Viral Encephalitis
Terminology

• Encephalopathy
  – Clinical syndrome of reduced consciousness
  – Many causes, incl. viral encephalitis

• Encephalitis
  – Acute, diffuse, inflammatory process affecting brain parenchyma
  – Most commonly viral
## Encephalopathy vs encephalitis?

<table>
<thead>
<tr>
<th></th>
<th>Encephalopathy</th>
<th>Encephalitis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical features</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fever</td>
<td>Uncommon</td>
<td>Common</td>
</tr>
<tr>
<td>Headache</td>
<td>Uncommon</td>
<td>Common</td>
</tr>
<tr>
<td>Depressed mental status</td>
<td>Steady deterioration</td>
<td>May fluctuate</td>
</tr>
<tr>
<td>Focal neurological signs</td>
<td>Uncommon</td>
<td>Common</td>
</tr>
<tr>
<td>Type of seizure</td>
<td>Generalised</td>
<td>Generalised or focal</td>
</tr>
<tr>
<td><strong>Laboratory findings</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood</td>
<td>Leucocytosis uncommon</td>
<td>Leucocytosis common</td>
</tr>
<tr>
<td>CSF</td>
<td>Pleocytosis uncommon</td>
<td>Pleocytosis common</td>
</tr>
<tr>
<td>EEG</td>
<td>Diffuse slowing</td>
<td>Diffuse slowing and focal abnormalities</td>
</tr>
<tr>
<td>MRI</td>
<td>Often normal</td>
<td>Focal abnormalities</td>
</tr>
</tbody>
</table>
Primary and Secondary Encephalitis

- There are **two ways** that viruses can infect brain cells and cause encephalitis:

  - **Primary encephalitis**, also called Acute viral encephalitis, is when the virus directly affects the brain or spinal cord. The resulting inflammation can occur in one area (focal) or can occur throughout the brain (diffuse).

  - **Secondary encephalitis**, also called post-infectious encephalitis, is when the virus first attacks another part of the body and the infection then spreads to the brain.
CNS virus pathogenesis

Exposure
  ↓
Dissemination
  ↓
CNS Entry
  ↓
Inflammation
  ↓
Clinical Disease

Pathogenic event
- Epithelial layer disruption
- Local replication
- Viremia Secondary amplification
- Blood-brain barrier disruption
- Axonal transport
- Direct and indirect cell damage
- Target cells (neurons, glial cells, endothelial cells)
Causes of acute viral encephalitis

**Geographically restricted causes**

- **Arboviruses** — Japanese B, St Louis, West Nile, Eastern equine, Western equine, Venezuelan equine, tick borne encephalitis viruses
- **Bunyaviruses** — La Crosse strain of California virus
- **Reoviruses** — Colorado tick fever virus

**Sporadic causes (not geographically restricted)**

- **Herpes viruses**
  - HSV-1, HSV-2, VZV, CMV, EBV, HHV6, HHV7
- **Enteroviruses**
  - Coxsackie, echoviruses, enteroviruses 70/71, parechovirus, poliovirus
- **Paramyxoviruses**
  - Measles, mumps
- **Others (rarer causes)**
  - Influenza viruses, Adenovirus, JC virus (PML), rabies, parvovirus, lymphocytic choriomeningitis virus, rubella virus,
Primary Cause

• Arboviruses are the most common causes of viral encephalitis
• Arbovirus stands for arthropod-borne viruses
• There are 3 virus families associated with encephalitis
  – *Togaviridae (Alphavirus)* – most common
  – *Flaviviridae (Flavavirus)*
  – *Bunyaviridae (Bunyavirus)*
Arboviruses

- Arthropod-borne viruses

- 534 registered arboviruses
  - 134 documented human pathogens

- Major vectors
Arbovirus Families

- **Flaviviruses** (single-stranded positive-sense RNA viruses)
  - *West Nile virus*
  - *St. Louis encephalitis virus*
  - *Japanese encephalitis virus*
  - Yellow fever virus
  - Dengue virus

- **Togaviruses** (single-stranded positive sense RNA viruses)
  - *Eastern, western, and Venezuelan equine encephalitis viruses*

