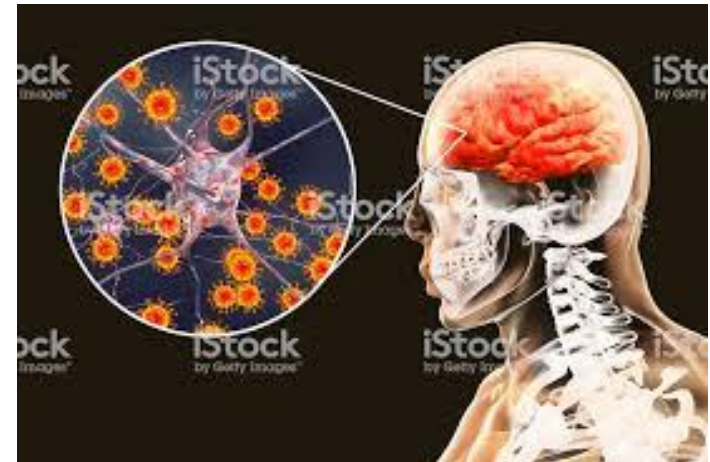


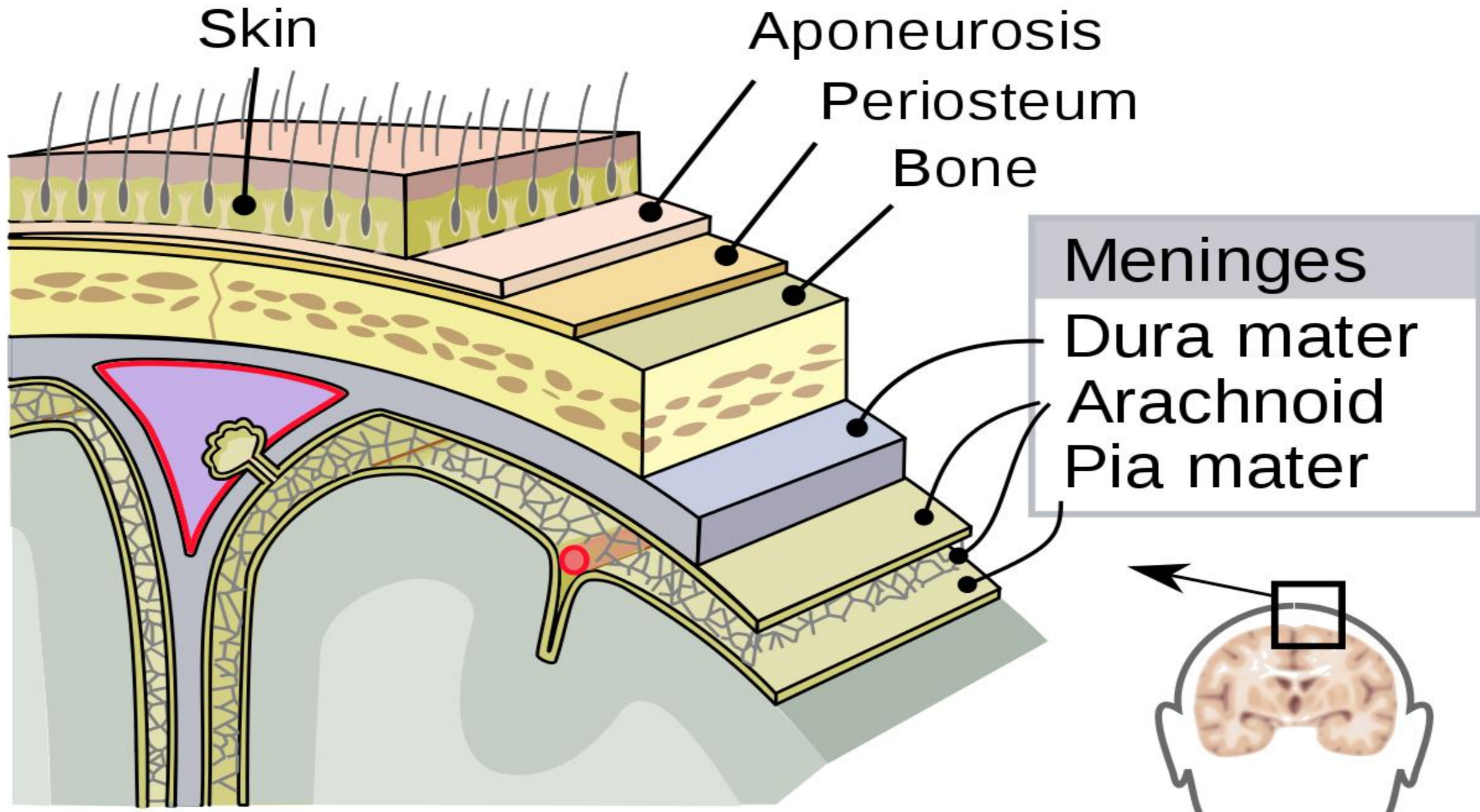
VIRAL INFECTIONS OF THE CENTRAL NERVOUS SYSTEM

