

Virus Name: Dengue 3		Abbreviation: DENV
Status Arbovirus	Select Agent No	SALS Level 2
SALS Basis Results of SALS surveys and information from the Catalogue.		
Other Information DOC Permit Required		
Antigenic Group B		

SECTION I - Full Virus Name and Prototype Number

Prototype Strain Number / Designation H-87 (1,2)	Accession Number	Original Date Submitted 1/27/1985
Family Flaviviridae	Genus Flavivirus	
Information From W.McD. Hammon	Address Graduate School of Public Health, Univ. of Pittsburgh, Pittsburgh, PA 15213	
Information Footnote Reviewed by editor		

Section II - Original Source

Isolated By (name) W.McD. Hammon; reviewed by ed.	Isolated at Institute Graduate School of Public Health, Univ. of Pittsburgh, Pittsburgh, PA 15213	
Host Genus Man	Species	Host Age/Stage 5 years
Sex Female		
<u>Isolated From</u>	<u>Isolation Details</u>	
Serum/Plasma		
Signs and Symptoms of Illness Fever (39.3C), chills, twitching, headache, abdominal pain, delirious*	Arthropod	
Time Held Alive before Inoculation		
Collection Method Venipuncture	Collection Date 8/21/1956	
Place Collected (Minimum of City, State, Country) Maternity and Children's Hospital		
Latitude 14° 35' N	Longitude 121° E	
Macrohabitat Tonda, Manila, Philippines	Microhabitat	Method of Storage until Inoculated Dry ice, then Revco mechanical freezer at -55dC or lower
Footnotes		

Section III - Method of Isolation

Inoculation Date
5/1/1957

Animal (Details will be in Section 6)
nb mice

Route Inoculated Intracerebral	Reisolation No
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Other Reasons
Eight similar viruses isolated from people infected in same epidemic

Homologous Antibody Formation by Source Animal
Not tested

Test(s) Used

Footnotes

Section IV - Virus Properties

Physicochemical
RNA

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)	

Stability of Infectivity (effects)

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) 1:1000	After Treatment Titer <2.0 dex	Control Titer 3.7 dex (5)

Other (formalin, radiation)
Probably similar to types 1 and 2

Virion Morphology

Shape Spherical	Dimensions 45-50 nm	
Mean nm	Range nm	
Measurement Method By electron microscopy of LLC-MK2 cells	Surface Projections/Envelope Envelope and spikes present	Nucleocapsid Dimensions, Symmetry

Morphogenesis

Site of Constituent Formation in Cell Virions in crystalline formations in cytoplasm (3,4)	Site of Virion Assembly Membranes of endoplasmic reticulum	Site of Virion Accumulation Cisternae of endoplasmic reticulum
Inclusion Bodies	Other	

Hemagglutination

Hemagglutination Yes	Antigen Source SMB ext. by sucrose-acetone	Erythrocytes (species used) Goose
pH Range 6.0-7.0	pH Optimum 6.4	
Temperature Range 24dC and 37dC	Temperature Optimum 24dC (5)	

Remarks

See DEN-1 and 2 for HA's and CF antigens fractions. * Incomplete clinical record; seen during epidemic of hemorrhagic fever.

Serologic Methods Recommended

PRNT, CF, HI, immunodiffusion

Footnotes

See DEN-1 and 2 for HA's and CF antigens fractions. * Incomplete clinical record; seen during epidemic of hemorrhagic fever.

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

See DEN-1 and 2 for general antigenic relationships with other Group B viruses and dengue viruses.

Several viruses isolated in the West Indies and Tahiti are reported as most closely related to type 3 but significant differences have been shown with some of these from the Philippine prototype H-87. Whether these are strain differences or whether new types are involved remains to be determined.

Type 3 was first isolated, together with type 4 from patients during an outbreak of what was called Philippine hemorrhagic fever ([1], [2]). Since it differed antigenically from the only two previous types recognized and was the etiological agent of a far more serious disease than classical dengue it was considered that the agent differed not only antigenically from types 1 and 2 but also in pathogenic properties. However since type 3 viruses or viruses closely related to the prototype have been found in India [9], Pakistan [10], the West Indies ([10], [11], [12]), and Tahiti, producing mild and classical dengue without serious or obvious hemorrhagic manifestations the pathogenicity and antigenic properties no longer appear related.

