

MICROBIOLOGY

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Number

2

Subject

Viral Encephalitis

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Viral Encephalitis

At the end of the sheet, there are 4 questions from 2016 exam. The order of this sheet is veryyy different from that in the record (sec. 1 record) and hopefully made easier.

Last time we talked about Aseptic Meningitis, which is inflammation of the meninges but with negative bacterial cultures.

Myelitis - Inflammation of the spinal cord.

Encephalitis - Inflammation of the brain parenchyma.

* Viral encephalitis is of two types:

1) **Primary (acute) encephalitis**

More common, caused by viruses that pass from blood stream into the CSF then directly to the brain, causing tissue damage in the brain parenchyma.

2) **Secondary (post-infectious) encephalitis**

Occurs following an acute, systemic infection (that caused inflammation in other organ/s in the body) and after recovering remnants of the virus remain and eventually go to the brain and get attacked by the body's immune cells.

* How to differentiate between meningitis and encephalitis?

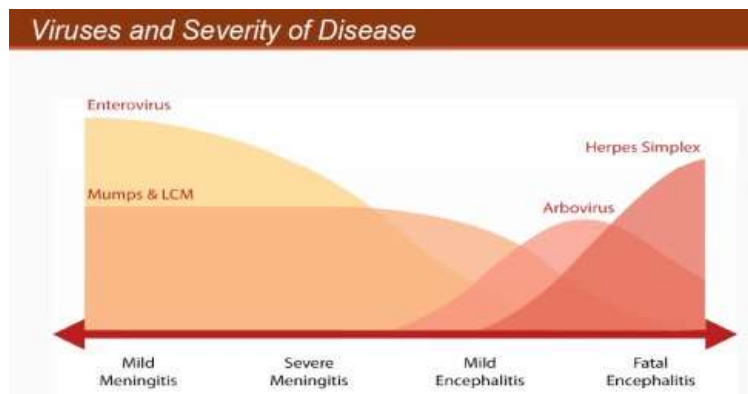
Meningitis patient presents with fever, headache, photophobia, lethargy, stiff neck (These can be present in encephalitis too!)

Encephalitis patient presents with clear neurological symptoms such as: altered level of consciousness, neural dysfunction, nerve palsies, paralysis, seizures, confusion & coma.

➔ A patient with symptoms of meningitis and encephalitis is diagnosed with "meningoencephalitis".

❖ What are the viruses that cause "Meningoencephalitis"?

- Herpesviridae
- Paramyxoviridae (parainfluenza, mumps, measles)
- Adenoviridae
- Rhabdoviridae
- Retroviridae (HIV)
- Enteroviruses



❖ Relating the severity of the disease to the causative agent:

- Mild meningitis → Enteroviruses
- Mild-moderate meningitis → Mumps & LCM
- Severe meningitis - moderate encephalitis → Arboviruses
- Fatal encephalitis → Herpes Simplex Virus (HSV)

❖ Secondary (post-infectious) encephalitis are caused by:

- I. **Measles** → “Subacute sclerosing panencephalitis” (1 in 100,000) characterized by: personality change, intellectual deterioration, spasticity, tremor.
- It occurs 2-10 years after infection.
- II. **Rubella** → “Progressive postrubella encephalitis” Associated with either persistent rubella infection of the CNS **or** late sequela of congenital rubella (transmitted to the fetus from his mother when she was pregnant) but manifested in him when he became an adult.
- III. **Polyomavirus JC** → “Progressive multifocal encephalopathy”
- In immunodeficient patients (requiring immunosuppressive therapy / AIDS).
- IV. **Enteroviruses** → They cause acute systemic infections that recover normally in most of the times but a very rare percentage develop secondary encephalitis.
- Characterized by: Headache, lethargy, confusion.
- It occurs in immunodeficient patients.
- Symptoms improve with immunoglobulins, but relapse on withdrawal.

➔ *There are no specific (antiviral) treatments for any of these secondary encephalitis.*

Arboviruses (ARthropod-BORne viruses)

- RNA viruses, most are enveloped.
- Arboviruses are not a family of viruses, **but a group of families**.
- They consist of: **Bunyaviridae, Flaviviridae & Togaviridae (Alphavirus)**

There are over 100 types of viruses in these 3 families and they were named according to the geographical location of where they were first identified.

e.g.) viruses of the Togaviridae family have very similar characteristics (structural, presentational, prevention, way of treatment and diagnosis) but they have different names because they were identified in different geographical regions.