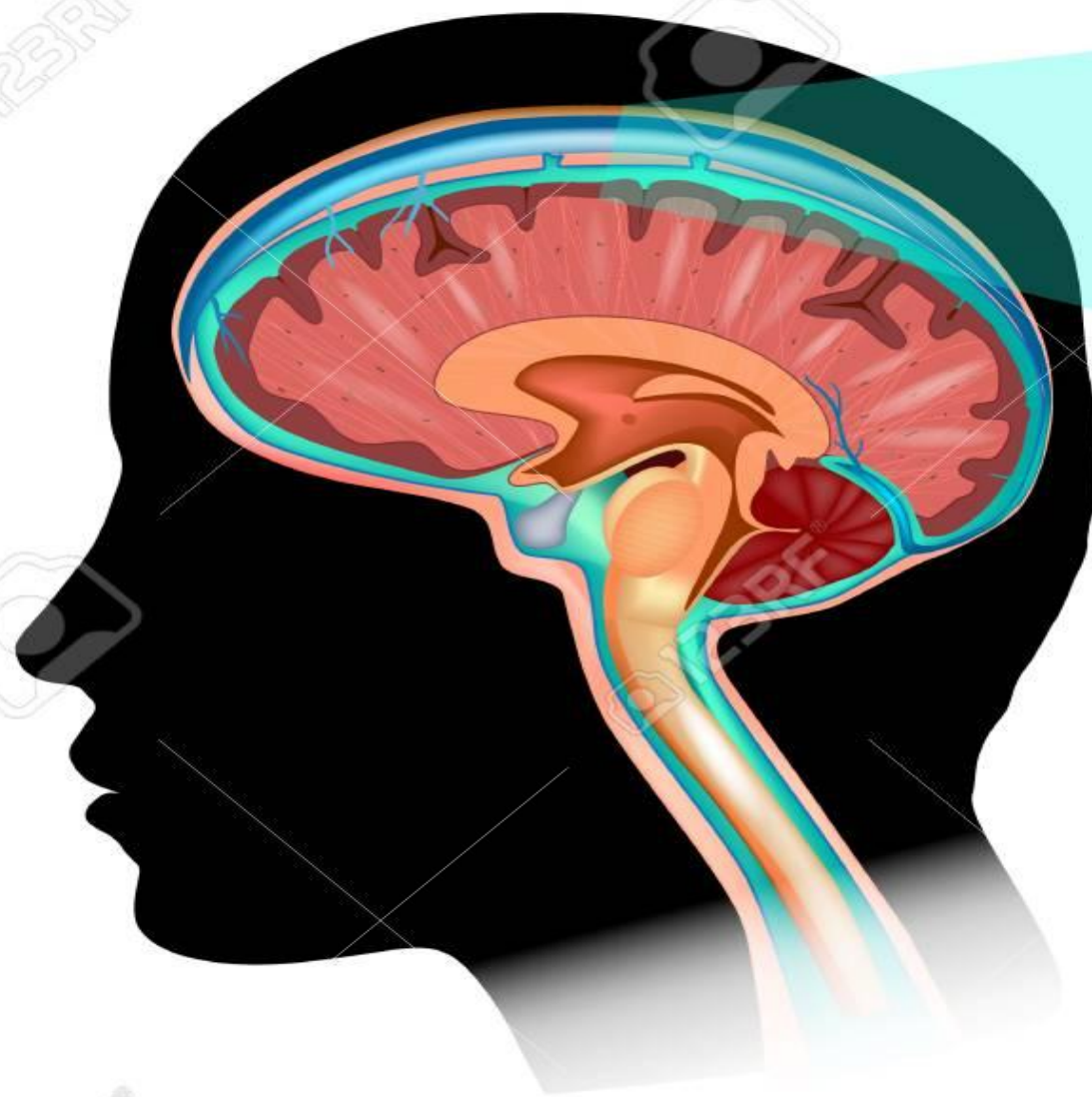
Asso. Prof Biljana Popovska Jovičić

Viral infections of the central nervous system

- Viral infections of the CNS include several different clinical syndromes that are divided depending on the symptoms that follow them in certain anatomical structures:
- Viral meningitis
- Encephalitis
- Meningoencephalitis
- Encephalomyelitis
- Cerebellitis







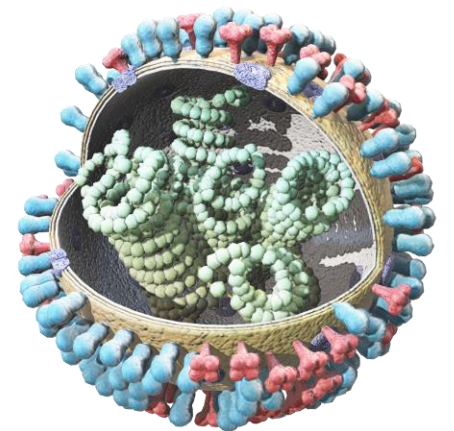
Labels for the detailed view of the meninges:

- Periosteal dura mater
