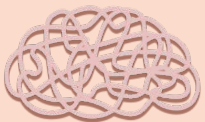
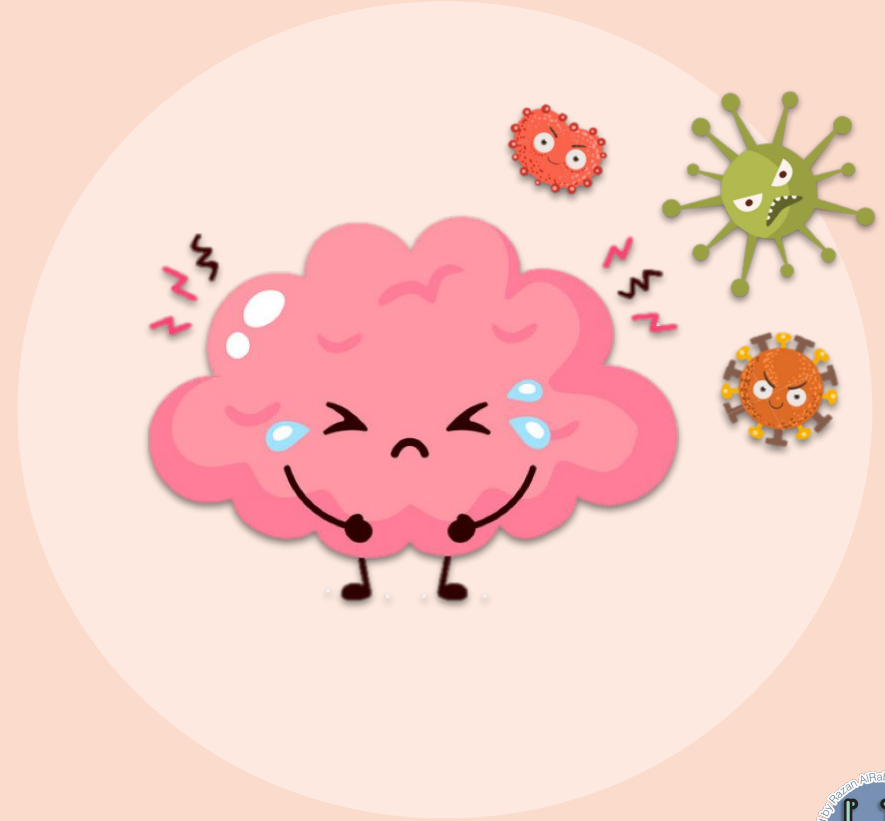


