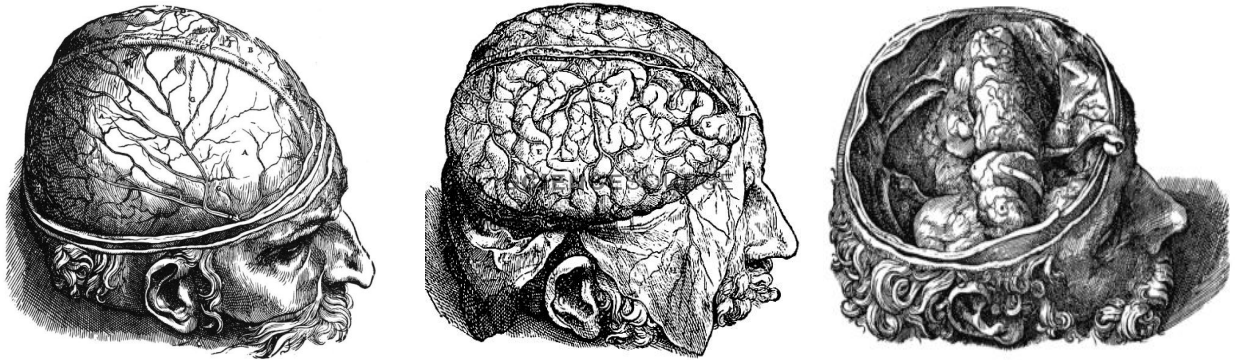


Microbiology

435's Teamwork
Neuropsychiatry Block



-
- Kindly check our [Editing File](#) before studying the document.
 - Please contact the team leaders for any suggestion, question or correction.
 - Pay attention to the statements highlighted in **red**.
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 - **Footnotes color code:** General | **Females** | **Males**

Revised by

خولة العماري & هشام الغفيلي



Viral infections of the CNS

Resources: Sherris Medical Microbiology, Notes on Medical Microbiology By Morag C, Prof. Malak's & Dr. Alhatheel's 2017 lectures.

Learning Objectives:

By the end of this lecture, you should know the...

1. Definition
2. Structure
3. Epidemiology
4. Pathogenesis
5. Clinical Presentations
6. Lab Diagnosis
7. Treatment
8. Prevention

Of CNS viral infections.

Viruses:

Viruses are obligate intracellular parasites that do not have a cellular structure, instead, they have a protein coat, and occasionally an envelope which derives from the host's cell plasma membrane. They have DNA molecule(s), or RNA molecule(s), but not both. Viruses contain the genetic information necessary for directing their own replication, but require host's cellular structure and enzymatic machinery to complete process.

Introduction:

Viruses that infect the central nervous system include Herpes Simplex Virus (HSV), Arboviruses, Coxsackieviruses, Echoviruses, and Enterovirus.

- Some of these infections affect primarily the meninges and result in meningitis.
- Viral meningitis is sometimes called aseptic meningitis.
- Other infections affect primarily the brain and result in encephalitis.
- Infections that affect both the meninges and brain result in meningoencephalitis.
- Meningitis is far more common among children than is encephalitis.

Meningitis Classification			
Infectious			Non-infectious
Bacteria ¹	Viruses ²	Fungi & protozoa	Caused by disorders that are not infections, probably drugs.
Septic Meningitis is quite severe and may result in: <ul style="list-style-type: none"> a) brain damage. b) hearing loss. c) learning disability. It would also causes death ³ .	<ul style="list-style-type: none"> • Aseptic meningitis. • Less severe.⁴ • Resolves without specific treatment within a week or two⁵. 		

	Findings of CSF analysis		
	Normal	Aseptic meningitis	Septic meningitis
Colour	Clear	Clear	Cloudy
Cells/mm³	< 5	Increase 100-1000 Lymphocytes	Increase 200-20,000 Neutrophils
Glucose mg/dl	45-85	Normal ⁶	Low <45
Protein mg/dl	15-45	Normal/High 50-100	High >100
Causes	-	Viruses (or others)	Bacteria

Classification of CNS Viral Infections		
Acute	Chronic	Precipitated ⁷
Meningitis, Paralysis and Encephalitis ⁸	SSPE ⁹ PML ¹⁰ C-J disease ¹¹ Tropical Spastic Paraparesis ¹² HIV dementia ¹³	Reye's syndrome ¹⁴ Guillain-Barré syndrome ¹⁵

¹ Should be treated with antibiotics.