- **Bunyaviruses** (segmented single-stranded negative sense RNA viruses)
  - *La Crosse virus*
  - Rift Valley fever virus
<table>
<thead>
<tr>
<th>Disease</th>
<th>Mosquito Vector</th>
</tr>
</thead>
<tbody>
<tr>
<td>EEE</td>
<td><em>Culiseta melanura, Aedes spp., Culex (Cx.) nigrapalpus, Coquilletidia spp.</em></td>
</tr>
<tr>
<td>WEE</td>
<td><em>Culex tarsalis, Aedes melaninon, Aedes dorsalis, Aedes campestris</em></td>
</tr>
<tr>
<td>VEE</td>
<td><em>Culex (Melanoconion) spp.</em></td>
</tr>
<tr>
<td>LAC</td>
<td><em>Ochleratatus triseriatus</em></td>
</tr>
<tr>
<td>SLE</td>
<td><em>Culex pipiens, Cx. quinquefasciatus, Cx. nigrapalpus, Cx. tarsalis</em></td>
</tr>
</tbody>
</table>
Arboviral Diseases in Humans

**Systemic febrile illness**
- West Nile virus
- Dengue virus
- Rift Valley fever virus
- Chikungunya virus

**Hemorrhagic fever**
- *Yellow fever virus*
- Dengue virus
- Rift Valley fever virus

**Encephalitis**
- West Nile virus
- Japanese encephalitis virus
- Eastern equine encephalitis virus
- La Crosse virus
Arbovirus Meningoencephalitis Pathogenesis

• **Exposure route/dissemination**
  – Replication within insect vector required
  – Primary exposure is cutaneous
  – Respiratory transmission demonstrated experimentally
  – Local replication followed by viremia

• **CNS entry**
  – Hematogenous
    • Traverse blood brain barrier (BBB) endothelium through unknown mechanism
  – Direct neuronal spread for respiratory exposure (olfactory bulb)

• **Cell damage**
  – Neurons are primary targets for many viruses
  – Direct cell death and inflammatory responses
Arbovirus Epidemiology

• Seasonal (summer/fall)

• Incidence varies with virus and time

• Extremes of age more susceptible to severe disease

• Mortality rate varied with virus
  – Eastern equine encephalitis virus (EEEV) ~50%
  – West Nile virus (WNV) ~10%
  – La Crosse virus (LACV) <1%
Arbovirus Meningoencephalitis Clinical Manifestations

• **Primary symptoms**
  – Most infections asymptomatic or produce non-specific “viral syndrome”
  – Fever, headache, seizures
  – Neuronal targets dictate clinical symptoms
    • Anterior motor neurons (WNV) – poliomyelitis
    • Basal ganglia neurons (JEV) – Parkinsonian

• **Long-term neurological sequelae possible**
Arbovirus Meningoencephalitis Diagnosis, Treatment, and Prevention

• **Diagnosis**
  – Clinical suspicion
  – Social history/exposure/travel provide important clues
  – CSF profile
    • Lymphocytic pleocytosis, high protein
  – CSF PCR, intrathecal IgM
  – Acute and convalescent serologies useful for epidemiology

• **Treatment**
  – Supportive

• **Prevention**
  – Inactivated vaccine available for JEV
  – Live attenuated YFV vaccine also available
  – Vector control efforts
Other CNS viruses

--Herpes simplex, type 1 and type 2
  – Epstein-Barr virus (EBV)
  – Cytomegalovirus (CMV)
  – Varicella zoster virus (VZV)
  – Human herpes virus 6 (HHV-6)
  – Herpes B virus (simian herpesvirus)
  – Rabies
  – Influenza A and B
  – JC virus (PML)

