Virus Name: Seoul	Abbreviation: SEOV

Status
Probably not Arbovirus

Select Agent
No

SALS Level

SALS Basis

Other Information
DOC Permit Required

Antigenic Group
Hantaan

SECTION I - Full Virus Name and Prototype Number

Prototype Strain Number / Designation
80-39

Accession Number

Original Date Submitted
1/29/1985

Family
Bunyaviridae

Genus
Hantavirus

Information From
Ho Wang Lee and Joel M. Dalrymple

Address
Korea University Medical College, Seoul, Korea and USAMRIID, Frederick, MD 21701, USA

Information Footnote

Section II - Original Source

Isolated By (name)
Ho Wang Lee, et al. (1)

Isolated at Institute
Seoul, Korea

Host Genus
Rattus norvegicus

Species

Host Age/Stage
Adult

Sex
Female

Isolated From	Isolation Details
Organs/Tissues	**Lungs**

Signs and Symptoms of Illness
None (IFA antigen detectable in tissues when sacrificed)

Arthropod

Time Held Alive before Inoculation

Collection Method
Trapped

Collection Date
4/15/1980

Place Collected (Minimum of City, State, Country)
Apartments, Ahyundong, Mapoku, Seoul, Korea

Latitude
37° 30' N

Longitude
127° 0' E

Macrohabitat
In and around houses

Microhabitat
Inside sewage area around housing where people and animals live

Method of Storage until Inoculated
Kept alive until processed

Footnotes

Section III - Method of Isolation

Inoculation Date
4/23/1980

Animal (Details will be in Section 6)
animal (Tissue Culture)

Route Inoculated
Intramuscular

Reisolation
Yes

Other Reasons
Numerous isolations from this same species and Rattus rattus

Homologous Antibody Formation by Source Animal
Yes

Test(s) Used
Indirect IFA

Footnotes

Section IV - Virus Properties

Physicochemical
RNA, Single Strand

Pieces (number of genome segments)
3 (22)

Infectivity

Sedimentation Coefficients(s) (S)

Percentage wt, of Virion Protein

Lipid

Carbohydrate

Virion Polypeptides: Number
4

Details
Nucleocapsid protein: 50,000 MW; glycoproteins (G1): 76,000 MW, (G2): 54,000 MW; (L) approx.200,000 MW

Non-virion Polypeptides: Number

Details

Virion Density
1.18-1.20 in sucrose

Sedimentation Coefficients(s) (S)

Nucleocapsid Density

Sedimentation Coefficients(s) (S)

Stability of Infectivity (effects)

pH (infective range)
Maximum stability at pH 7.6, inactivated completely at pH 4.0

Lipid Solvent (ether - % used to test) **20%**	After Treatment Titer **<1.0 dex**	Control Titer **5.8 dex**
Lipid Solvent (chloroform) **5%**	After Treatment Titer **<1.0 dex**	Control Titer **5.8 dex**
Lipid Solvent (deoxycholate) **0.1%**	After Treatment Titer **<1.0 dex**	Control Titer **5.8 dex**

Other (formalin, radiation)
Inactivated with 0.4% formalin, 70% ethanol, 0.5% iodine and UV irradiation

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Virion Morphology

Shape
Spherical particles

Dimensions
100 nm

Mean
100 nmnm

Range
90-140nm

Measurement Method	Surface Projections/Envelope	Nucleocapsid Dimensions, Symmetry
Electron microscopy (4.5)	**Surface projections and enveloped**	

Morphogenesis

Site of Constituent Formation in Cell	Site of Virion Assembly	Site of Virion Accumulation
Cytoplasm		
Inclusion Bodies	Other	

Hemagglutination

Hemaggiutination	Antigen Source	Erythrocytes (species used)
Yes	**SMB ext. by sucrose-acetone* (6); Vero E6 cell cultures**	**Goose**
pH Range	pH Optimum	
5.8-6.4	**6.0-6.2**	
Temperature Range	Temperature Optimum	
20-37dC	**37dC**	