- Superior sagittal sinus (venous blood)
- Meningeal dura mater
- Subarachnoid space
- Arachnoid mater
- Cerebral cortex
- Arachnoid villus



Meningeal syndrome

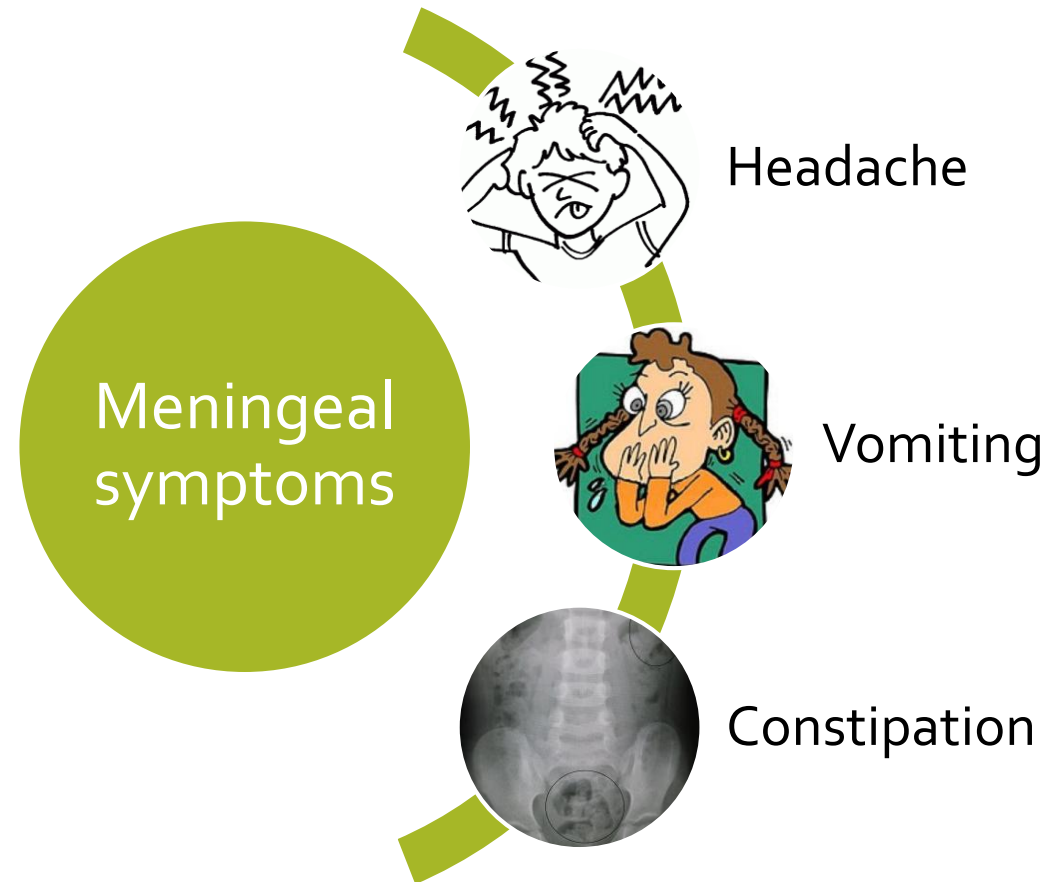
- Meningeal syndrome is a set of symptoms and signs that occur as a result of increased intracranial pressure. During a CNS infection, increased intracranial pressure occurs
- **Possible causes of increased intracranial pressure are:**
 - Disorder of cerebrospinal fluid dynamics
 - Brain edema
 - Disorder of cerebral circulation



