

Status: Arbovirus

SALS Level: 2

Antigenic Group: B

Taxonomic status: *Flavivirus*

Other Information: None.

Select Agent:

SALS Basis: S

HEPA Filtration:

Section I - Full Virus Name and Prototype Number**Full Virus Name:****Prototype Number:**

Langat

TP-21

Information from: C.E. Gordon Smith**Date:**

6/1/1984

Address: London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C.1

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Section II - Original Source**Isolated by:** C.E. Gordon Smith (1) **at:** Kuala Lumpur, Malaysia**Genus and species:** *Ixodes granulatus* Supino **Sentinel X****Age/Stage:** Adult **Sex:** F

| Isolated From | Isolation detail |
|---------------|------------------|
|---------------|------------------|

Signs and symptoms of illness: Nil**Arthropod engorged depleted gravid****Time held alive before inoculation:****Collection date:** 4/17/1956 **Method:** From trapped ground rats***Place collected:** Ulu Langat Forest Reserve, Malaysia**Latitude:** 3° 0' " N **Longitude:** 101° 50' " E**Macrohabitat:** Forest**Microhabitat:** Forest floor**Method of storage until inoculated:** Live ticks**Footnotes:****Section III - Method of Isolation and Validity****Inoculation Date:** 4/18/1956**Animal:** nb mice **Embryonated egg:** **Tissue Culture:**

(Details in Section VI - Biologic Char.)

Route inoculated: Intracerebral**Reisolation:** Yes**Other reasons:** No virus of Russian spring-summer group had ever been used in the laboratory.**Homologous antibody formation by source animal (See Section II):****Test used:** HI CF NT**Other:****Footnotes:**

Section IV - Virus Properties

Physicochemical:

| | | | |
|----------------------------------|--------------|--|----------------|
| RNA: | DNA: | Single Strand: | Double Strand: |
| Pieces: | Infectivity: | Sedimentation coefficient(s): /strong> | |
| Percentage wt. of virion protein | | , lipid | carbohydrate |
| Virion polypeptides: | | | |
| Number: | Details: | | |
| Non-virion polypeptides: | | | |
| Number: | Details: | | |
| Virion density: | | Sedimentation coefficient: | |
| Nucleocapsid density | | Sedimentation coefficient: | |

Stability of infectivity (effects) pH

| | | |
|------------------------------|---|------------------------|
| Lipid solvent: | | |
| (ether) 1:2 | After treatment titer 5.5 dex | Control titer 8.0 dex |
| (chloroform) | After treatment titer | Control titer |
| Detergent: | | |
| (deoxycholate) 0.1% | After treatment titer <5.0 dex | Control titer 8.0 dex |
| Other (formalin, radiation): | Trypsin 0.05% After treatment: <2.7 dex | Control titer: 8.0 dex |

Virion morphology:

| | | |
|-----------------------------------|---------------------|--|
| Shape | Spherical particles | Dimensions About 33 nm; 35-42 nm |
| Mean (nm) | range (nm) | how measured Electron microscopy (negative stain; sections(8)) |
| Surface projections, envelope | | |
| Nucleocapsid dimensions, symmetry | | |

Morphogenesis:

Site of constituent formation in cell
Site of virion assembly
Inclusion bodies
Other

Hemagglutination:

| | | | |
|-------------------------------|---|--|--------------------|
| Hemagglutination | Yes | Antigen source SMB ext. by sucrose-acetone | |
| Erthrocytes | Goose | pH range 5.9-7.0 | pH optimum 6.5-6.7 |
| Temperature optimum | 4dC | range 4dC-37dC | |
| Remarks | Also used centrifugation, protamine precipitation and calcium phosphate chromatography to purify HA (2,3) * Rattus mulleri validus, R.sabanus vociferans. | | |
| Serologic methods recommended | HI, CF, NT, agar gel precipitation (7) | | |
| Footnotes: | Also used centrifugation, protamine precipitation and calcium phosphate chromatography to purify HA (2,3) * Rattus mulleri validus, R.sabanus vociferans. | | |

Section V - Antigenic Relationship And Lack of Relationship To Other Viruses

Langat falls into Group B and as far as is known is not related to any viruses not in this group. It is more closely related to the tick-borne viruses than others in Group B.

| Immune Seras | Langat Antigen | | | Antigens | Langat Antiserum | |
|-----------------------|----------------|---------|-------------|--------------|------------------|---------|
| | HI Ht/Ho | Index | NT Ht/Ho | | HI Ht/Ho | Index |
| JE | 40/320 | 0.125 | 0/3.4 | JE | 20/320 | 0.0625 |
| Dengue 1 | 20/320 | 0.0625 | 0.5/2.4 | Dengue 1 | <20/320 | <0.0625 |
| Dengue 2 | 20/320 | 0.0625 | | Dengue 2 | 40/320 | 0.125 |
| Yellow fever | <20/320 | <0.0625 | | Yellow fever | 20/320 | 0.125 |
| Russian spring summer | | | 2.9/3.8 | | | |

For information on relationship to other tick-borne viruses consult References [7] and [19].

