

<b>Virus Name: Hypr</b>		<b>Abbreviation: HYPRV</b>
Status <b>Arbovirus</b>	Select Agent <b>No</b>	SALS Level <b>4</b>
SALS Basis <b>Results of SALS surveys and information from the Catalogue.</b>		
Other Information <b>Vaccination Recommended</b>		
Antigenic Group <b>B</b>		

**SECTION I - Full Virus Name and Prototype Number**

Prototype Strain Number / Designation <b>Tick-borne encephalitis</b>	Accession Number	Original Date Submitted <b>3/13/1985</b>
Family <b>Flaviviridae</b>	Genus <b>Flavivirus</b>	
Information From <b>H. Libikova</b>	Address <b>Institute of Virology, Czechoslovak Academy of Sciences, Bratislava 9</b>	
Information Footnote <b>Reviewed by editor</b>		

**Section II - Original Source**

Isolated By (name) <b>L. Popisil, et al. (1)</b>	Isolated at Institute <b>Brno, Czechoslovakia</b>	
Host Genus <b>Man</b>	Species	Host Age/Stage <b>5 years</b>
Sex <b>Male</b>		
<u>Isolated From</u> <b>Whole Blood</b>	<u>Isolation Details</u>	
Signs and Symptoms of Illness <b>Typical tick-borne encephalitis (not paralytic)</b>	Arthropod	
Time Held Alive before Inoculation		
Collection Method	Collection Date	
Place Collected (Minimum of City, State, Country) <b>Vicinity of town of Brno, Moravia, Czechoslovakia</b>		
Latitude <b>49° N</b>	Longitude <b>18° E</b>	
Macrohabitat	Microhabitat	Method of Storage until Inoculated <b>Inoculated immediately</b>
Footnotes		

**Section III - Method of Isolation**

Inoculation Date	
Animal (Details will be in Section 6) <b>wn mice</b>	
Route Inoculated <b>Intracerebral</b>	Reisolation <b>Not tried</b>
Other Reasons <b>Clinical picture, patient bitten by ticks</b>	
Homologous Antibody Formation by <u>Source Animal</u>	
Test(s) Used	
Footnotes	

**Section IV - Virus Properties**

Physicochemical		
<b>RNA</b>		
Pieces (number of genome segments)	Infectivity	Sedimentation Coefficients(s) (S)
Percentage wt, of Virion Protein	Lipid	Carbohydrate
Virion Polypeptides: Number	Details	
Non-virion Polypeptides: Number	Details	
Virion Density	Sedimentation Coefficients(s) (S)	
Nucleocapsid Density	Sedimentation Coefficients(s) (S)	
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<b><u>Stability of Infectivity (effects)</u></b>		
pH (infective range)		
Lipid Solvent (ether - % used to test)	After Treatment Titer	Control Titer
Lipid Solvent (chloroform)	After Treatment Titer	Control Titer
Lipid Solvent (deoxycholate)	After Treatment Titer	Control Titer
Other (formalin, radiation)		
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<b><u>Virion Morphology</u></b>		
Shape	Dimensions <b>55 - 80 nm</b>	
Mean nm	Range nm	
Measurement Method <b>Negative stain, electron microscopy (2)</b>	Surface Projections/Envelope <b>Envelope observed</b>	Nucleocapsid Dimensions, Symmetry <b>Spherical nucleocapsid; diameter</b>

**Morphogenesis**

Site of Constituent Formation in Cell      Site of Virion Assembly      Site of Virion Accumulation

Inclusion Bodies      Other

**Hemagglutination**

Hemagglutination      Antigen Source      Erythrocytes (species used)  
**Yes**      **SMB ext. by acetone-ether; purified by calcium phosphate columns**      **Goose**

pH Range      pH Optimum  
 6.2-6.8      6.6

Temperature Range      Temperature Optimum  
    Room (22dC)

Remarks

Serologic Methods Recommended  
**HI, CF, NT**

Footnotes

**Section V - Antigenic Relationship and Lack of Relationship to Other Viruses**

I. Neutralizing indices of immune hamster sera in cross-neutralization tests in mice (intraperitoneal inoculation):

Virus	Serum			
	Hypr	RSSE (Sofin)	Absettarov	Louping ill
Hypr	158.5 *	158.5	158.5	158.5
RSSE (Sofin)	67.6	67.6	67.6	67.6
Absettarov	1,600	1,600	1,600	1,600
Louping ill	1,400	1,400	1,400	1,400

\* In thousands

II. Cross-complement fixation tests with immune hamster sera:

Antigen	Serum			
	Hypr	RSSE (Sofin)	Absettarov	Louping ill

Hypr	32 **	8	8	16
RSSE (Sofin)	16	16	8	8
Absettarov	32	32	16	16
Louping ill	16	32	4	16

\*\* Serum of titers

I. and II. See Reference [4] .

III. Neutralization tests with immune horse gamma globulin (1:1000) against the strain Hypr [5] in HeLa cells:

**Neutralizing titers with viruses**

Hypr	512	Absettarov	512
RSSE (Sofin)	512	OMSK	1024
Kyasanur Forest dis	512		

IV. Negative results:

- a) Cross-neutralization tests in mice with WEE, EEE and Theiler FA viruses
- b) Cross-CF tests with SLE, Jap. B, EMC, LCM and FA viruses

**Section VI - Biologic Characteristics**

Virus Source (all VERTEBRATE isolates)  
 Blood (M), cerebro spinal fluid (M), CNS (M)(LV),

Lab Methods of Virus Recovery (ALL ISOLATIONS)  
 Newborn and weanling mice; chick embryos and primary avian cell cultures

Cell system (a)	Virus passage history (b)	Evidence of Infection						
		CPE			PLAQUES			Growth Without CPE +/- (g)
		Day (c)	Extent (d)	Titer TCD50/ml (e)	Day (c)	Size (f)	Titer PFU/ml (e)	
HeLa (CL)	HeLa 36		3+	7.7 <sup>a</sup> (23)				
PS (CL)	P-47				6	2-3 mm (24)		

The virus can be propagated in chick, human and pig embryo cell cultures (all PC); HeLa, Detroit-6 and human amnion cell lines (all CL).