² CANNOT be treated with antibiotics. Viruses are the most common cause of meningitis.

³ Can be fatal if not treated.

⁴ The symptoms are present but they are less severe compared to bacterial meningitis.

⁵ Self-limiting.

⁶ Normal / slight change.

⁷ Neurological diseases precipitated by viral infections are syndromes associated with viral infections & risk factors.

⁸ Inflammation of the brain.

⁹ Subacute sclerosing panencephalitis is a progressive and deadly brain disorder related to measles (rubeola) infection.

¹⁰ Progressive multifocal leukoencephalopathy. Due to JC virus.

¹¹ Creutzfeldt-Jakob disease (CJD) is a rare, degenerative, invariably fatal brain disorder. It is a prion.

¹² Weakness, muscle spasms, and sensory disturbance by Human T-lymphotropic virus.

¹³ Decline in mental processes is a common complication of HIV infection.

.Rapidly progressive encephalopathy ¹⁴

في الأطفال الذين يتناولون الأسبرين، عندما يصابون بالإنفلونزا يكونون عرضة للإصابة بـ **Reye's syndrome**.
Rapid-onset muscle weakness caused by the immune system damaging the peripheral nerves ¹⁵

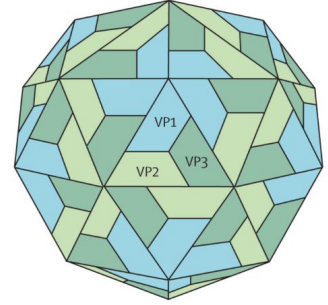
مؤخرًا وجدوا علاقة بين **Guillain-Barré syndrome** و **Zika virus**

1. Aseptic Meningitis

Etiology:

It mainly caused by *Enterovirus*¹⁶ (EV) and many other viruses, such as:

- *Mumps Virus*¹⁷.
- *Arbovirus*¹⁸.
- *Herpes Simplex Virus - type 2 (HSV)*¹⁹.
- *Human Immunodeficiency Virus (HIV)*.
- *Lymphocytic Choriomeningitis Virus (LCM)*.



Enterovirus				
Definition	<i>Picornavirus</i> ²⁰ family Nonenveloped Icosahedral ssRNA +ve polarity			
Includes	<i>Poliovirus</i> (Type 1,2,3)	<i>Coxsackieviruses</i> (A&B)	<i>Echoviruses</i>	<i>Enteroviruses</i> (Type 68-71)

Epidemiology:

- **Spreads in:** Crowded, poor hygiene and sanitation areas.
- **Affects:** Children more than adults.
- **Reservoir:** Human
- **Seasonal distribution:** Summer and fall.

Pathogenesis²¹:

Transmitted²² through the oral/fecal route → Replication²² in the GIT → Viremia affect many organs causing the clinical manifestation.

At the CNS and Peripheral Nerves:

- Causing destruction of motor neurons²³ of AHCs.
- **Rarely** affects brainstem (bulbar poliomyelitis).
- Immunity: IgA²⁴ and IgG²⁵ = Lifelong type-specific immunity.

7 to 14 days for incubation → 5 days systemic symptoms (non specific symptoms²⁶) → 5 days of neural symptoms (specific symptoms).

¹⁶ Enteroviruses is a large group and it contains (poliovirus) GPA Cox, and GPB Cox, echovirus and enteroviruses) and that they can cause aseptic meningitis, paralysis and encephalitis.

¹⁷ يسبب النكاف.

¹⁸ تنتقل عن طريق vectors (ناقل) مثل: sandfly, tick, mosquitoes.

¹⁹ And type 1.

²⁰ هذه عائلة كبيرة من الفيروسات وتنتقل لجميع أنحاء الجسم.

Another example from the Picornaviridae family is the Rhinovirus which is small, non-enveloped virus with single stranded RNA with positive polarity. Non-enveloped viruses can survive in the environment for a long time because they are protected by the capsid (unlike enveloped viruses).

²¹ تنتقل عن طريق الـ oral-fecal route أو الـ inhalation و تسبب respiratory tract infection أو تسبب gastroenteritis إذا انتقلت للـ GIT ومن الممكن أيضا أن تنتقل للدم و تسبب systemic viremia وتنتقل أيضا للـ lymph nodes وتسبب secondary viremia. إذا انتقلت للكبد تسبب hepatitis و إذا انتقلت للـ CNS تسبب meningitis أو encephalitis و في حال انتقلت للعضلات تسبب myocarditis أو pericarditis و تسبب rash إذا انتقلت للـ skin وغيرها حسب المنطقة.