Viral Infections of CNS



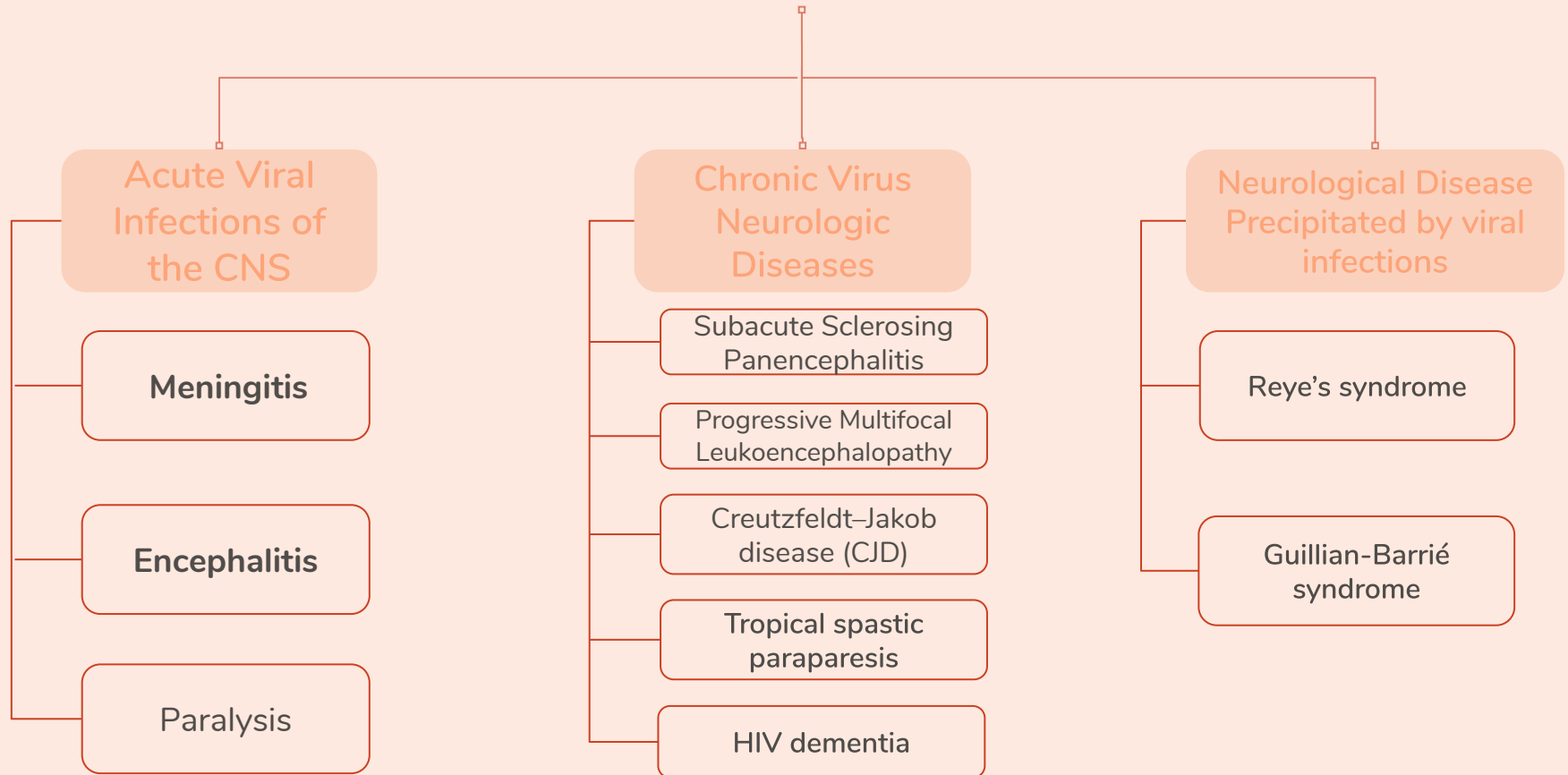
Objectives

- ★ Understand the different acute viral infections of the CNS (Meningitis, paralysis and encephalitis).
- ★ Differentiate between the clinical presentation and cerebrospinal fluid finding in the viral meningitis (aseptic meningitis) and bacterial meningitis (septic meningitis).
- ★ Understand the common viruses causing aseptic meningitis and encephalitis with regard to classification, structure, epidemiology pathogenesis, infections, clinical presentation, lab diagnosis and prevention.
- ★ Understand general information of arboviruses and giving some example of arboviruses causing CNS infection.

Color index:

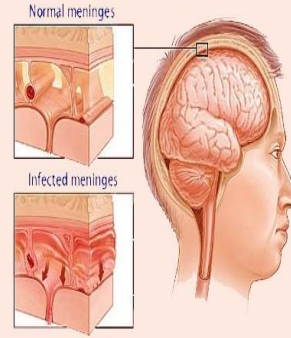
- Important
- Doctors note
- Extra

Virus Neurological Diseases



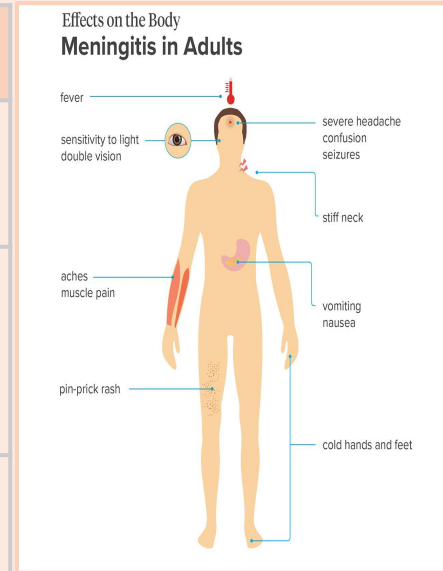
Meningitis

- Inflammation of leptomeninges (affect Pia, Arachnoid, & Subarachnoid space).
- Etiology:
 - **Infectious agents:**
 - Bacteria (In APM lecture)
 - Viruses
 - Fungi
 - Protozoa
 - **Non-infectious agents.**