Meningeal syndrome

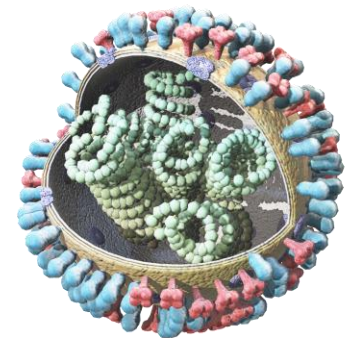
- **The consequences of increased intracranial pressure are a decrease in cerebral perfusion pressure (CPP), brain hypoxia, and neuronal damage.**
- **Meningeal symptoms and signs occur due to increased intracranial and intraspinal pressure** on the brain, anterior and posterior roots of the spinal cord (defensive reflexes to additional increased intracranial and intraspinal pressure)

Meningeal symptoms



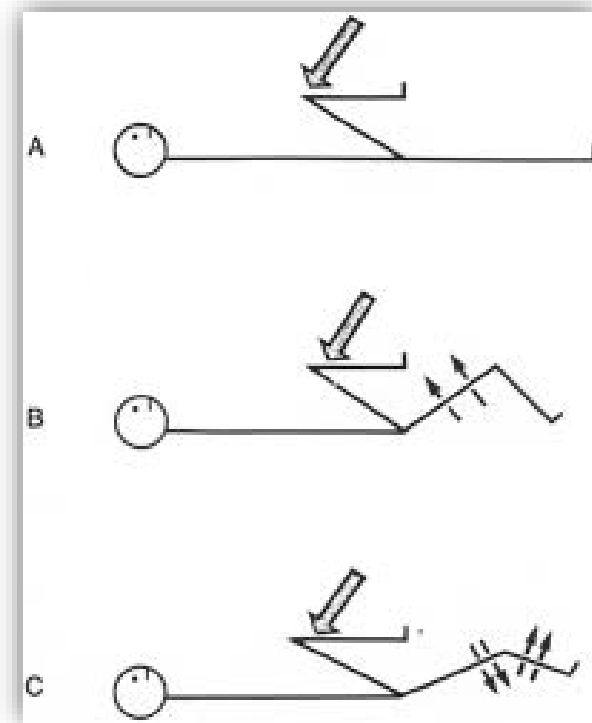
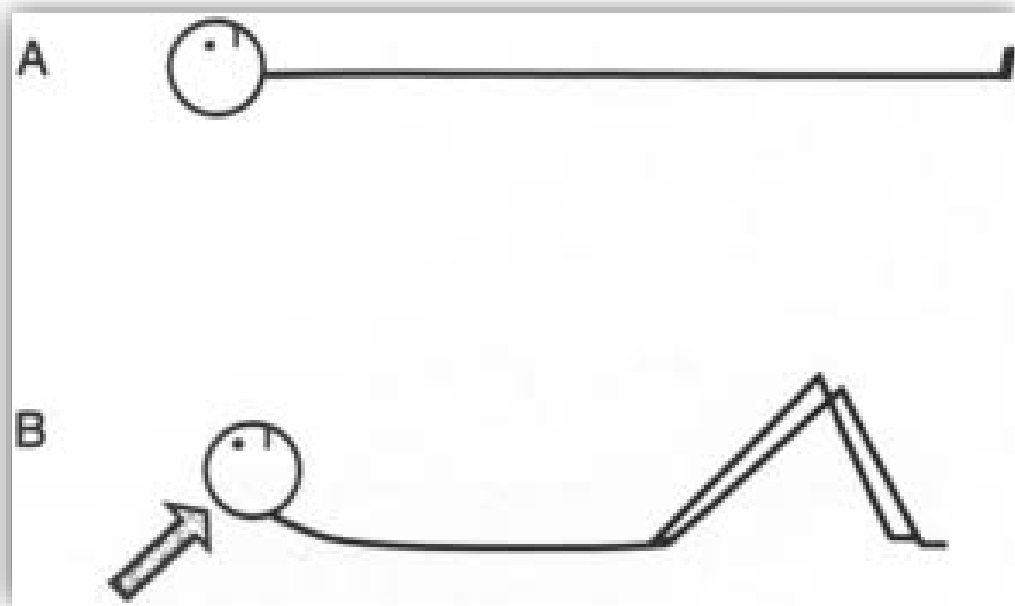
Meningeal signs