²² Mode of transmission: fecal-oral route mainly → replicate in intestines then gets to the brain through viremia → then it takes up to 15 days → recovery → causes destruction of motor neurons

²³ The result will be paralysis in the muscle.

²⁴ Intestinal igA. Because it replicate in the intestine.

²⁵ Humoral igG.

²⁶ Characterised by non specific illness such as fever, nausea, headache.

Enteroviral infections: (Asymptomatic Infections ²⁷)	
Neurologic diseases	Non-neurologic diseases
<p>Aseptic meningitis²⁸</p> <p>Paralysis</p> <p>Encephalitis</p> <p>Seizures</p>	<p>Respiratory tract infections</p> <p>Skin and mucosal infections</p> <p>Cardiac infections</p> <p>Acute hemorrhagic conjunctivitis... etc.</p>

Poliovirus Infections		
No illness	Minor illness	Major illness
90-95%	4-8%	1-2%
Asymptomatic	Abortive poliomyelitis ²⁹ . (No CNS involvement)	<ul style="list-style-type: none"> Nonparalytic poliomyelitis³⁰ (Aseptic meningitis). Paralytic poliomyelitis³¹ (Flaccid paralysis).

Lab Diagnosis of Enteroviruses		
Virus isolation ³²	CSF in aseptic meningitis	Serology
<p>1. Samples:</p> <ul style="list-style-type: none"> Stool (best)³³. Rectal or throat swabs. CSF³⁴. <p>2. Inoculate in cell cultures: All Enteroviruses grow except some strains of Cox-A viruses.</p> <p>3. Observe for CPE³⁵: Identify the type by Neutralization Test.</p>	<ul style="list-style-type: none"> Lymphocytosis. Glucose level is normal or slightly ↓ Protein level is normal or slightly ↑ Isolation rate is variable. EV RNA detected in CSF³⁶ by RT-PCR.³⁷ 	Limited value ³⁸

²⁷ Most common enteroviral infection are asymptomatic.

²⁸ Most common diseases in the nervous system that is caused by enteroviruses.

²⁹ Failing to produce symptoms. Non specific symptoms such as nausea headache.

³⁰ Its mild usually in children.

³¹ No sensory loss. it affects only motor neuron.usually in adults so the severity of the disease increase with age.

³² The Gold standard.

³³ Because this virus sheds in stool.

³⁴ CSF specimen taken in case of meningitis.

³⁵ We see in cell culture: CPE (cytopathic effect)→ but keep in mind that CPE is not a definite diagnosis of viral infection→ it must be confirmed by immunofluorescence or other techniques.

³⁶ CSF clear in appearance

³⁷ عينة الـ CSF صعب تأخذها من المريض بشكل متكرر (بخلاف الدم) فنحاول نستفيد منها و ما نضيعها في culture مثلا.

³⁸ لأسباب: ما فيه antigen و لأننا نتعرض لهذه الفيروسات باستمرار، فإذا عملنا screening للـ population كثير بيطلع عندهم (موجود) و مع ذلك ما عندهم infection، فضلا عن أنه الناس تأخذ الـ polio vaccine --> كثير صار عندهم antibody و هذا الـ antibody تعطي تفاعل في ELISA

Treatment → No antiviral available.

Prevention → Sanitation, Hygienic measures and Poliovirus vaccines.

Poliovirus Vaccines			
Vaccine	Advantages	Disadvantages	Both are
Inactivated (killed) Polio Vaccine (IPV) ❖ For Adults. ❖ IM/Subcutaneous.	<ul style="list-style-type: none"> • Does not revert to virulence. • Does not cause disease in the immunocompromised. • Co-infection with other EVs Does not impair immunization. • Does not require refrigeration. 	<ul style="list-style-type: none"> • Does not induce intestinal IgA. • Does not interrupt transmission. • Does not afford 2nd protection. • Short duration of immunity. 	<ul style="list-style-type: none"> • 3 types (trivalent) Give protection against all 3 types of polio.
Live-Attenuated Polio Vaccine (OPV or Sabin) ❖ For Children. ❖ Oral.	<ul style="list-style-type: none"> • Induces intestinal IgA.³⁹ • Interrupts transmission. • Affords 2nd protection⁴⁰ by spread to others. • Long duration of immunity⁴¹ 	<ul style="list-style-type: none"> • May revert to virulence (rare) • Cause disease in the immunocompromised. • Co-infection with other EVs may impair immunization. • Requires refrigeration⁴². 	<ul style="list-style-type: none"> • Prevent disease. • Induce humoral IgG.