• Measles
• Mumps
• Rubella
• Human immunodeficiency virus (HIV)
# Herpesviridae

<table>
<thead>
<tr>
<th>Subfamily</th>
<th>Growth &amp; Cytopathology</th>
<th>Latent infections</th>
<th>Genus</th>
<th>Official name (herpes virus)</th>
<th>Common name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alphaherpesvirinae</td>
<td>Short, cytolytic</td>
<td>Neurons</td>
<td>Simplexvirus</td>
<td>1 2</td>
<td>HSV-1 HSV-2</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Varicellivirus</td>
<td>3</td>
<td>VZV</td>
</tr>
<tr>
<td>Betaherpesvirinae</td>
<td>Long, cytomegalic</td>
<td>Glands, kidneys</td>
<td>Cytomegalovirus</td>
<td>5</td>
<td>CMV</td>
</tr>
<tr>
<td></td>
<td>Long, lymphoproliferative</td>
<td>Lymphoid tissue</td>
<td>Roseolovirus</td>
<td>6 7</td>
<td>HHV-6 HHV-7</td>
</tr>
<tr>
<td>Gamaherpesvirinae</td>
<td>Long, lymphoproliferative</td>
<td>Lymphoid tissue</td>
<td>Lymphocryptovirus</td>
<td>4</td>
<td>EBV</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Rhadinovirus</td>
<td>8</td>
<td>Kaposi’ sarcoma virus</td>
</tr>
</tbody>
</table>

- **Herpesviridae**
- **Subfamily Growth & Cytopathology**: Short, cytolytic, Long, cytomegalic, Long, lymphoproliferative
- **Latent infections**: Neurons, Glands, kidneys, Lymphoid tissue
- **Genus**: Simplexvirus, Cytomegalovirus, Roseolovirus, Lymphocryptovirus, Rhadinovirus
- **Official name (herpes virus)**: HSV-1, HSV-2, CMV, HHV-6, HHV-7
- **Common name**: HSV-1, HSV-2, VZV, CMV, HHV-6, HHV-7
Herpes simplex encephalitis

- HSV encephalitis (HSE) most common cause of viral encephalitis in industrialised nations

- Annual incidence 1 in 250,000-500,000

- 90% HSV-1

- HSV-2 more common in immuno-compromised, neonates
HSV-1

• Primary infection occurs in oral mucosa
  – 30% people get clinically apparent cold sores
  – 90% healthy people have been infected with HSV-1
• Virus then travels along trigeminal nerve to ganglion in most those infected
• 70% cases of HSV-1 encephalitis already have antibody present suggesting reactivation of virus most common mechanism
• Why HSV-1 reactivates not known
• In children, HSV-1 encephalitis occurs during primary infection
HSV-2

• Transmitted via genital mucosa
  – Genital herpes in adults
  – USA, 20% of adults sero-positive for HSV-2

• HSV-2 may cause
  – Meningitis (esp. recurrent meningitis)
  – Encephalitis (esp in neonates)

• Neonates can be infected during delivery: neonatal herpes (disseminated infection often with CNS involvement)
HSV Encephalitis Pathogenesis

• Exposure route/dissemination
  – Primary exposure (cutaneous)
  – Reactivation from latency (sensory ganglion)

• CNS entry
  – Direct neuronal spread

• Cell damage
  – Direct cell lysis and inflammatory responses
HSV Encephalitis Clinical Manifestations

• **Primary symptoms**
  – Fever, headache
  – Progressive neurological symptoms
  – Focal symptoms represent region of brain involvement (temporal lobe common)
  – Mental status changes frequent
  – Seizures

• **Meningitis and myelitis also seen**
  – Primary genital HSV
  – Recurrences possible (Mollaret’s meningitis)

• **Long-term neurological sequelae possible**
  – Especially without prompt therapy
HSV Encephalitis Diagnosis, Treatment, and Prevention

• **Diagnosis**
  – Clinical suspicion
  – **CSF profile:**
    • Lymphocytic pleocytosis, increased RBCs common, high protein
  • WBC: 20-300 cells/mm³
  • Protein: median 80 (normal<60)
  • Glucose usually normal
    – **CSF PCR is gold-standard diagnostic test**
    – MRI and EEG also helpful but not specific

• **Treatment**
  – Acyclovir

• **Prevention**
  – No vaccine available
Varicella Encephalitis - 1

- **Incidence**
  - 1-2/10,000 cases of varicella
  - Incidence is highest in adults and infants

- **Presentation**
  - Symptoms usually appear about one week after rash (though may be earlier or later).
  - Acute or gradual onset.
  - Fever, headache, vomiting, altered mental status
  - Focal neurologic findings, hyper/hyporeflexia, hemiparesis, and sensory changes
  - Seizures 29-52% of cases
Varicella Encephalitis - 2

• Pathogenesis
  – Role of active viral replication in CNS?
  – Pathologic findings are more consistent with a post-infectious demyelinating process. Inclusion bodies are rarely seen.