Remarks
*** HA demonstrated by this method with prototype Hantaan virus**

Serologic Methods Recommended
PRNT, IFA, ELISA

Footnotes
*** HA demonstrated by this method with prototype Hantaan virus**

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

Seoul virus infected tissue culture cells and sections of rat lungs react extensively by IFA with convalescent sera from HFRS patients in Korea, Japan, China, USSR, and nephropathia epidemica in Scandinavia [7] - [10] . Seoul virus cross-reacted with Hantaan virus and Prospect Hill virus by IFA but differentiable by plaque-reduction test, ELISA test and passive hemagglutination inhibition test. Seoul and Hantaan viruses are differentiated serologically by IFA with monoclonal antibodies to Hantaan virus.
Antigenic relations of HFRS-related virus: PRNT were performed on Vero E6 cell monolayers with rat antisera and cell culture-adapted viruses. Approximately 100 PFU of virus were incubated with twofold dilutions of sera for 1 hour at room temperature before inoculation of 25-cm2 flasks. Inoculated cells were further incubated for 1 hour at 37/C before addition of overlay containing 0.6% agarose (Seakem ME) and 10% heated fetal bovine serum (FBS). Following incubation for 7 to 14 days after infection, a second overlay identical to the first, except for a reduced FBS concentration (2%) and inclusion of neutral red (final concentration, 0.167 mg/ml), was applied. Plaques were counted as they became visible 1 to 5 days after addition of the second overlay. Titers were expressed as the reciprocal of the highest dilution of antibody, resulting in greater than 80% reduction of approximately 100 plaques.

Serum pools	Virus							
	HTN	LEE	UR	TCH	GP	SR-11	PH	PUU
HTN	4000	4000	0	160	80	40	0	0
LEE	4000	2000	20	160	160	200	0	0
UR	2000	80	4000	16000	16000	8000	160	0
TCH	2000	200	4000	32000	8000	8000	200	0
GP	200	80	2000	8000	8000	8000	200	0

SR-11	2000	20	2000	2000	2000	2000	200	0
PH	0	0	0	0	20	20	4000	0
PUU	0	0	0	0	0	0	0	1280

Tchoupitoulas, Girard Point and Sapporo rat viruses are unregistered.

HTN = Hantaan virus (76-118)

LEE = Human isolate from Korea

UR = Seoul virus

TCH = Tchoupitoulas

GP = Girard Point

SR-11 = Sapporo rat

PH = Prospect Hill

PUU = Puumala

Section VI - Biologic Characteristics

Virus Source (all VERTEBRATE isolates)
Blood (LV) lungs (LV), kidneys (LV), parotid glands (LV), saliva (LV), urine and feces (LV)(1) Pancreas (23)

Lab Methods of Virus Recovery (ALL ISOLATIONS)
Vero E6 cells, laboratory rats, and Apodemus agrarius by intramuscular inoculation (weanling or adult)

Cell system (a)	Virus passage history (b)	Evidence of Infection							
		CPE			PLAQUES			Growth Without CPE	
		Day (c)	Extent (d)	Titer TCD50/ml (e)	Day (c)	Size (f)	Titer PFU/ml (e)	+/- (g)	
E6 cells(CL)	Vero P2	7-10	0	8.3 [a,b]	7	1 mm	6.3 [b]	+ (5)	
A549 cells (CL)		7-10	0	5.0	9	1 mm	4.2	+ (11)	

[a] Fluorescent foci-forming infectious doses 50

[b] Expressed in dex

Section VII - Natural Host Range (Additional text can be added below table)

Vertebrate (species and organ) and arthropod	No. isolations/No. tested	No. with antibody/No. tested Test used	Country and region
Rattus norvegicus (lungs)	37/477	63/477 IFA	Seoul and 4 nearby cities, Korea
Rattus rattus (lungs)	2/47	5/47 IFA	
Rattus norvegicus (lungs)	2/208	64/208 IFA	Tokyo bay area, Japan
Rattus norvegicus	1		New Orleans, Louisiana USA (23)
Rattus norvegicus	1		Philadelphia, Pennsylvania, USA(28)
Rattus norvegicus	1		Houston, Texas USA(28)
Sprague-Dawley rats (lungs)	2/501	208/501 IFA	Seoul, Korea
Wistar rats (lungs)	1/480	165/480 IFA	
Wild rats		112/1,262 IFA	Various states USA(23)
Man (blood)	Not tested	293/356 * IFA	Seoul, Korea; 1980-84
Man (blood)	Not tested	19/20 IFA	Osaka, Japan

Other isolations: laboratory rat, 1 Japan (25); laboratory rat tumor, 1 Japan (26); Rattus nitidus 1 China (27); Bandicota indica, 1 Thailand (24). Other Rattus spp. isolates have been obtained in Brazil, Thailand and the United States. It has not been established that the bandicoot rat isolate is identical to other rat isolates or to Hantaan virus.

