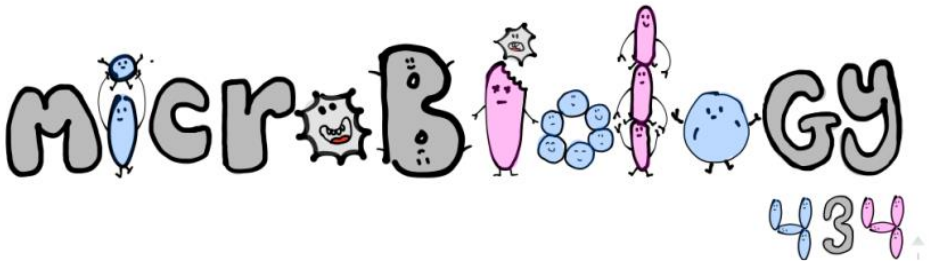
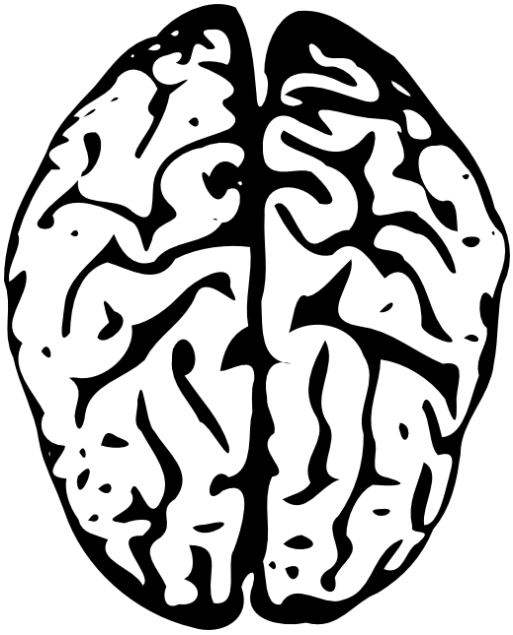
Viral CNS Infection





- **Important**
- Extra explanation

1- **Acute viral infections of the CNS.**

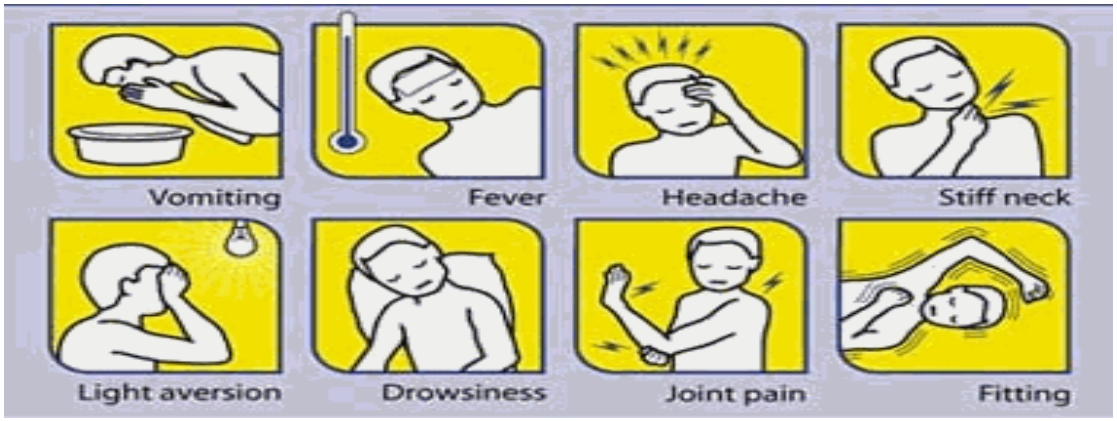
Meningitis , paralysis & encephalitis.
2- **Chronic virus neurological diseases.**
SSPE, PML, C-J disease, tropical spastic paraparesis, HIV dementia.
3- **Neurological diseases precipitated by viral infections.**
Reye's syndrome, Guillian-Barré syndrome.

Meningitis:

Caused by:

- **Infectious agents :** bacteria - Viruses - Fungi - protozoa
- **Non-infectious agents** [tumor – bleeding – abscess]

Signs and symptoms:



Viral Meningitis: Most common

- Aseptic meningitis [No gram stain]
- **Less severe**
- Resolves without specific treatment within a week or two