Section VI - Biologic Characteristics

Virus Source (all VERTEBRATE isolates)
Blood (M)

Lab Methods of Virus Recovery (ALL ISOLATIONS)
Newborn mice (blind passage); LLC-MK2 and mosquito cell cultures; inoculation of adult mosquitoes

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)	

Forms plaques in Vero (CL) and LLC-MK2 (CL)(13); RMK (PC) and PS-Y-15(CL) (14); MA-104 (CL) and MA-111 (CL)(15); forms plaques and produces CPE in PS (CL)(16); produces CPE in BHK-21 (CL)(17); multiplies and probably produces CPE in C6/36 (CL), Aedes albopictus (CL)(18) and AP-61 (CL)(19,20). Forms plaques in Aedes albopictus (21).

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
Man *	Many	Many	SE Asia(1,2), India(9), Pakistan(10), Philippine Is. (1,2), West Indies(10,11,12), Tahiti
Man			Previously, not presently: Australia, Currently: Indonesia,
Aedes aegypti	Numerous		SE Asia, Philippine Islands, India
Culex tritaeniorhynchus	1/8,686		Philippine Islands (1)

* Numerous isolations from acute phase blood, days 1-5. Principal source of mosquito infection.

Note: Aedes niveus and Anopheles (Cel) balabacensis introlatus most likely jungle canopy vectors for dengue in Gunong Begout Forest, Malaysia (25).

Experimental host and age	Passage history and strain	Inoculation Route-Dose	Evidence of infection	AST (days)	Titer log ₁₀ /ml
Mice (nb)	P >21	ic 0.01	Death	4-6	5.0-6.0
Mice (nb)		ip 0.03	Occasional death		
Mice (nb)		sc			
Mice (wn)	P >21	ic 0.03	Death	6-8	5.0
Mice (wn)		ip 0.1	None		
hamster (nb)		ic	Death		
hamster (nb) (3-4 wk)		ic	Occasional illness or death		
hamster (nb) (3-4 wk)		ip	None		
rabbit (yg)	P >21	ic	None		
guinea pig (yg)		ic	None		
chick embryo		various	None		
monkey (yg)		P 4	ic		
monkey (yg)	P >21	sc,intracut.	None		

Section IX - Experimental Arthropod Infection and Transmission

Arthropod species & virus source(a)	Method of Infection log10/ml (b)		Incubation period (c)		Transmission by bite (d)		Assay of arthropod, log10/ml (e)		
	Feeding	Injected	Days	°C	Host	Ratio	Whole	Organ	System
<p><i>Aedes aegypti</i>; experimental transmission to suckling mice by mosquitoes fed on brain-virus suspension after extrinsic incubation period (6). Cannot be passed in <i>Blattella germanica</i>, <i>Cimex lectularis</i>, <i>Attegenus Piceus</i>, <i>Plodia interpuctella</i>, <i>Culex tritaeniorhynchus</i>, <i>Ornithodoros savignyi</i> (7).</p>									

Section X - Histopathology

Character of lesions (specify host)

In man: (See DEN-1). sm: localized, circumscribed areas of neuronolysis in the cerebral cortex. Prominent vascular alterations-marked endothelial cell swelling and proliferation, slight perivascular cuffing and edema in cerebrum (8)

Inclusion Bodies

Intranuclear

Organs/Tissues Affected

Brain (LV), spinal cord (LV); no significant alterations recognized in viscera of inoculated suckling mice (8)

Category of tropism

Neurotropic in mice

Section XI - Human Disease

In Nature
Significant

Residual

Death
Significant

Subclinical
Reported

Overt Disease
Reported

Clinical Manifestations

Fever, headache, prostration, stiff neck, myalgia, arthralgia, CNS signs (including encephalitis), hemorrhagic signs, respiratory involvement, leukopenia, CNS pleocytosis, rash, lymphadenopathy, jaundice, vomiting, melena, hematemesis, hemoptysis, etc.

Number of Cases

Probably millions but type specificity seldom dete

Category (i.e. febrile illness, etc.)

Febrile illness with rash; hemorrhagic fever

Section XII - Geographic Distribution

Known (Virus detected)

SE Asia, incl. Philippine Is., Sri-Lanka; Pakistan, India, Bengladesh, Rep. of China, Tahiti, Colombia, Jamaica, Puerto Rico, Hispaniola Indonesia, New Guinea and previously in Australia

Suspected (Antibody only detected)

Section XIII - References

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Remarks

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