Indications of Polio adults vaccination:

Travelers to polio-endemic countries and Health care workers.

Doses:

2 Months, 4 Months, 6-18 Months and 4-6 years.

Combinations⁴³:

IPV, DTaP⁴⁴, HiB⁴⁵, and HB⁴⁶ vaccines.

Adverse reactions:

- Local reactions of (IPV) at the site of injection.
- Vaccine-Associated paralytic poliomyelitis⁴⁷ with (OPV), therefore adults, and immunocompromised need to get the killed one (IPV).

³⁹ Live-attenuated induces both IgA and IgG; and having them both is a good thing. It is better than having only IgG (like in killed vaccine) because IgG is in circulation and IgA is in mucus; so having them both gives more protection.

⁴⁰ Because is not killed (it is live-attenuated).

⁴¹ Given orally because of the nature of transmission or the acquired infection; it goes to GIT. So now I have live-attenuated virus → I need the virus to replicate at low level → so I need it to get to the GIT → that's why live-attenuated is given orally; (if live-attenuated given IM there will be no benefit of that). While in adults it is given IM or subcutaneously because it is killed (not live-attenuated).

⁴² To preserve it so it won't change into active virus.

⁴³ Pediatric → combination → it is killed (not live-attenuated); but for children it is recommended to use live-attenuated.

⁴⁴ Helps children younger than age 7 develop immunity to three deadly diseases caused by bacteria: diphtheria, tetanus, and whooping cough (pertussis).

⁴⁵ Haemophilus influenzae type b vaccine.

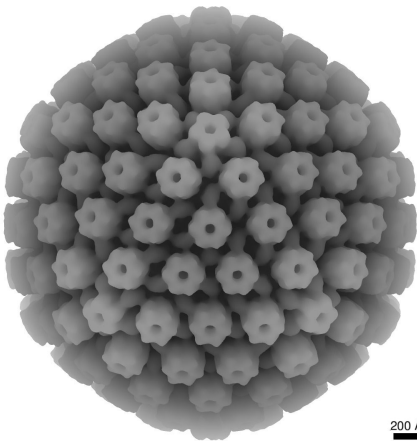
⁴⁶ Hepatitis B vaccine.

⁴⁷ It happens with oral polio vaccine when taken by adults and patients with low immunity → that's why oral (live-attenuated) is not recommended for adults.

2. Viral Encephalitis

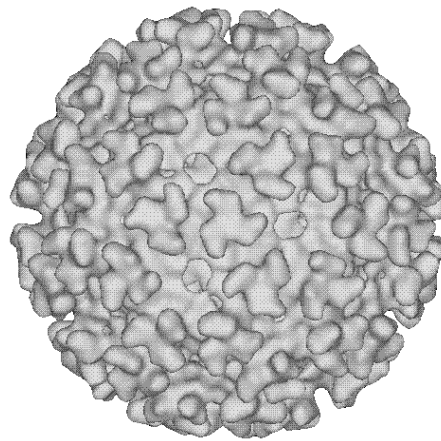
Etiology:

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

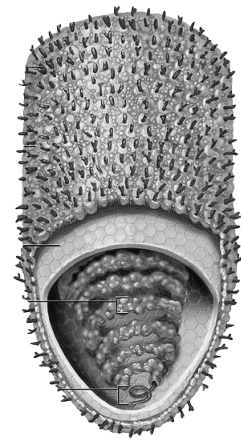


Herpes viruses

200 Å



Arbovirus



Rabies

Herpes Simplex Virus (HSV) Encephalitis	
Features	HSV Type 1 dsDNA Enveloped Icosahedral
Clinical findings ⁴⁸	Fever, headache, vomiting, seizures and altered mental state.
Diagnosis	<ul style="list-style-type: none"> • MRI → CSF (Lymphocytes, normal glucose, high protein). • PCR⁴⁹ (Detect HSV-1 DNA).
Treatment	<ul style="list-style-type: none"> • High mortality rate⁵⁰ • Acyclovir (treatable)

⁴⁸ Clinical manifestations are similar to encephalitis and meningitis; you can't distinguish based on clinical manifestations.