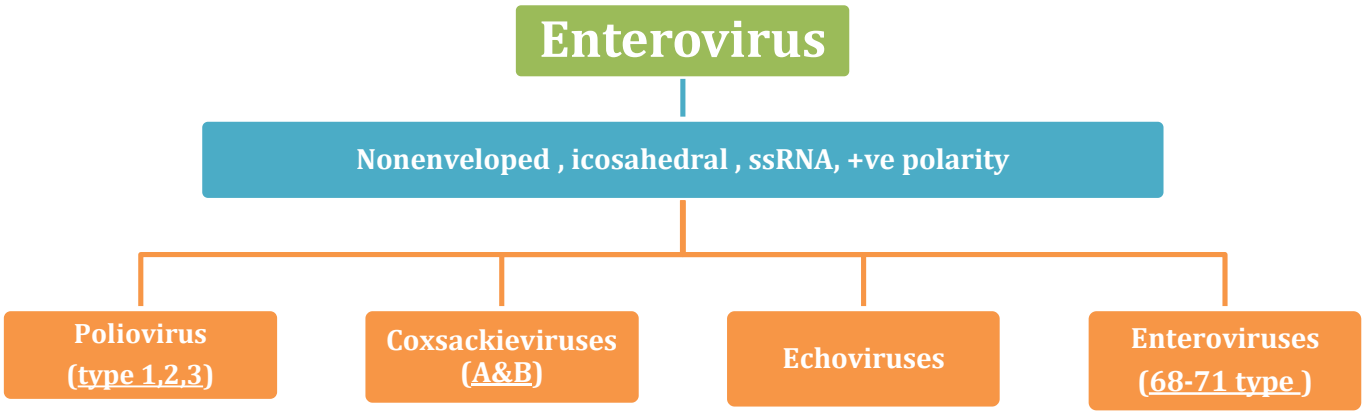
Bacterial Meningitis: Emergency

- Septic meningitis
- Quite **severe** and may result in
  a) Brain damage
  b) Hearing loss
  c) Learning disability
- It would also cause death!

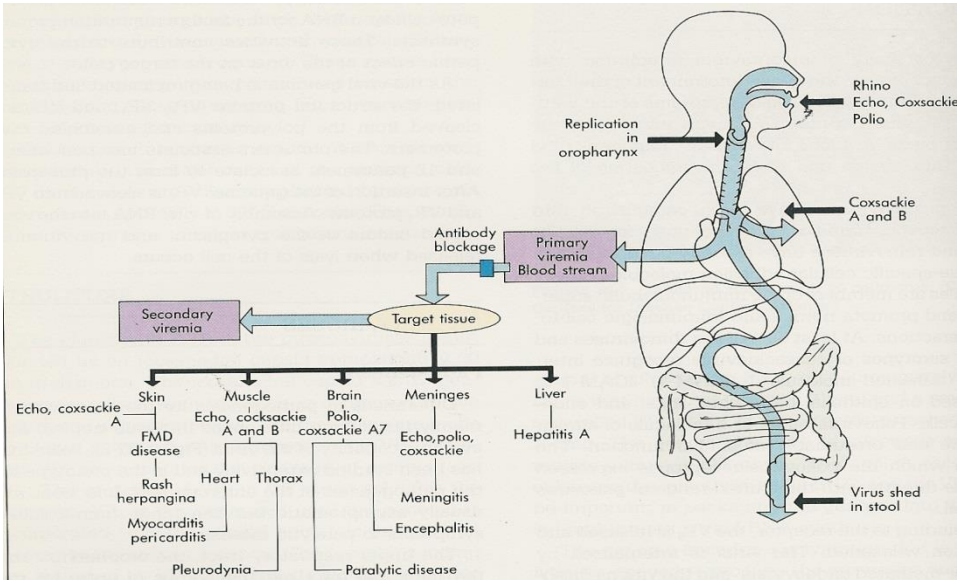
	Normal	Aseptic meningitis	Septic meningitis
Colour	Clear	Clear	Cloudy
Cells/mm³	< 5	increase 100-1000 Lymphocytes	High/v. high 200-20,000 Neutrophils
Glucose mg/dl	45-85	Normal*	Low<45
Protein mg/dl	15-45	Normal/high 50-100	High>100
Causes		Viruses* , others	Bacteria

Viral (Aseptic) meningitis:

- It caused mainly by **Enterovirus**, and other viruses such as Arbovirus ,herpes and HIV.
  enteroviruses is a large group and it contains (polioviruse, GPA Cox. , and GPB Cox. , echovirus and enteroviruses) and that they can cause aseptic meningitis, paralysis and encephalitis



Epidemiology	
Reservoir	Human
Spread	• Fecal - oral route **(mainly)** • Inhalation of infectious aerosols (Crowded, Poor hygiene & Sanitation)
Age	Children > Adults
Seasonal distribution	Summer & Fall



Pathogenesis:

Transmitted through the oral – fecal route → replication in the GIT → viremia →affect many organs → causing the clinical manifestation

[even though they replicate in the GIT they don't cause GIT disease]

Enteroviral infections:

Neurologic diseases	Non-neurologic diseases
Aseptic meningitis – Paralysis – encephalitis - seizures	Respiratory tract infections – skin &mucosa infections – cardiac infections – acute hemorrhagic conjunctivitis