- Stiff neck
- Kernig's sign
- Bružinski (upper and lower)
- Vujić's sign
- Meningeal position
- Tense fontanelle



Meningeal signs

Bružinski (upper and lower)

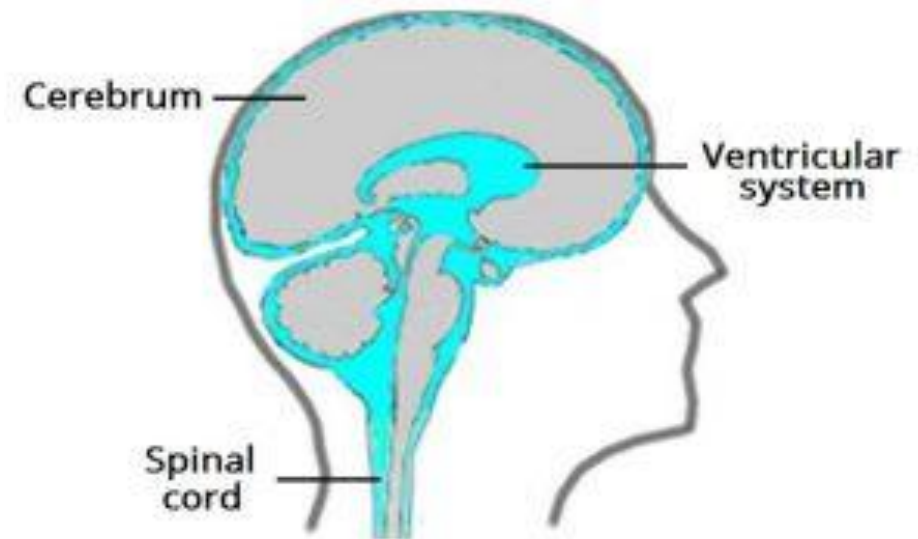


CSF SYNDROME

- CSF pressure
- Cerebrospinal fluid appearance
- Number and type of cellular elements
- Proteins in cerebrospinal fluid
- CSF glucose or glycorrachia
- Chlorides

NORMAL APPEARANCE OF CSF

- NORMAL PRESSURE
- CLEAR COLORLESS LIQUID CONTAINS UP TO 5 LYMPHO-MONOCYTES IN 1 mm³
- PROTEIN RATE LESS THAN 0.40 g/L
- CSF glucose – $\frac{1}{2}$ TO $\frac{2}{3}$ OF SERUM GLYCEMIA
- CHLORIDES DEPEND ON THE DEGREE OF DEHYDRATION