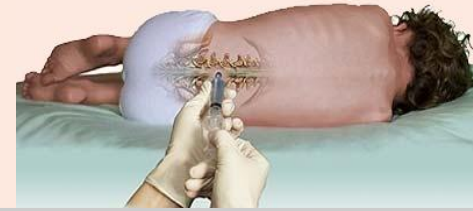
Symptoms:

	Viral Meningitis <small>more common</small>	Bacterial Meningitis
Type	Aseptic meningitis CSF result is negative with routine bacterial cultures	Septic meningitis
Severity	Less severe	Quite severe & may result in: <ol style="list-style-type: none"> 1. Brain damage 2. Hearing loss 3. learning disability
Prognosis	Resolves without specific treatment within a week or 2.	medical emergency & would also cause death!!



Cerebrospinal fluid (CSF) analysis

Cerebrospinal fluid drawn
from between two vertebrae



	Normal	Aseptic meningitis	Septic meningitis
Colour	Clear	Clear/Normal	Cloudy
Cells/mm ³	<5	↑ Lymphocytes 100-1000 mm³	high Neutrophils 200-20,000 mm³
Glucose mg/dl	45-85 mg/dl	within the normal range.	Low <45
Protein mg/dl	15-45 mg/dl	Normal or high (50-100)	High >100
Causes	-	Viruses , others.	Bacteria

Etiology

Viral (Aseptic) meningitis

Enteroviruses ,
most common
cause

Others:

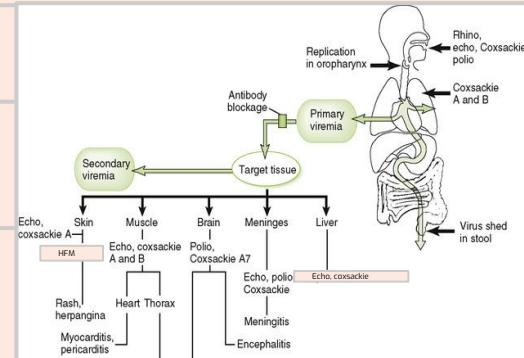
- Mumps virus. it was the most common cause but not any more due to vaccination.
- Arboviruses.
- Herpes viruses.
- Human Immunodeficiency Virus (HIV).
- Lymphocytic Choriomeningitis Virus (LCM).

Viral Encephalitis

- Enteroviruses.
- Herpes viruses.
- Rabies virus.
- Arboviruses.
- Others

Enteroviruses

Family	Picornaviridae. pico = small			
Structural features	<ol style="list-style-type: none"> 1. Non-enveloped 2. Icosahedral capsule 3. +ve Single Stranded RNA genome (+ssRNA). 			
Viruses included	Poliovirus (1,2,&3 types).	Coxsackieviruses (A&B).	Echoviruses	Enteroviruses (68-71).
Epidemiology	Reservoir	Humans.		
	Spread	<ul style="list-style-type: none"> • Mainly fecal - oral route. • Inhalation of infectious aerosols (In crowded, poor hygiene & sanitation). 		
	Age	affect Children more than Adults.		
	Seasonal distribution	Summer & fall.		
Pathogenesis	<p>the main route for enterovirus is the fecal oral route → replicate in the GIT (oropharynx) → reaches the blood (viremia) → it targets many organs such as meninges, brain, muscles and skin</p>			