⁴⁹ Molecular testing → viral nucleic acid

⁵⁰ High mortality rate if not treated; this is the only virus (from this group) that can be treated.

Rabies Encephalitis ⁵¹ → (A fatal acute encephalitis - Zoonotic disease ⁵²)	
Features	Bullet shaped virus Enveloped virus ss (-) RNA genome ⁵³ Helical nucleocapsid
Reservoir⁵⁴	Raccoons, foxes, wolves, bats, cats and dogs.
Transmission	<ul style="list-style-type: none"> ● Common route: Bite of a rabid animal. ● Uncommon route: Inhalation while in a bat-infested cave / Corneal transplant.
Phases of the disease (4 phases)	1. The incubation period⁵⁵ 1-3 months or longer (depending on the bite).
	2. The prodromal phase Fever, headache, malaise, anorexia, nausea, vomiting and abnormal sensation around the wound.
	3. Neurological phase <u>Encephalitis:</u> Nervous, lacrimation, salivation, hydrophobia, convulsion, coma and death. <u>Paralytic illness:</u> Ascending, death, associated with Bat bite.
	4. Recovery: Extremely rare
Laboratory Diagnosis	<ul style="list-style-type: none"> ● PCR: Rabies RNA in saliva. ● Rapid virus antigen detection (IF⁵⁶): Neck skin biopsy, Corneal impressions, Brain tissue. ● Histopathology: Brain cells, intracytoplasmic inclusions (Negri bodies). ● Virus cultivation⁵⁷.
Prevention (Untreatable)	<p>Control measures against canine rabies include:</p> <ul style="list-style-type: none"> ● Stray animals control. ● Vaccination of domestic animals. <p>Pre-exposure prophylaxis (Vaccine): Persons at increased risk of rabies⁵⁸ e.g. vets, animal handlers... etc.</p> <p>Post-exposure prophylaxis:</p> <ul style="list-style-type: none"> ● Wound treatment. ● <u>Passive immunization⁵⁹:</u> human anti-rabies immunoglobulin applied around the wound and IM. ● <u>Active immunization:</u> Human Diploid Cell Vaccine (HDCV) 5-6 doses.

⁵¹ اسم عائلة ال rabies virus هو rhabdoviridae.

⁵² ينتقل من الحيوان إلى الإنسان

⁵³ Reminder: -ve polarity → needs transcription then translation. While +ve polarity → translation immediately

⁵⁴ Reservoir is the nature host of the virus (habitat).

⁵⁵ إذا في الفترة هذه (شهر-3 شهور) المريض ما زار الطبيب و لم يأخذ ال vaccine و ال immunoglobulin (يعني إذا ظهرت الأعراض) لأنها لو ظهرت الأعراض يكون صعب أن ينجو، ولكن فترة الحضانة طويلة، فيمكن علاجه -إن شاء الله- لو الشخص أول ما تعرض مباشرة يروح للمستشفى و يأخذ ال vaccine و ال immunoglobulin. و recovery is extremely rare if not treated immediately.

⁵⁶ Immunofluorescence.

⁵⁷ ممكن نسوي culture للفيروس، لكن المريض لما يجي عنده إصابة يعملون له PCR على طول (قبل ظهور الأعراض) لأنها لو ظهرت الأعراض يكون الفيروس قد تمكن من الشخص، فلا يوجد طريقة تمنع المضاعفات و ممكن يموت، أساسا الشخص المصاب سواء ظهرت الأعراض أم لم تظهر يجب أن يأخذ ال vaccine.

⁵⁸ الأشخاص الذين يتعاملون مع الحيوانات يأخذون ال vaccine و هو human diploid cell vaccine وهذا يعتبر active immunization. Active immunization → stimulates the body to produce antibody (takes time to produce antibody → about 2-3 weeks to produce antibody). I give antigen to the body to produce antibody or cellular or humoral immunity.

⁵⁹ Passive (immediate action) → We give the body antibody to neutralize.

