of haemorrhagic fever with renal syndrome, nephritis and/or influenza. The results of immunofluorescent (IFA) tests are shown in Table 1. Out of 6 patient's sera examined by IFA tests, 5 have been positive. Higher antibody titres to Hantaan 76—118 virus strain (the eastern type of HFRS) were detected in 3 patient's sera; on the other hand, higher antibody titres to CG—1820 virus strain (the western type of HFRS) were found in the sera of 2 patients.

The results of class IgM HI antibodies to the Fojnica antigen of HFRS virus are presented in Table 2. The positive control sera (acute — phase sera collected from patients in Bulgaria and Yugoslavia) were found to possess IgM antibodies along with 2 out of 9 patient's sera examined to the eastern

serotype of HFRS.

It has been proved that the eastern type of HFRS occurs in Far Eastern Asia (Korea, China, Far East of the U.S.S.R.) while the western type of HFRS in Europe (Gajdusek, 1982; Baškircev et al., 1984). Yugoslavian sera from febrile nephropathy patients reacted as high with Hantaan antigen as with Puumala antigen (Gajdusek, 1982). The European form of HFRS is considered to be less haemorrhagic than the Korean haemorrhagic fever. However, in Slovakia, the first HFRS cases had fatal outcome (Plank et al., 1961).

Both the eastern type (Hantaan) and the western type (Puumala) of HFRS virus have been already detected in small rodents in Slovakia (Grešíková et al., 1984; Daneš et al., 1986; Grešíková et al., 1988). Clethrionomys glareolus and Microtus arvalis have been the common hosts for the western type of

Serum	Clinical diagnosis	HI titres	HI titres after 2-mercaptoethanol treatment	
Patient from	HFRS	80	10	
Bulgaria				
Patient from	$_{ m HFRS}$	80	< 10	
Yugoslavia				
Human from	$\mathbf{HFRS}$	40	20	
the U.S.A.				
Negative	${f Healthy}$	0	0	
human				
D.L.	MFRS	10	< 10	
R.M.	Nephritis	160	40	
T.L	Nephritis	80	10	
M.M.	Influenza	< 10	< 10	
B.R.	$_{ m HFRS}$	10	10	
Z.J.	$_{ m HFRS}$	< 10	< 10	
š.s.	$_{ m HFRS}$	< 10	< 10	
U.L.	HFRS	< 10	< 10	

Table 2. Haemagglutination-inhibiting (HI) titres to haemorrhagic fever with renal syndrome (HFRS) antigen in patient's sera

HFRS and correlated with the mild form of disease. Apodemus species seems to be the host for the eastern type of HFRS and related with severe form of HFRS.

It is of interest that we have been able to demonstrate specific IgM antibodies to Hantavirus (Fojnica strain) by HI tests. By IFA tests, however, antibodies were detected to both the eastern and western types of HFRS.

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## References

Baškircev, V. N., Tkačenko, E. A., Dzagurova, T. K., and Rylceva, E. V. (1984): Vydelenie štammov virusa gemorragičeskoj lichorodky s počečnym syndromom v kulture kletok. Vopr. virusol. 29 (4), 497-502.

Brummer-Korvenkontio, M., Vaheri, A., Hovi, T., von Bonsdorf, C. H., Vuorimies, J., Manni, T., Penttinen, K., Oker-Blom, N., and Lahdevirta, J. (1980): Nephropathia epidemica: Detection of antigen in bak voles and serologic diagnosis of human infection. J. infect. Dis. 140, 131-134.

Brummer-Korvenkontio, M., Henttonen, H., and Vaheri, A. (1982): Haemorrhagic fever with renal syndrome in Finland: ecology and virology of nephropathia epidemica. Scand. J. infect. Dis. Suppl. 36, 88.

Clarke, D. H., and Casals, J. (1958): Technique for haemagglutination and haemagglutination-inhibition with arthropod-borne viruses. Am. J. trop. Med. Hyg. 7, 561-573.

Daneš, L., Tkachenko, E. A., Ivanov, A. P., Lim, D., Rezapkin, G. V., and Dzagurova, T. K. (1986): Haemorrhagic fever with renal syndrome in Czechoslovakia: Detection of antigen in small terrestrial mammals and specific serum antibodies in man. J. Hyg. Epid. Microbiol. Immunol. 30, 79-85.

- Gajdusek, D. C. (1982): Rodent-borne viral nephropathy haemorrhagic fever with renal syndrome; nephropathia epidemica. Report by the World Health Organization Working group on Haemorrhagic Fever with Renal Syndrome, Tokio, February 22-24, 3.
- Grešíková, M., Rajčáni, J., Sekeyová, M., Brummer-Korvenkontio, M., Kožuch, O., Labuda, M., Turek, R., Weismann, P., Nosek, J., and Lysý, J. (1984): Haemorrhagic fever virus with renal syndrome (HFRS) in small rodents in Czechoslovakia. *Acta virol.* 28, 416-421.
- Grešíková, M., Sekeyová, M., Brummer-Korvenkontio, M., Kožuch, O., Labuda, M., Rajčáni, J., and Lysý, J. (1986): Serological survey with antigen of haemorrhagic fever with renal syndrome in small rodents in Slovakia. *Acta virol.* 30, 158-160.
- Grešíková, M., Kožuch, O., Sekeyová, M., Tkachenko, E. A., Rezapkin, G. V., Lysý, J. (1988): Detection of the antigen and antibodies to the eastern subtype of haemorrhagic fever with renal syndrome virus in small rodents in Slovakia. *Acta virol.* 32, 164-166.
- Karabatsos, N. (1985): (Ed.) International Catalogue of Arboviruses Including Certain Other Viruses of Vertebrates, 4th ed., Am. Soc. Trop. Med. Hyg., San Antonio, Texas.
- Plank, J., Režucha, M., and Rojkovič, D. (1961): Occurrence of haemorrhagic fevers in Europe, pp. 291-301 (in Slovak). In Zborník krajovej patológie Východného Slovenska. I. Niektoré prírodnochniskové nákazy na Východnom Slovensku. Krajské nakladateľstvo všeobecnej literatúry, Košice.
- Tkachenko, E. A., Ivanov, A. P., Dzagurova, T. K., Donets, M. A., Rezapkin, G. V., and Leshchinskaya, E. V. (1981): Immunosorbent assay for diagnosis of haemorrhagic fever with renal syndrome. Lancetii (8240), 257-258.