1.Asymptomatic Infections

Types are not important

they cause

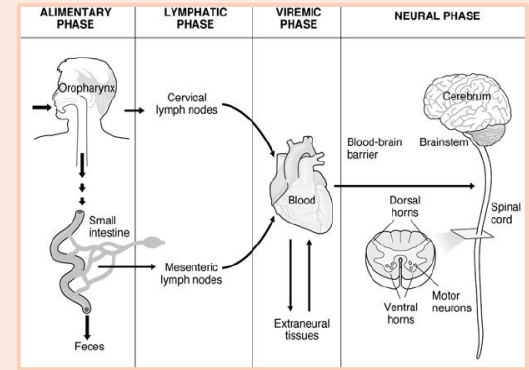
2.Diseases
mild
benign self
limiting

virus / disease	Polio types 1-3	GPA COX. types 1-24	GPB COX. types 1-6	Echo types 1-34	Entero types 68--71
Aseptic meningitis most common	1-3	Many	1-6	Many	71
Paralysis	1-3	7,9	2-5	2,4,6,9,11,30	70,71
Encephalitis	-	2,5-7,9	1-5	2,6,9,19	70,71
Non-neurologic Diseases	Cardiac & Muscular:		<ul style="list-style-type: none"> • Pleurodynia (epidemic myalgia) • Myocarditis, pericarditis. 		
	Skin & Mucosa infections:		<ul style="list-style-type: none"> • Herpangina • Hand-foot-and-mouth disease • Exanthems 		
	Acute hemorrhagic conjunctivitis.				
	Respiratory tract infections.				
	Others.				

Poliovirus

Pathogenesis

- Pathway to CNS by:
 - Blood (viraemia).
 - Peripheral nerves.
- Causing destruction of **motor neurons AHCs**.
- Rarely affects brain stem (bulbar Poliomyelitis) **which result in respiratory failure** .
- Immunity:
 - IgA & IgG = Lifelong type-**specific** immunity.



Infections

- No illness (90-95%):
 - Asymptomatic , **but can spread to others**.
- Minor illness (4-8%):
 - Abortive poliomyelitis (**No CNS involvement**) . **it causes slight fever, malaise, headache, sore throat and vomiting**.
- Major illness (1-2%):
 - Non-paralytic poliomyelitis (**Aseptic meningitis**).
 - Paralytic poliomyelitis (**Flaccid paralysis**) **asymmetrical without sensory loss**.

Lab diagnosis of EVs	Virus isolation	<ul style="list-style-type: none"> • Samples: Stool (best), rectal, throat swabs, & CSF. • Inoculate in MKC & HDF. (all EVs grown except some strains of Cox A viruses) • Observe for Cytopathic effect (CPE). • Identify the type by Neutralization Test.
	CSF in Aseptic meningitis	<ul style="list-style-type: none"> • Lymphocytosis • Glucose: Normal to slightly decreased • Protein: Normal or slightly high. • Isolation rate is variable. • RT-PCR to detect Enteroviruses RNA in CSF. the best diagnostic method for the neurological disease .
	Serology	<ul style="list-style-type: none"> • Limited value , Preformed antibodies (e.g. due to vaccine) can give false positive results
Management of EVs	Treatment	<ul style="list-style-type: none"> • No antiviral therapy.
	Prevention	<ul style="list-style-type: none"> • Sanitation & Hygienic measures • Poliovirus vaccines: <ol style="list-style-type: none"> 1. Inactivated polio vaccine (IPV): <ul style="list-style-type: none"> ○ (Salk, Killed), can be injected Subcutaneous, or IM. ○ Adverse reactions: Local reactions. 2. Live-attenuated polio vaccine (OPV): <ul style="list-style-type: none"> ○ Sabin, oral. ○ Adverse reactions: Vaccine-Associated Paralytic Poliomyelitis in adult and low immune. • 4 doses of PV: 2, 4, 6-18 ms, & 4-6 yrs. • Pediarix contains; IPV, DTaP, HB vaccines. • Poliovirus vaccines for adults: <ul style="list-style-type: none"> ○ Indications: Travelers to polio-endemic countries, Health care workers. ○ Vaccine: Inactivated polio vaccine (IPV)