The Arthropod Borne Virus (Arbovirus)

Features	ssRNA More than 500 viruses Icosahedral capsule
Vector⁶⁰	Mosquito, ticks and sandflies.
Reservoir	Wild birds and mammals.
Transmission	A bite of an infected vector.
Infection	<ul style="list-style-type: none"> ● Asymptomatic Infections⁶¹ “MOST COMMON” → 80% ● Diseases: <ul style="list-style-type: none"> - Fever, rash and arthralgia. - Hemorrhagic fever ± hepatitis. - CNS disease [meningitis & encephalitis] < 1% - West Nile Fever → 20%
Arbo Vs Associated with CNS Disease (West Nile)⁶²	<p>Vector: Mosquitos.</p> <p>Reservoir: Birds.</p> <p>Distribution: Europe, Africa, Middle East⁶³, Asia and America.</p> <p>Flaviviridae: Enveloped + ssRNA.</p> <p>Cause febrile illness “yellow fever and Dengue fever” eventually meningitis and encephalitis.</p>
Lab Diagnosis	<ul style="list-style-type: none"> ● Isolation⁶⁴ (Gold standard): <ul style="list-style-type: none"> - <u>Samples:</u> Blood, CSF or Viscera. - <u>Cell culture:</u> by CPE or Identify by Immunofluorescence. ● IgM → ELISA and Immunofluorescence. ● Arbovirus RNA⁶⁵ by RT-PCR.
Prevention	<ul style="list-style-type: none"> ● Vector Control⁶⁶: <ul style="list-style-type: none"> - Elimination of vector breeding sites using insecticides. - Avoidance contact with vectors (repellants, net)⁶⁷. ● Vaccines: <ul style="list-style-type: none"> - Tick-borne encephalitis vaccine. - Japanese encephalitis vaccine. <p style="text-align: right; color: #9e9e9e;">These vaccines are not specific but it is proven to produce an effective antibody cross-reaction.⁶⁸</p>

⁶⁰ Carrier, do not have the disease themselves.

⁶¹ غالب ال viral infections تكون asymptomatic و ممكن تسبب mild or severe symptoms

⁶² The most common in middle east.

⁶³ قبل فترة صار outbreak في جنوب المملكة (حمى الوادي المتصدع = Rift valley virus) و (حمى الضنك = Dengue) و هذه كلها من نفس فصيلة ال West nile virus و هي Flavivirus.

⁶⁴ In cell culture.

⁶⁵ كل فيروس له طريقة خاصة: specific kit for RNA detection by molecular testing

⁶⁶ The best

⁶⁷ Avoid contact especially at night

⁶⁸ وجدوا أنه إذا الشخص أخذ ال vaccines تعطي حماية ضد ال west nile virus

Summary

Aseptic meningitis

Etiology	Enteroviruses mainly, might be by Mumps, Arbo, Herps viruses & HIV. - The most common cause of meningitis.		
Enteroviruses			
- Picornaviridae family. - Non-enveloped, icosahedral, ss (+) RNA. - Include: Poliovirus, Coxsackieviruses, Echoviruses, Enteroviruses.			
Epidemiology	- Reservoir → Human. - Children > adult. - Summer & Fall. - Spread → Fecal-oral route, inhalation of infectious aerosols (in crowded, poor hygiene & sanitation)		
Pathogenesis	Fecal-oral route → GIT → spread hematogenously → target organs (liver, meninges, brain, muscle, skin).		
Enteroviral infections	- Asymptomatic. - Most of the neurologic infections are caused by enteroviruses types (68-71).		
Poliovirus	Pathogenesis	- GIT → spread to CNS by blood or peripheral nerves → destruction of AHCs (LMNL) → paralysis. - Rarely affect brainstem. - IgA & IgG → Lifelong type-specific immunity. - 7 days → incubation, after 5 days → spread systematically, after 5 days → to neural tissue.	
	Response of infection	- 90% → Asymptomatic. - 4-8% → minor illness → Abortive poliomyelitis (No CNS involvement). - 1-2% → major illness → 1- Nonparalytic poliomyelitis (Aseptic meningitis). 2- Paralytic poliomyelitis: (Flaccid paralysis).	
Lab diagnosis	Virus isolation	Stool sample → Inoculate in cell cultures (all EV grow except Cox A) → Observe for CPE → Identify the type.	
	CSF	Lymphocytosis, ↓ glucose or N, ↓ protein or N.	RT-PCR. Serology-limited value
Management	No Rx.	<u>Prevention:</u> Sanitation & Hygienic measures, Poliovirus vaccines.	<u>Poliovirus vaccines:</u> 1- IPV → killed, IM, adult and ↓ immunity, No IgA, local reactions. 2- OPV → Live, oral, children, ✓ IgA, Vaccine, Associated Paralytic Poliomyelitis (OPV),
Viral Encephalitis			
HSV	- HSV-1: dsDNA, Enveloped, Icosahedral Virus. - High mortality rate. - Dx: MRI, CSF, PCR (HSV-1 DNA) - Rx: Acyclovir		
Rabies encephalitis	- one of Rhabdoviridae. - ss (-) RNA, Helical nucleocapsid, Enveloped. - Bullet shaped virus.		
	Epidemiology	- Reservoir → major: Raccoons, cats, dogs. → Zoonotic disease. - Fatal acute encephalitis. - <u>Transmitted by 2 routes:</u> 1- Common → Bite of a rabid animal. 2- Uncommon → Inhalation while in a bat infested cave, Corneal transplantation.	
		<u>Dx:</u> PCR, IF, Histopathology: Negri bodies, Virus cultivation, serology.	<u>Prevention:</u> Control measure against canine rabies, vaccine.
Arthropod-borne Viruses (Arbovirus)	Epidemiology	- Reservoir → Wild birds & Mammals. - Vector → Mosquito, ticks & Sandfly. - Transmission → bite of infected vector.	
	Arboviruses associated with CNS disease → West Nile V → distributed in middle east.		West Nile V → Flaviviridae. → meningitis, encephalitis.
	Dx	- Isolation (Gold standard). - ELISA, IF (most used) → IgM antibodies.	<u>Prevention:</u> - Vector control.