- They are transmitted to humans via arthropod vectors (mosquitoes, ticks).
- Reservoirs are animals (birds, cattle, rodents, etc...).
- There are 2 transmission cycles
 - **Man – arthropod – man (Urban cycle)**
 - ⇒ e.g.) Dengue & urban yellow fever
 - ⇒ Reservoir is either man or arthropod (Transovarial transmission from arthropod).
 - **Animal – arthropod – man (Sylvatic/Jungle cycle)**
 - ⇒ e.g.) Japanese encephalitis, WEE, EEE & jungle yellow fever
 - ⇒ Reservoir is an animal.

WEE = Western equine encephalitis
EEE = Eastern equine encephalitis
VEE = Venezuelan equine encephalitis
✓ Both cycles is seen in the yellow

Arthropods acquire the virus by ingesting the blood of a viremic vertebrate and the virus replicates inside the arthropod **without causing any disease** and get excreted in their faeces. Both mosquitoes & ticks transmit the virus via biting.

Tick bites are itchy! When you itch your skin, faeces will get into the circulation carrying the virus then the virus spreads into your organs and sometimes to the CNS.

❖ *Examples of arthropod vectors:*

- **Aedes Aegypti** → They carry dengue, chikungunya, yellow fever & **zika virus**.
- **Culex Mosquito** → They can travel up to 15-20 km, and can cause an outbreak. They carry Japanese encephalitis & St. Louis encephalitis viruses.
- **Sandfly**
- **Ticks**

Zika virus

An old virus, many outbreaks happened decades ago.

Causes mild symptoms in children & adults, manifested by fever, rash & flu-like symptoms and recover with symptomatic treatment.

∞ Who are the most ones in risk of developing severe illness?

➔ Neonates; they get the virus from their pregnant mothers during pregnancy and they are born with microencephaly, CNS anomalies.

∞ An outbreak in South America happened last year; pregnant women were advised to avoid getting pregnant until the next 1-2 years so that the outbreak is gone.

∞ The old vaccine is not working anymore, scientists are currently working on making a new “killed-virus vaccine” and will be done in the next 5-10 years and this vaccine is safe for pregnant women, unlike the live-attenuated vaccines which are risky.

❖ *Diseases caused by Arboviruses* (الترتيب حسب الظواهر الأكثر شيوعاً)

- 1) Most commonly, the infection is subclinical (asymptomatic) * mentioned in sheet 1*
- 2) Minimal symptoms stage: fever, rash & flu-like symptoms
- 3) Encephalitis: Japanese encephalitis, St. Louis encephalitis, EEE & WEE
 - CNS symptoms in EEE develop 4-10 days after being bitten.
 - Mortality rate is 40-50% if any of these infections progressed to encephalitis
 - West Nile infection: 1/5 will develop symptoms & 1/150 will get encephalitis.
- 4) Hemorrhagic fever: Dengue, Yellow fever, or Crimean-Congo fever.
 - The patient will bleed externally or internally, might get a hypovolemic shock but our most concern of hemorrhagic fever is multi-organ failure.

❖ *Structure of Togaviruses (Alphavirus)*

- (+ sense) ss-RNA, encapsulated, with Icosahedral capsid
- They have two glycoproteins (spikes): E1 & E2
- Examples: EEE, WEE, VEE; they are common in North & South America and they are transmitted via animal-**mosquito**-human cycle.