<sup>a</sup> Expressed in dex

Vertebrate (species and organ) and arthropod	No. isolations/No. tested	No. with antibody/No. tested Test used	Country and region
Ixodes ricinus	Many		(6,7,8,9 and others)
Dermacentor marginatus	1		(10)
Haemaphysalis inermis	1		(12)
Small rodents:			
Clethrionomys glareolus (blood)	2	NT	(22;11)
Apodemus flavicollis (blood)	2/25		(11)
Apodemus sylvaticus	Virus pos.		(15)
Insectivores:			
Talpa europaea (blood; brain)	7/46		(13)
Erinaceus roumanicus (blood)	2/53		(11)
Sorex araneus (blood)	2/18		(14)
Bird: Anas querquedula		NT	
Man	Many		
Deer, hare, fox		NT	
Goats, sheep, cows		NT	
Bats		NT	USSR findings listed only.
Haemaphysalis punctata	1		Bulgaria (21)
Dermacentor marginatus	1		

Experimental host and age	Passage history and strain	Inoculation Route-Dose	Evidence of infection	AST (days)	Titer log <sub>10</sub> /ml	
Mice (nb)	40-50 passages	ic 0.03	Fatal encephalitis		8-9	
Mice (nb)	ic in mice	ip 0.05	Fatal encephalitis		8-9	
Mice (nb)		sc				
Mice (wn)		ic 0.03	Fatal encephalitis		7-9	
Mice (wn)		ip 0.1	Fatal encephalitis		7-8	
white rats (2 days)		ic 0.05	Fatal encephalitis		9.5	
white rats (11 days)		ic 0.05	Fatal encephalitis		6.5	
white rats (30 days)		ic 0.05	Fatal encephalitis		4.5	
Syrian hamsters		After adaptation	ic 0.05	Fatal encephalitis		8-9
rhesus monkey			ic 0.1	Fatal encephalitis		
cynomologus monkey			in 1.2	Viremia, antibody formation		
		sc 1.0	Viremia, antibody formation			
goats, sheep (yg)		ic	Clinical symptoms of encephalitis (10)			
goats, sheep (ad)		sc	Viremia, excretion of the virus into the milk, antibody formation(10)			
swine		sc	Antibody formation (10)			
embryonated eggs			Virus multiplication			

Also susceptible (viremia) are wood mice, harvest mice, bats, hedgehog, European hares, chickens, domestic ducks, passerine, gallinaceous and predatory birds and lizards.

**Section IX - Experimental Arthropod Infection and Transmission**

Arthropod species & virus source(a)	Method of Infection log <sub>10</sub> /ml (b)		Incubation period (c)		Transmission by bite (d)		Assay of arthropod, log <sub>10</sub> /ml (e)		
	Feeding	Injected	Days	°C	Host	Ratio	Whole	Organ	System
	Ixodes ricinus ticks experimentally transmit the virus and transovarial transmission demonstrated in this vector.								

**Section X - Histopathology**

Character of lesions (specify host)  
**Diffuse meningoencephalomyelitis more pronounced in gray than white matter. Degeneration, necrosis of neurons, perivascular and leptomenigeal infiltration, glial focal proliferation. Characteristic for nat. infection in man, exp. in mice (ic and peripheral) and other suscept. (LV) (20)**

Inclusion Bodies Intranuclear

Organs/Tissues Affected  
**Brain (M)(LV), spinal cord (M)(LV)**

Category of tropism  
**Neurotropic**

**Section XI - Human Disease**

In Nature <b>Significant</b>	Residual <b>Reported</b>	Death <b>Reported</b>
Subclinical	Overt Disease <b>Significant</b>	
Clinical Manifestations <b>Fever (S), headache (S), prostration (S), stiff neck (S), CNS signs (including encephalitis) (S), respiratory involvement (R), CNS pleocytosis (S); Biphasic illness</b>		
Number of Cases <b>100 - 1000 per year in Czechoslovakia</b>	Category (i.e. febrile illness, etc.) <b>Febrile illness, encephalitis</b>	

**Section XII - Geographic Distribution**

Known (Virus detected) <b>Czechoslovakia, Hungary, Poland, Yugoslavia, Austria, Bulgaria, Sweden, Finland. (For references, see Reference 25)</b>
Suspected (Antibody only detected) <b>Germany</b>

## Section XIII - References

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## Remarks

**Two special lines of the strain Hypr were widely used in practice: (a) Variant Hy-HeLa (16,17) used as highly cytopathic antigen for In vitro NT in cell lines; (b) Clone Hy-HK 28"2" of the attenuated variant of the strain Hypr with detailed description of genetic markers (18), used as live vaccine for large domestic animals (19).**