Poliovirus infections:

No illness 90-95%	**Asymptomatic** but can infect others
Minor illness 4-8%	Abortive poliomyelitis (**No** CNS involvement)
Major illness 1-2%	• Nonparalytic poliomyelitis (Aseptic meningitis) • Paralytic poliomyelitis (Flaccid paralysis) asymmetrical w/ no sensory loss

Pathogenesis:

Reach CNS by:

- Blood.
- Peripheral nerves.
- **7 days** for incubation
- **5** days → systemic symptoms (non specific symptoms)
- **5** days → neural symptoms (specific symptoms)

- Causing **destruction** of motor neurons of **AHCs.**
- **Rarely** affects brain stem (**bulbar poliomyelitis**).
  Accompanied w/ respiratory depression
- Lifelong type-specific immunity = IgA & IgG.
  [Depends on which type of poliovirus]

Lab Diagnosis:

Virus isolation

- **Samples:** stool (best) -[rectal or throat] swab - CSF inoculate in cell cultures.
  [**All EVs grown except some strains of Cox A viruses**] .
- Observe for CPE. cytopathic effect
- Identify the **type**.

CSF findings

- **lymphocytosis**
- **Glucose level** : normal to slightly decreased.
- **Protein level:** normal to slightly increased.
- EV RNA detected in CSF by **RT-PCR**.

Serology

- **Limited** value

Management:

- **Treatment (Rx):** No antiviral Rx.
- **Prevention:** Sanitation & Hygienic measures - Poliovirus vaccines

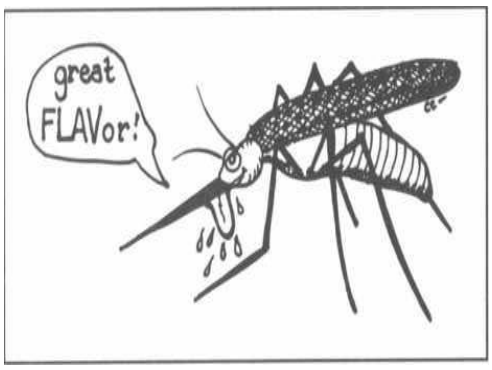
Type of vaccine	Route	advantages	disadvantages	Common in both
Inactivated polio vaccines IPV (salk, killed) For adults	Subcutaneous or IM	• **Doesn't** Revert to virulence • **Doesn't** Cause disease in the immunocompromised pt. • **Co-infection** with other EVs **Doesn't** impair immunization. • **Doesn't** require refrigeration.	• **Doesn't** induce intestinal IgA . • **Doesn't** interrupt transmission. • **Doesn't** afford 2nd protection. • **Short** duration of immunity	• 3 types (trivalent) Give protection against all 3 types of polio . • Prevent disease. • Induce humoral **IgG**
Live-atteuated polio vaccine OPV (sabin) For children	Oral	• Induces intestinal IgA. • Interrupts transmission. • **Affords** 2nd protection by spread to others. • **Long** duration of immunity.	• **May** revert to virulence (rare) • **Cause disease** in the immunocompromised pt. • **Co-infection** with other EVs may impair immunization • **Requires** refrigeration.	

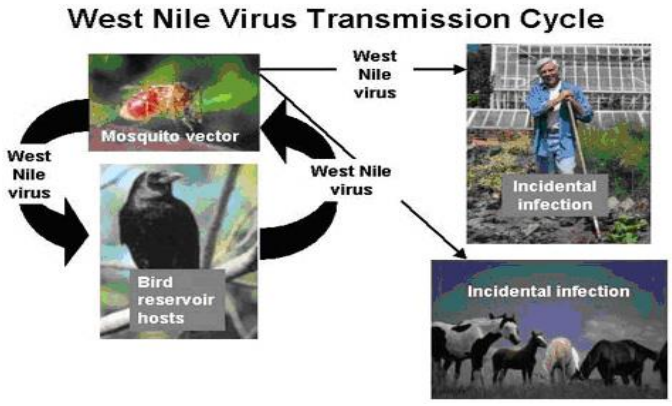
- **Adverse reactions:**
  - Local reactions. (IPV) at the site of injection
  - **Vaccine-Associated paralytic poliomyelitis.** (OPV) adult, immunocompromised. They need to get the killed one
- **4 doses:** 2,4,6-18 months. & 4-6 years
- **Combination vaccine:** IPV,DTaP,Hib,&HB vaccines.
- **Polio vaccination of adults:**
  - **Indications:** travelers to polio-endemic countries & Health care workers.
  - **IPV.**