4/1,788 humans had IFA, ELISA and NT antibodies; neutralizing antibody titrations indicated that infections were caused by a rat-associated virus(30).

* Clinically severe and moderate hospitalized cases in Seoul City where only urban rats were found. The patients have never been in rural endemic areas of HFRS for two months prior to illness. Inapparent infection rates, as indicated by significant levels of IF antibody, are 1% among urban residents of Seoul and 10% among urban residents of Incheon. Many cases of HFRS occurred among urban residents of Osaka and several outbreaks of HFRS occurred in animal rooms of medical centers in Japan (12-17).

4/1,788 humans had IFA, ELISA and NT antibodies; neutralizing antibody titrations indicated that infections were caused by a rat-associated virus(29).

Section VIII - Susceptibility to Experimental Infection (include viremia)

Experimental host and age	Passage history and strain	Inoculation Route-Dose	Evidence of infection	AST (days)	Titer log10/ml
Mice (nb)	80-39; E6 P-4	ic 0.01	Develop viremia, antibodies, die	14	6.3
Mice (nb)		ip 0.1	Develop viremia and antibodies		
Mice (nb)		sc 0.1	Develop viremia and antibodies		
Mice (wn)		ic 0.03	Develop viremia and antibodies		
Mice (wn)		ip 0.3	Develop viremia and antibodies		
Balb C mice (nb)		ic 0.01	Develop viremia, antibodies; die	12	6.8
Balb C mice (nb)		ip 0.1	Develop viremia and antibodies		
Balb C mice (wn)		ic 0.03	Develop viremia and antibodies		
Wistar rat (nb)	Wistar rat P-3 Strain 80-39	ic 0.02	Develop viremia, antibodies, die	21	3.0
Wistar rat (wn)		ic 0.03	Develop viremia and antibodies		
Wistar rat (wn)		ip 0.5	Develop viremia and antibodies		
Apodemus agrarius (wn)		ic 0.01	Develop viremia and antibodies		
Apodemus agrarius (wn)		im 0.3	Develop viremia and antibodies		
Rattus norvegicus (wn)		ic 0.03	Develop viremia and antibodies		
Rattus norvegicus (wn)		im 0.5	Develop viremia and antibodies		
Rattus norvegicus (wn)		ic 0.03	Develop viremia and antibodies		
Rattus norvegicus (wn)		im 0.5	Develop viremia and antibodies		
Wistar female Rattus norvegicus			12-16 wks. old, infected by inhalation (29).		

NOTE: Except for nb rodents inoculated ic, all other test rodents do not display an apparent illness.

Section IX - Experimental Arthropod Infection and Transmission

Arthropod species & virus source(a)	Method of Infection log10/ml (b)		Incubation period (c)		Transmision by bite (d)		Assay of arthropod, log10/ml (e)		
	Feeding	Injected	Days	°C	Host	Ratio	Whole	Organ	System

Section X - Histopathology

Character of lesions (specify host)
Hemorrhagic lesions found in the pituitary, right atrium and the kidney. Intense capillary congestion and small areas of necrosis in viscera (M). Hemorrhagic lesions in viscera and encephalitis in nb mice and rats by inoculation of the virus ic (LV).

Inclusion Bodies — Intranuclear

Organs/Tissues Affected
Heart: hemorrhage in the right atrium;kidney: severe congestion of medulla;pituitary gland: congestion and necrosis in anterior lobe.Lung: edema (M). Brain: encephalitis; viscera: hemorrhagic lesions in nb mice and rats (LV).