• Prognosis
  – Mortality of about 5-10% (higher mortality in older literature probably due to Reye’s syndrome)
  – 10-20% of survivors will have neurologic sequelae

• Therapy
  – IV acyclovir recommended
Varicella in the Immunocompetent Host

• Serious neurologic complications occur in <1% of cases:
  – Aseptic meningitis
  – Cerebellar ataxia
  – Transverse myelitis
  – Encephalitis
  – Guillain-Barré syndrome
  – Arterial ischemic strokes
  – Optic neuritis
Diagnosis of VZV Encephalitis

• Both PCR on CSF and antibody testing for VZV IgG and IgM (EIA) on both serum and CSF

• Diagnosis of VZV infection of the CNS is supported by detection of VZV antibody in the CSF, even in the absence of PCR-amplifiable VZV DNA. Therefore, Clinicians should request both PCR and antibody analysis
Human herpesvirus 6 encephalitis

• Human herpesvirus (HHV) 6, the etiologic agent of roseola, is nearly universally acquired during childhood.

• The virus establishes lifelong infection, including within the central nervous system (CNS), and replicates within several CNS cell types.

• HHV-6 encephalitis is a significant consequence of transplant immunosuppression, although it is seen in immunocompetent patients as well.
Saliva Sample

Methods:

Collection

Swabs in 500ul VTM
Refrigerated up to 21 days

Centrifugation
Re-suspend in 200ul PBS

DNA Extractions
-Qiagen-200ul

Qualitative PCR
HHV-6 and 7differentation
U38 primers

Viral Quantification (if +)
-Light Cycler-
U38 Primers and Probes

Acute & Convalescent Saliva Samples

ELISA
(IgM, IgG, IgA)

IgG Avidity
Blood Sample
Methods:

Collection Processing within 24 hrs.

Ficoll-Paque Separation

Whole Blood
- RNA Extractions
  - Qiagen
  - 10,000,000 cells
- RT-PCR
  - Light Cycler
  - U38 Primers and Probes

Lymphocytes
- DNA Extraction
  - Qiagen
  - 1,000,000 cells or 200ul
- Qualitative PCR
  - U38 Primers
- Viral Quantification (if+)
  - Light Cycler
  - U38 Primers and Probes

Plasma
- ELISA
  - (IgM, IgG)
  - 10ul
- IgG Avidity
Adenoviruses

- First isolated in 1953 in a human adenoid cell culture.
- Approximately 100 serotypes have been recognized, at least 47 of which infect humans.
- Have been classified into seven subgroups (A through G).
<table>
<thead>
<tr>
<th>Species</th>
<th>Hemagglutination Groups</th>
<th>Types</th>
<th>Tumors in animals</th>
<th>Transformation in cell culture</th>
<th>% GC</th>
<th>Associated disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAdV-A</td>
<td>IV (little or none)</td>
<td>12, 18, 31</td>
<td>High</td>
<td>Positive</td>
<td>46–47</td>
<td>Cryptic enteric infection</td>
</tr>
<tr>
<td>HAdV-B</td>
<td>I (complete for monkey erythrocytes)</td>
<td>3, 7, 11, 14, 16, 21, 34, 35, 50</td>
<td>Moderate</td>
<td>Positive</td>
<td>49–51</td>
<td>Conjunctivitis, Acute respiratory disease, Hemorrhagic cystitis, Central nervous system</td>
</tr>
<tr>
<td>HAdV-C</td>
<td>II (partial for rat erythrocytes)</td>
<td>1, 2, 5, 6</td>
<td>Low or none</td>
<td>Positive</td>
<td>55</td>
<td>Endemic infection, Respiratory symptoms</td>
</tr>
<tr>
<td>HAdV-D</td>
<td>III (complete for rat erythrocytes)</td>
<td>8, 9, 10, 13, 15, 17, 19, 20, 22–30, 32, 33, 36–39, 42–49, 51, 53, 54</td>
<td>Low or none (mammary tumors)</td>
<td>Positive</td>
<td>55–57</td>
<td>Keratoconjunctivitis in immunocompromised and AIDS patients</td>
</tr>
<tr>
<td>HAdV-E</td>
<td>III</td>
<td>4</td>
<td>Low or none</td>
<td>Positive</td>
<td>58</td>
<td>Conjunctivitis</td>
</tr>
<tr>
<td>HAdV-F</td>
<td>III</td>
<td>40, 41</td>
<td>Unknown</td>
<td>Negative</td>
<td>51</td>
<td>Infantile diarrhea</td>
</tr>
<tr>
<td>HAdV-G</td>
<td>Unknown</td>
<td>52</td>
<td>Unknown</td>
<td>Unknown</td>
<td>55</td>
<td>Gastroenteritis</td>
</tr>
</tbody>
</table>