Important Features of Polio Vaccines

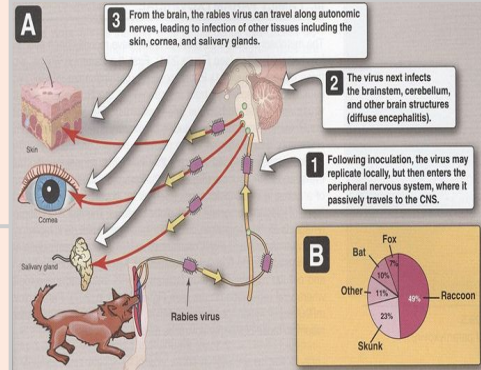
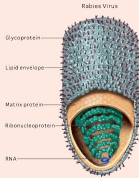
Attribute	Killed (IPV)	Live (OPV)
3 types (trivalent)	Yes	Yes
Prevents disease	Yes	Yes
Induces humoral IgG	Yes	Yes
Route of administration	Injection	Oral
Induces intestinal IgA	No	Yes
Affords secondary protection by spread to others	No	Yes
Reverts to virulence Vaccine-Associated Paralytic Poliomyelitis	No	Yes (rarely) , DON'T give it to adults or immunocompromised patients , it's ONLY for children
causes disease in low immune	No	Yes
Duration of immunity	Shorter	Longer

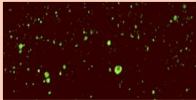

Herpes Simplex Encephalitis (HSV)

Family	<ul style="list-style-type: none">● Herpesviridae family.
Caused by	<ul style="list-style-type: none">● Herpes simplex virus -1 (HSV-1).<ul style="list-style-type: none">○ Double Stranded DNA genome (dsDNA).○ Enveloped. notice that all the viruses that will cause encephalitis are enveloped○ Icosahedral virus.○ It cause orofacial infection.
Clinical Presentation /feature	<ul style="list-style-type: none">● Fever, headache, vomiting, seizures & altered mental status.● High mortality rate.
Pathogenesis	It presents as skin lesions around the mouth and the nose → go to the sensory ganglion where it will replicated there → peripheral nerve → reaches the temporal area of the brain → result in a temporal lesion .
Diagnosis	Magnetic resonance imaging (MRI) <ul style="list-style-type: none">● for temporal lobe lesion.
	CSF <ul style="list-style-type: none">● ↑ in Lymphocytes, glucose is normal & protein is normal / ↑ .● detection of HSV-1 DNA by PCR.
Treatment	<ul style="list-style-type: none">● The only treatable CNS infection● Acyclovir

Rabies Encephalitis

<p>Caused by:</p>	<ul style="list-style-type: none"> ● Rabies virus ● It's zoonotic disease (infection that spread between animals & humans). ● A fatal acute encephalitis 	
<p>Family</p>	<ul style="list-style-type: none"> ● Rhabdoviridae. 	
<p>Structural features</p>	<ol style="list-style-type: none"> 1. Enveloped virus 2. Bullet shaped virus 3. Helical nucleocapsid 4. -ve Single Stranded RNA genome (-ssRNA). 	
<p>Epidemiology</p>	<p>Reservoir</p>	<ul style="list-style-type: none"> ● Major: Raccoons, Foxes, Wolves, & Bats. ● Imp: Cats & Dogs.
	<p>Transmission</p>	<ul style="list-style-type: none"> ● Common route: bite of rabid animal. ● Uncommon route: <ul style="list-style-type: none"> ○ Inhalation while in a bat infested cave, ○ Corneal transplant. <p style="text-align: center; color: green;">from undiagnosed donor</p>
<p>Pathogenesis</p>	<p>After getting a bite from a rabid animal that is infected rabies → the virus will enter the PNS → reaches spinal cord, medulla & brain → from the brain it travel down to infect other tissues like the cornea, skin & salivary glands</p>	



Phases	The incubation period	1-3 months ,needs to be treated within this period, its shorter if the bite is closer to the head	
	The prodromal phase	<ul style="list-style-type: none"> ● Fever ● Headache ● Malaise ● Anorexia 	<ul style="list-style-type: none"> ● Nausea ● Vomiting ● Abnormal sensation around the wound.
	Neurological phase	1- Encephalitis: more common Nervous, lacrimation, salivation, hydrophobia(fear of water), convulsion, coma & death.	
		2- Paralytic illness; Ascending, death, associated with Bat bite.	
	Recovery	Extremely rare	
Laboratory Diagnosis	1. RT-PCR:	Rabies RNA in saliva	
	2. Rabid viruses antigen detection (IF):	<ul style="list-style-type: none"> ● Neck skin biopsy ● Croneal impressions ● Brain tissue 	 <p>Rabid brain stained with Fluorescent anti-rabies antibody</p>
	3. Histopathology:	<ul style="list-style-type: none"> ● Neuronal brain cells ● Intracytoplasmic inclusions (negri bodies) 	 <p>Negri bodies are diagnostic of rabies.</p>

4. Virus cultivation

5. Serology

Control measures against canine rabies includes

- Stray animals control.
- Vaccination of domestic animals.