Section VI - Biologic Characteristics

Virus source (all VERTEBRATE isolates): Blood (LV), spleen (LV)

Lab Methods of Virus Recovery (ALL ISOLATIONS): Newborn mice

Susceptibility of Cell Culture Systems:

| 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) |
| Chick embryo(PC) | P-8 | 2-4 | | Viral multiplication; peak titers = 6.4-8.4** | | Plaques | | + (5,6) |
| Vero (CL) | P-4 | | | | 9 | 1 mm | 8.2** (14) | |
| LLC-MK2 (CL) | | | | | 4 | 3-4 mm | 9.4 (14) | |
| Rana temporaria tadpoles (PC) | P-10 TP64 | | | | | | | + (17) |
| Rhipicephalus appendiculatus(CL) (RA-243) | | | | | | | | + (18) |

** Expressed in dex

Section VII - Natural Host Range

| Vertebrate (species and organ) and arthropod | No. isolations/No. tested | No. with antibody/No. tested Test used | Country and region |
|--|---------------------------|---|---|
| Ixodes granulatus | 7/15 pools | | Ulu Langat, Malaysia |
| Ixodes granulatus | 0/16 pools | | Elsewhere, Malaysia |
| Haemaphysalis papuana | 1 | | Central Thailand (15) |
| Ixodes persulcatus | 7 | | Krasnoyarsk region, Central Siberia, USSR(20) |
| | | HI NT | |
| Rattus bowersi | | 2/6 | Ulu Langat Forest |
| R. sabanus | | 0/16 2/10 | Reserve, Malaysia |
| R. mulleri | | 3/14 3/7 | |
| R. rajah | | 2/22 2/15 | |
| R. jalorensis | | 0/4 0/1 | |
| R. argentiventer | | 0/15 | Elsewhere, Malaysia |
| R. bowersi | | 0/5 | |
| R. mulleri | | 1/17 0/4 | |
| R. sabanus | | 0/47 | |
| R. rajah | | 0/8 0/6 | |
| R. jalorensis | | 0/44 0/5 | |
| R. annandeli | | 1/27 1/27 | |
| R. whiteheadi | | 0/6 | |
| R.r. diardi | | 0/2 | |

Section VIII - Susceptibility To Experimental Infection (Record Viremia)

| Experimental host and age | Passage history and strain | Inoculation Route-Dose | Evidence of infection | AST (days) | Titer log10/ml |
|---------------------------|----------------------------|------------------------|--------------------------|------------|----------------|
| Mice (nb) | P-2 | ic 0.01 | Paralysis, death | 4 | |
| Mice (nb) | | ip 0.05 | Paralysis, death | 4-5 | |
| Mice (nb) | | sc | | | |
| Mice (wn) | P-5 | ic 0.03 | Paralysis, death | 5 | 9.3 |
| Mice (wn) | | ip 0.1 | Paralysis, death | 14 | 9.0 |
| albino rats (nb) | P-7 | ip 0.05 | Paralysis, death | 9-10 | |
| rhesus monkey (ad) | | ic | Fever, viremia, antibody | | |
| cynomologus monkey (ad) | | sc | Viremia, antibody | | |
| cynomologus monkey (ad) | | oral | Viremia, antibody | | |
| spider monkeys | | feeding | Viremia, antibody | | |
| man (ad) | | sc | Fever, viremia, antibody | | |
| chick (1 day) | | sc | Viremia, antibody | | |

Adult rats sc; R. bowersi sc; guinea pig ip, ic; rabbits ip, ic; sheep, ic, sc; and Microtus agreritis given 7-9th passage all exhibited antibody formation only.

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 |
| Dermocentor marginatus larvae; MB-7, TP64 | X | | | | | | Virus multiplication; transtadial transmission. (Up to 6.3/0.03 in nymphs)(16). | | |
| Ixodes ricinus | Virus fed to larvae; virus multiplication, transmission by bite. | | | | | | | | |
| Haemaphysalis spinigera | Virus fed to larvae; trans-stadial transmission (4) | | | | | | | | |

Section X - Histopathology

Character of lesions: Mice: Perivascular cuffing and neuronal damage in cerebrum and anterior horns of thoracic and cervical cord. Man (experimental): Encephalitis in 2/27. Sheep, monkeys: Nil.

Inclusion bodies:

Cytoplasmic:(M) (LV)

Intranuclear: (M)

(LV)

Organs-tissues affected: Brain (LV), spinal cord (LV),

Category of tropism: Neurotropic

Section XI - Human Disease

| | | | |
|------------------------|----------------|-----|-----|
| Human disease: | In nature: | (S) | (R) |
| | Death: | (S) | (R) |
| | Residual: | (S) | (R) |
| Laboratory infections: | Subclinical: | (S) | (R) |
| | Overt Disease: | (S) | (R) |

Clinical manifestations: Fever (R), leukopenia (S); based on experimental infection of patients with malignant disease (9).

Category: Encephalitis (9)

No. of cases: No natural cases known

Section XII - Geographic Distribution

Known (virus):

Malaysia; Thailand (15), Siberia, USSR (20)

Section XIII - References

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Section XIV - Remarks