		- RT-PCR → RNA.	- Vaccination: Tick-borne encephalitis vaccine, Japanese encephalitis vaccine.
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Multiple Choice and Short Answer Integrated Questions

-To open an answered sheet, please click [here](#)-

CASE - 1

A 15 years old teenager was admitted to the ER due to a dog's bite on his left leg. He had fever of 40°C. His parents reported that he was vomiting for the past three days after the incidence. On clinical examination, his leg appears swollen and erythematous. His lab results showed a viral infection manifested with Rabies.

At which phase of the disease is he?

- A. Incubation
- B. Neurological
- C. Prodromal
- D. Recovery

How can you treat a patient with such presentation?

Name five reservoirs that can cause Rabies Encephalitis:

What clinical manifestations are associated with the neurological phase of the disease?

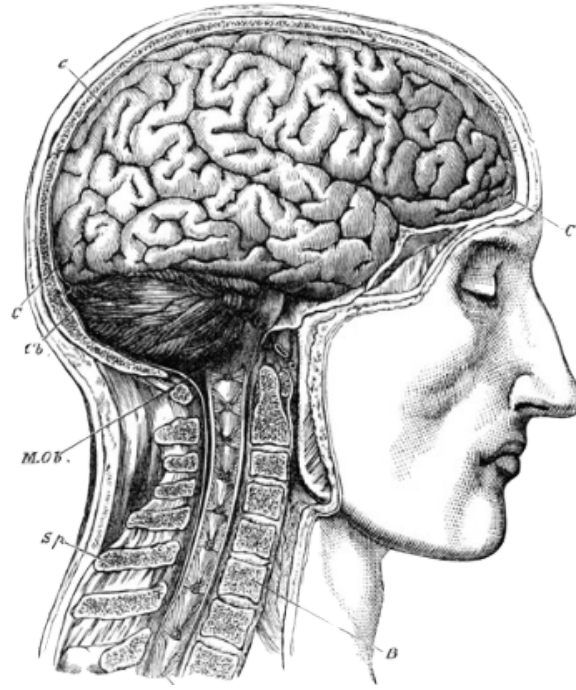
CASE - 2

A 27 year old female was presented to a hospital in the UK. After diagnosing her with meningitis, the doctor requested her an ICU stay with intravenous antibacterial and normal saline. After 24 hours, the patient died... In the mortgage, a group of doctors were investigating the cause of death, and their findings were as following:

- Multiple, small, red pigmentations on the skin, probably due to an insect bite.
- Immunofluorescence of her brain tissue showed evidence of a ssRNA viral infection.

Which virus of the following is the most probable cause of death?

- A. Herpes virus
- B. Enterovirus
- C. Rabies virus
- D. Arbovirus



كذَلِكَ يُبَيِّنُ اللَّهُ لَكُمْ آيَاتِهِ لَعَلَّكُمْ تَعْقِلُونَ ﴿٢٤٢﴾

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Heartful thanks to our phenomenal team members

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