Rabies encephalitis (- A fatal acute encephalitis - zoonotic disease) .	
Features of Virus	**1-**Bullet shaped virus. **2-**Enveloped virus. **3-**ss (-)RNA genome. 4- Helical nucleocapsid
Reservoir	- **Major**: Raccoons, Foxes, Wolves & Bats. - **Imp** : cats & dogs .
Transmission	**Common route** : Bite of a rabid animal. **Uncommon route** :Inhalation while in a bat-infested cave or Corneal transplant .
Phases of the disease (4 phases)	**1-The incubation period :** 1-3 months or longer [depending on the bite] **2-The prodromal phase**:(Fever, Headache, Malaise ,Anorexia ,Nausea & Vomiting , Abnormal sensation around the wound). **3-Neurological phase :** 1- Encephalitis (Nervous , lacrimation , salivation, hydrophobia, convulsion , coma & death). 2-Paralytic illness (Ascending , Death, associated with Bat bite). **4- Recovery** :Extremely rare
Laboratory Diagnosis	**1- PCR** : Rabies RNA in saliva **2- Rapid virus antigen detection (IF) : (**Neck skin biopsy ,Corneal impressions, Brain tissue). **3- Histopathology** :neuronal brain cells, intracytoplasmic inclusions (Negri bodies) →intra cytoplasmic **4-Virus cultivation .**
Prevention [Not treatable]	**Control measures against canine rabies include:** -Stray animals control. -Vaccination of domestic animals. **Pre-exposure prophylaxis (Vaccine):** -Persons at increased risk of rabies (e.g. vets, animal handlers etc). **Post-exposure prophylaxis :** -Wound treatment -Passive immunization: (human anti-rabies immunoglobulin applied around the wound & IM). -Active immunization: Human Diploid Cell Vaccine (HDCV) 5 - 6 doses

	Herpes simplex virus [HSV]
Cause	HSV-1 [ds DNA – enveloped – icosahedral]
Clinical findings	Fever – headache – vomiting – seizures – altered mental state – High mortality rate 70%
diagnosis	MRI – CSF [Lymphocytes – normal glucose – high protein] **PCR** [Detect HSV-1 DNA]
treatment	Acyclovir [treatable]

	The ARthropod Borne viruses [arboviruses]	
General	• ssRNA - more than 500 viruses – icosahedral capsul	
Epidemiology	Vectors (carrier, They do not have the disease themselves) Mosquito – ticks – sandflies	Reservoir [anything in which a disease lives and can multiply] Wild birds & Mammals
Transmition	a bite of an infected vector.	
infections	• **Asymptomatic Infections "MOST COMMON" → 80%** • **Diseases** ○ Fever, Rash & arthralgia ○ Hemorrhagic fever ± hepatitis ○ CNS disease [meningitis & encephalitis]→ **< 1%** ○ west Nile Fever → **20%**	
Arbo Vs associated with CNS disease [West Nile V]	" it is the most common " • **Vector: Mosquitos** • **Reservoir: Birds** • **Distribution:** Europe - Africa - **Middle East Asia** – America • Flaviviridae [**enveloped + ssRNA**] • cause **febrile** illness "yellow **fever** and Dengue **fever** " eventually → **Meningitis, Encephalitis**	
Lab Diagnosis	• Isolation (**Gold standard**) ○ **Samples:** Blood – CSF - Viscera ○ **Cell culture:** by CPE or Identify by IF • **IgM -AB** : ○ ELISA - IF → (**most used**) • Arbovirus RNA by **RT-PCR**	
Prevention	• Vector Control: ○ Elimination of **Vector breading sites** Using **insecticides** ○ Avoidance **contact** with vectors (**repellants , net**) • Vaccines: ○ **Tick-borne** encephalitis vaccine ○ **Japanese** encephalitis vaccine these vaccines are not specific but it is proven to produce an effective antibody cross-reaction.	





MCQs:

1…… infection of meningitis can cause brain damage and lead to death:

a) Viral
b) Bacterial
c) Fungal

2. A patient with CSF analysis (glucose 20, protein 150) is diagnosed with:

a) Septic meningitis
b) Aseptic meningitis

3. A viral isolation sample is taken from:

a) Stool
b) Blood
c) Saliva

4. Arbovirus comes from:

a) Bats
b) Mosquitos
c) Flies

5. A 7 year old male child came to the hospital with inability to move and limited sensation , he has a history of fever headache and nausea .The lab PCR results came with positive Non enveloped , icosahedral , ss (+) RNA , what is the most likely causative agent :

a. Poliovirus
b. Arboviruses
c. HSV(Herpes simplex virus -1)

6. What is the only viral infection of the CNS that can be treated through drugs?

A- Rabis encephalitis
B- HSV encephalitis
C- Arboviral encephalitis
D- Meningitis caused by Coxsackievruses A

ANSWERS :
1-B 2-B 3-A 4-B 5-A 6-B

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