❖ *Structure of Flaviviruses*

- (+ sense) ss-RNA, encapsulated, with Icosahedral capsid
- Examples:
 - * Murray valley virus – Australia
 - * Powassan virus – Canada
 - * St. Louis encephalitis – America
 - * Japanese encephalitis – Japan, China & South-East Asia
 - * Tick-borne encephalitis – Europe & Asia
 - * West Nile virus – World-wide

Japanese encephalitis

- ✓ Most infectious are subclinical, just like other Arboviruses
 - ⇒ Unapparent (asymptomatic) to clinical cases ratio is 300:1 and this means that for every 1000 cases, only 3 will develop symptoms.
- Life-threatening encephalitis occurs in clinical cases
- No specific antiviral therapy is available

❖ *Structure of Bunyaviruses*

- (- sense) ss-RNA spherical, enveloped viruses
- They have two glycoproteins: G1 & G2
- They contain three nucleocapsids: S, M, L (small, medium, large)
 - In some references, you might read that Bunyaviridae are segmented viruses, although they are NOT but the nucleocapsid surrounding them is segmented into 3 parts and each part can encode for more than one protein;
 - M → encodes for G1, G2 & non-structural proteins
 - S → encodes for non-structural proteins
 - L → encode for L protein
- Examples: California encephalitis, Rift valley fever & La crosse → They all can cause encephalitis and travel via mosquito vector.
- They can cause hemorrhagic fever with renal syndrome.
- Rift valley fever can cause retinitis & hepatitis.
- Hantavirus can cause pulmonary syndrome.

❖ *Diagnosis for all Arboviruses*

The golden rule is Serology.

Culturing & antigen/nucleic acid detection in cell line can be used but it's not done routinely due to safety issues; they need to be done a lab with a bio-safety level of 3 or 4.

❖ *Prevention*

- Surveillance (مراقبة) of disease and vector populations.
- Control of vector – pesticides, elimination of breeding grounds.
- Personal protection – house screening, bed nets, insect repellants, protective clothes
- Vaccination - Yellow fever, Japanese encephalitis, Russian tick-borne encephalitis, Dengue (developed in 2010)

❖ *Treatment*

Treatment of all Arbovirus infections is symptomatic, depending on the presented case (antipyretics for fever, plasma/fluids for blood loss, painkillers for pain, etc...)

No specific antiviral therapy.

Now we finished talking about Arboviruses. Let's talk about other causes of viral encephalitis...

Herpes Simplex Encephalitis

- HSV-1 is more associated with encephalitis
- HSV-2 is more associated with meningitis

Keep in mind that both HSV types can cause either of the diseases!

There are two types of HSV encephalitis:

- Neonatal HSV encephalitis
 - The baby gets the virus from his mother passing the birth canal during labour
 - Brain becomes liquefied. With a mortality rate of 100% even with treatment :(
 - Avoided by giving birth via Caesarean-section.
- Focal HSV encephalitis
 - Can occur in children or adults
 - Temporal lobe is commonly affected
 - IV acyclovir is given when suspected, Mortality rate is 70% without treatment.

Paramyxoviridae Encephalitis

- Genus Henipaviruses – consists of Hendra virus & Nipha virus.
 - Outbreaks in Malaysia, Singapore & Bangladesh
 - They can cause severe, rapidly progressing encephalitis with high mortality rate.
 - Main reservoir is fruit bats (flying fox) and the virus sheds in their urine
- Pigs get infected with henipaviruses when exposed to excretions of fruit bats and develop severe RS tract infection.
- Transmission to humans:
 - Direct contact with infected pigs or with their respiratory/urinary secretions
 - No bat-to-human transmission
 - No human-to-human transmission

❖ Human illnesses caused by *Henipaviruses*:-

- Incubation period of 1-2 weeks
- Most patients present with fever, headache, respiratory symptoms & encephalitis (drowsiness, dizziness & comatose in 1-2 days)
- Few patients get infected but asymptotically.

Later on, when asymptomatic patient's immunity drops, encephalitis might relapse and then he will develop symptoms.

In a little percentage of those asymptomatic patients, remnants of the virus stay in the CNS and get attacked by body's immune cells, resulting in: residual neurological deficits (Secondary post-infectious encephalitis).

- Treatment is supportive, some patients respond to ribavirin.
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Dr. Ashraf's questions in last year's exam, first 2 are for the first 2 lectures:-

- 1- True – HSV-2 is harder to diagnose due to absence of genital infection
- 2- A question about "What is not caused by Arboviruses"
- 3- A patient with CJD, wrong – his survival median is 14 months
- 4- Only bad thing about OPV compared to IPV – rarely can cause paralytic poliomyelitis

The sheet is over, good luck.