Category of tropism
Kidney and parotid glands (M); lung, kidney and parotid glands(LV)

Section XI - Human Disease

In Nature	Residual	Death
Significant	**Significant**	**Significant**

Subclinical	Overt Disease
Significant	**Significant**

Clinical Manifestations
fever, headache, vertigo, pharyngeal injection, nausea, rash, backache, proteinuria, hyposthenuria, polyuria, hematuria, atypical lymphocytes, oliguria, azotemia, constipation, hypotension, leukocytosis (>10,000/mm3), thrombocytopenia (<100,000/mm3)

Number of Cases	Category (i.e. febrile illness, etc.)
70-100 cases/year in Seoul; 126 cases in Osaka.	**Hemorrhagic fever with renal syndrome**

Section XII - Geographic Distribution

Known (Virus detected)
Korea, Japan, China, Thailand, Brazil, and USA. Similar illness exist in China, USSR, Eastern and Norther Europe (18-21).

Suspected (Antibody only detected)
Hong Kong; Philippines; Malaysia; Singapore; Australia; Fiji; Hawaii, USA.; Belgium; Greece; Egypt; Sudan and Uganda (some data are not published)

Section XIII - References

1. LEE, H.W., et al. 1982. J. Inf. Dis. 146:638-644.
2. SCHMALJOHN, C.S., et al. 1983. Virol. 131:482-491.
3. SCHMALJOHN, C.S., et al. 1983. J. Inf. Dis. 148:1005-1012.
4. WHITE, J.D., et al. 1982. Lancet 1:768-771.
5. MCCORMICK, J.B., et al. 1982. Lancet 1:765-768.
6. TSAI, T.F., et al. 1984. J. Inf. Dis. 150:895-898.
7. LEE, H.W., et al. 1978. J. Inf. Dis. 137:298-308.
8. LEE, H.W., et al. 1979. Lancet 1:100.
9. UMENAI, T., et al. 1979. Lancet 1:1314-1316.
10. LEE, H.W., et al. 1979. Biken J. 22:41-45.
11. FRENCH, G.R., et al. 1981. Science 211:1046-1048.
12. LEE, H.W., et al. 1980. Korean J. Virol. 10:1-6.
13. LEE, H.W. 1982. In: Prog. Med. Virol., Vol. 28. J.L. McInick, ed. S. Karger AG, Basel. 1982. pp. 96-113.
14. LEE, H.W., et al. 1982. J. Inf. Dis. 146:645-651.
15. TAMURA, M., et al. 1964. Biken J. 7:79-94.
16. SUGIYAMA, K., et al. 1984. J. Inf. Dis. 149:472.
17. TAKEUCHI, T.H., et al. 1982. Jap. J. Inf. Dis. 56:466.
18. LEE, P.W., et al. 1980. Lancet 1:1025-1026.
19. GAJDUSEK, D.C. 1962. J. Pediatrics 60:841-857.
20. GAON, J., et al. 1968. Folia Medica Faculatatis Medicinae Universitatis Saraeviensis 3:23-41.
21. MYHRMAN, G., et al. 1951. Acta Med. Scand. 140:52-56.
22. SCHMALJOHN, C.S., et al. 1985. Science 227:1041-1044.
23. TSAI, T.F., et al. 1985. J. Inf. Dis. In press.
24. LEDUC, J.W. Personal communication. 1984.
25. KITAMURA, T., et al. 1983. Japan J. Med. Sci. Biol. 36:17-25.
26. YAMANISHI, K., et al. 1984. J. Virol. 52:231-237.
27. ZHU, Z.Y., et al. 1984. Acta Microbiol. Sinica. 24:92-95.
28. LEDUC, J.W., et al. 1984. Am. J. Trop. Med. Hyg. 33:992-998.
29. NUZUM, E.O., et al. 1988. Am. J. Trop. Med. Hyg. 38:636-640.
30. CHILDS, J.E., et al. 1988. Am. J. Epidemiol. 127:875-878.

Remarks

Synonyms of human disease: Korean Hemorrhagic Fever, Epidemic Hemorrhagic Fever, Songo Fever, Hemorrhagic Nephroso-Nephritis, and Nephropathia Epidemica, serologically related and clinically similar diseases, are referred to as Hemorrhagic Fever with Renal Syndrome.