Pre-exposure prophylaxis (Vaccine)

- For persons at increased risk of rabies (e.g. vets, animal handlers etc.)
- Use: Active immunization; **Human Diploid Cell Vaccine (HDCV)**

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.**

Prevention of Rabies:
its preventable but not treatable

Arthropod-borne Viruses

Include

Arboviruses >500 viruses.

Epidemiology

Reservoir

Wild birds & Mammals.

Vector

Mosquito, Tick, & Sandfly.

Transmission

Bite of infected vector.

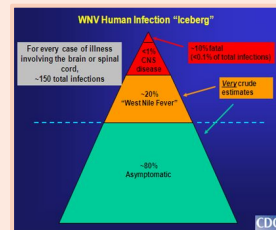
Infections

- Asymptomatic infections , most commonly (80%)
- Diseases:
 - Fever, Rash, & Arthralgia.
 - Hemorrhagic fever ± hepatitis.
 - **CNS diseases** (in the next table, and they are not imp)
(meningitis & encephalitis).

Virus	Vector	Reservoir	Distribution
Eastern equine (encephalitis EEEV)	Mosquito	Birds	America
Western equine (encephalitis WEEV)	Mosquito	Birds	America
Venezuelan equine (encephalitis VEEV)	Mosquito	Rodent	America
Japanese encephalitis V	Mosquito	Birds, Pigs	Orient
Murray Valley (encephalitis V)	Mosquito	Birds	Australia
West Nile Virus	Mosquito	Birds	Europe , Africa , Middle East, Asia, America

West Nile Virus

Family	Flaviviridae.
features	<ol style="list-style-type: none"> 1. Enveloped virus 2. +ve Single Stranded RNA genome (+ssRNA). 3. Febrile illness → meningitis, encephalitis.



Diagnosis of Arboviruses

- Lab Methods (reference lab):
 - **Isolation** (Gold standard)
Samples: blood, CSF, Viscera.
Cell culture → CPE (cellular pathological effect)→ Identify by IF.
 - **IgM -AB, ELISA, IF (most used)**
 - Arbovirus RNA by RT-PCR.

Vector Control

- Elimination of vector breeding sites
- using insecticides
- Avoidance contact with vectors (repellants, net)

Prevention Of Arboviruses

Vaccines

there is no specific vaccine against west nile virus

- Tick-borne encephalitis vaccine
- Japanese encephalitis vaccine

Quiz :

Q1/ What is the most common etiology for meningitis?

- A. Viral infection.
- B. Fungal infection.
- C. Bacterial infection.
- D. A & C.

Q2/ Enteroviruses are :

- A. Non-enveloped viruses
- B. have ss -ve RNA genome
- C. Icosahedral in shape
- D. A & C.

Q3/ Which type of herpes can cause CNS infection?

- A. HSV-2
- B. HSV-1
- C. Both
- D. Non of them

Q4/ Common route for transmission of Rabies virus ?

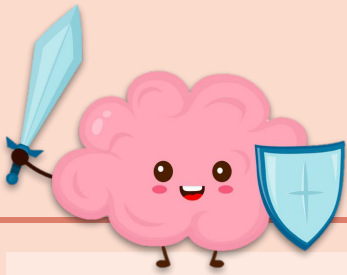
- A. Inhalation while in a bat-infested cave
- B. Bite of rabid animal
- C. Corneal transplant
- D. Sexually

SAQ/ A 2 years old child came to the hospital complaining from headache , fever , photosensitivity and neck stiffness the doctor took a sample of CSF and it showed clear CSF with normal glucose and slightly increased protein . under the microscope there was a non-enveloped +RNA virus .

1. What is your diagnosis?
2. what is the organism?
3. how would the doctor treat it?
4. if the patient was 43 how would we prevent it?


Q1/A
Q2/D
Q3/B
Q4/B


SAQ:
1. viral aseptic meningitis
2. poliovirus
3. its a self-limiting virus
4. IPV



THANK YOU

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