Clinical Syndromes

1. Pharyngitis 1, 2, 3, 5, 7
2. Pharyngoconjunctival fever 3, 7
3. Acute respiratory disease of recruits 4, 7, 14, 21
4. Pneumonia 1, 2, 3, 7
5. Follicular conjunctivitis 3, 4, 11
6. Epidemic keratoconjunctivitis 8, 19, 37
7. Pertussis-like syndrome 5
8. Acute haemorrhagic cystitis 11, 21
9. Acute infantile gastroenteritis 40, 41
10. Intussusception 1, 2, 5
• 11. Severe disease in AIDS and other immunocompromized patients 5, 34, 35
• 12. Meningitis 3, 7
Adenovirus Virus Meningoencephalitis

Adenovirus is a common pathogen in the pediatric population.

Several neurologic syndromes have been attributed to adenovirus, such as adenovirus: aseptic meningitis, myelitis, subacute focal encephalitis, and Reye-like syndrome.

It is rare to isolate any of the adenoviruses from either the cerebrospinal fluid (CSF) or the brain.

In immunosuppress and transplantation

Several reports, however, have directly demonstrated adenoviruses in CSF (Ad3, 5, 6, 7, 7A, and 12).
Laboratory Diagnosis

- Should be obtained from a site or secretion relevant to the disease symptoms.

- Fluorescent antibody assays and the polymerase chain reaction can be used to detect, type, and group the virus.

- Serologic testing is rarely used except for epidemiologic purposes.
Rhabdoviridae

**Classification**

Four genera: *Lyssavirus*, *Vesiculovirus*, *Ephemerovirus*, and *Novirhabdovirus*

**Genus: Lyssavirus** – 6 serotypes
- Rabies virus - distributed worldwide
- Mokola virus – Central Africa
- Lagos bat virus – Central and southern Africa
- Duvenhage virus – South Africa
- European bat lyssavirus 1 and 2 – Europe
- Australian bat lyssavirus – Australia
Rabies Virus Encephalitis Pathogenesis

- Rabies virus multiplies in muscle or connective tissue at the site of inoculation

- Rabies enters peripheral nerves through sensory and motor nerve endings – primarily through neurotransmitter acetylcholine as receptor. Also uses gangliosides and phospholipids.

- Virus enters the brain through the limbic system

- Multiplies in CNS and progressive encephalitis develops
- The virus then spreads through peripheral nerves to the salivary glands and other tissues

- Susceptibility to infection and incubation period may depend on the host’s age, genetic, immune status, viral strain, amount of inoculation, the severity of laceration
Rabies Virus Encephalitis Clinical Manifestations

• **Epidemiology**
  – Disease recognized for thousands of years (2300 B.C.)
  – Only handful of cases in U.S. per year
  – More common in underdeveloped countries
  – Only 10-20% of “true” exposures will result in disease

• **Reservoir (U.S.)**
  – Bats, skunks, raccoons, and foxes
  – Rodents, lagomorphs, and domestic dogs/cats almost never infected

• **Primary symptoms**
  – Fever, dysphagia, hydrophobia, increased muscle tone
  – Progression to coma and death
Rabies Virus Encephalitis Clinical Manifestations

- Rabies is an **acute, fulminant, fatal encephalitis**, incubation period 1-2 months
- **Short prodromal phase**: 2-10 days, malaise, anorexia, headache, **photophobia**, nausea and ting, sore throat and fever
- **Acute neurologic phase**: 2-7 days, nervousness, apprehension, hallucinations and bizarre behavior; lacrimation, pupillary dilation, salivation, perspiration, **hydrophobia**
- **Coma**: death by respiratory paralysis
Rabies Virus Encephalitis Diagnosis, Treatment, and Prevention

• **Diagnosis**
  – Clinical suspicion with exposure history
  – CSF profile (cell count, glucose, protein) often unhelpful
  – CSF/tissue RT-PCR
  – DFA of neck skin biopsies
  – Serologies can be helpful

• **Treatment**
  – None (universally fatal once symptoms develop)

• **Prevention**
  • Preexposure vaccination for all persons at high risk of contact with rabid animals
  • Postexposure prophylaxis
**Polyomaviridae**

- **Species**
  - BK polyomavirus
  - Bovine polyomavirus
  - Canary polyomavirus
  - Chimpanzee polyomavirus
  - Goose hemorrhagic polyomavirus
  - Hamster polyomavirus
  - Human Polyomavirus
  - **JC polyomavirus**
  - Merkel cell polyomavirus
  - Murine polyomavirus
  - Rabbit kidney vacuolating virus
  - Simian virus 40
FIGURE 52-8. Mechanisms of spread of polyomaviruses within the body. PML, Progressive multifocal leukoencephalopathy.
**JC virus**

- JC virus (JCV) is a polyomavirus infecting greater than 80% of the human population early in life.
- Replication of this virus in oligodendrocytes and astrocytes results in the fatal demyelinating disease **progressive multifocal leukoencephalopathy (PML)** in immunocompromised individuals, most notably acquired immunodeficiency syndrome (AIDS) patient.

JCV can cross the **blood–brain barrier** into the central nervous system, where it infects oligodendrocytes and astrocytes, possibly through the **serotonin receptor**.
Diagnosis Clinical Samples and Biopsies
JCV and PML

• viral protein was detected in biopsy tissue using antibody to the capsid protein, VP1.

• *in situ* DNA hybridization ➔ Use of biotin-labelled DNA probes helped identify in biopsy and autopsy brain tissue

• PCR for JCV DNA was then applied to CSF samples of patients with PML ➔ a high degree of correlation with biopsy results
Orthomyxoviridae

– Three types of flu virus
  • Genus *Influenzavirus* A – 8 genome segments
  • Genus *Influenzavirus* B - 8 genome segments
  • Genus *Influenzavirus* C - 7 genome segments, no NA

- *On the basis of antigenic differences between NP and M: A, B and C*

- *type A, B, C : NP, M1 protein sub-types: HA or NA protein*
INFLUENZA
Encephalopathy -Mechanisms

• Direct virus infection of ependymal cells, vascular endothelium, neurons (rarely found in CSF)

• Cytokine-mediated destruction of blood-brain barrier

• Autoantibody production
INFLUENZA
Encephalopathic Syndromes

• encephalopathy
• liver and CNS
  – Reye’s syndrome
• peripheral nervous system
  – Guillian-Barré syndrome
• Post-encephalitic Parkinson’s

• MERS: mild encephalopathy with promptly reversible splenial lesions
### Typical CSF findings in CNS infections

<table>
<thead>
<tr>
<th></th>
<th>Viral</th>
<th>Bacterial</th>
<th>TB</th>
<th>Fungal</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Opening pressure</strong></td>
<td>Normal/high</td>
<td>High</td>
<td>High</td>
<td>High/v. high</td>
<td>10-20 cm</td>
</tr>
<tr>
<td><strong>Colour</strong></td>
<td>Clear</td>
<td>Cloudy</td>
<td>Cloudy/yellow</td>
<td>Clear/cloudy</td>
<td>Clear</td>
</tr>
<tr>
<td><strong>Cells/mm³</strong></td>
<td>Sl. increase 5-1000</td>
<td>High/v. high 100-50,000</td>
<td>Sl. increase 25-500</td>
<td>Normal/high 0-1000</td>
<td>&lt; 5</td>
</tr>
<tr>
<td><strong>Differential</strong></td>
<td>Lymphocytes</td>
<td>Neutrophils</td>
<td>Lymphocytes</td>
<td>Lymphocytes</td>
<td>Lymphocytes</td>
</tr>
<tr>
<td><strong>CSF/plasma glc ratio</strong></td>
<td>Normal</td>
<td>Low</td>
<td>Low/v. low (&lt;30%)</td>
<td>Normal/low</td>
<td>66%</td>
</tr>
<tr>
<td><strong>Protein (g/l)</strong></td>
<td>Normal/high</td>
<td>High</td>
<td>High/v. high</td>
<td>Normal/high</td>
<td>&lt;0.45</td>
</tr>
</tbody>
</table>

- Normals are given in parentheses.