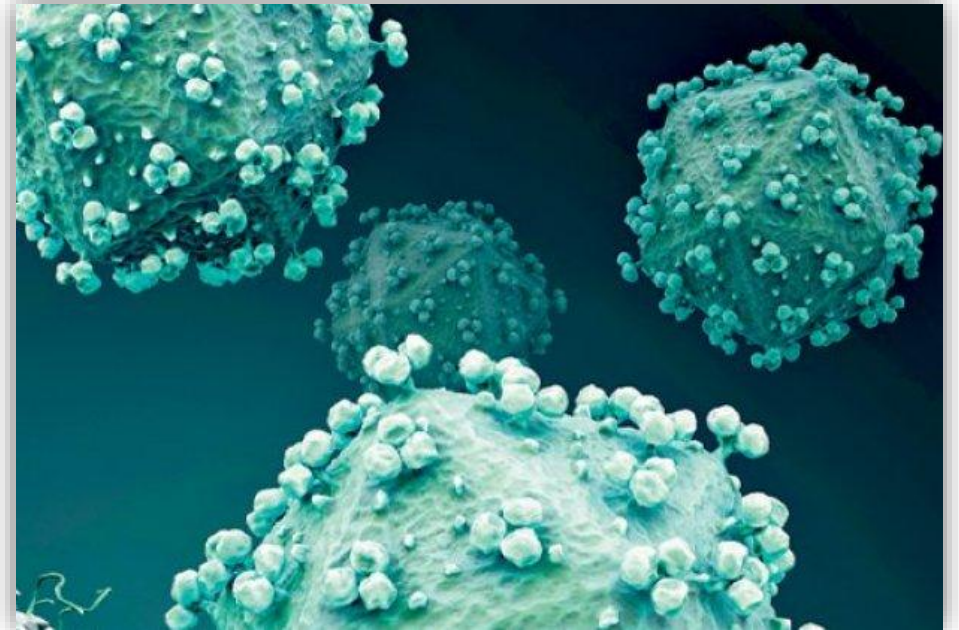
Viral meningitis

- It represents inflammation of the soft meninges, caused by various viruses with a favorable clinical course and good prognosis
- Aseptic meningitis - lymphocyte dominance, the cause of which cannot be determined after initial clinical examinations and cerebrospinal fluid culture
- Viral meningitis can be caused by various viruses



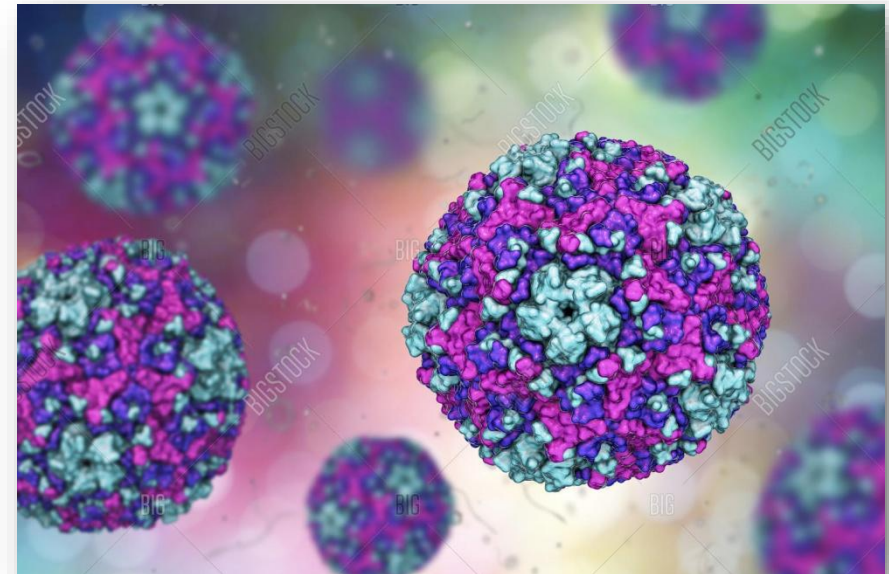
Etiology and epidemiology of viral meningitis

- PICORNAVIRIDAE – ENTEROVIRUSES
- PARAMYXOVIRIDAE - MUMPS VIRUS
- ARBO (St. Louis)
- ARENA VIRUSES – LCM
- HERPES VIRUSES (VZV, CMV, EBV, HSV)
- HIV
- ADENOVIRUSES
- VIRUS INFLUENZAE A, B
- PARAINFLUENZA VIRUS



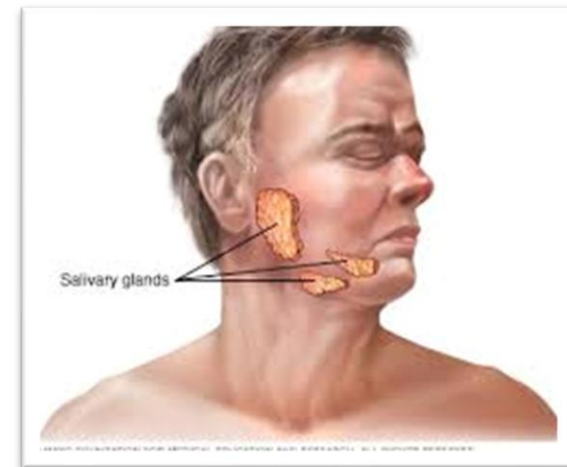
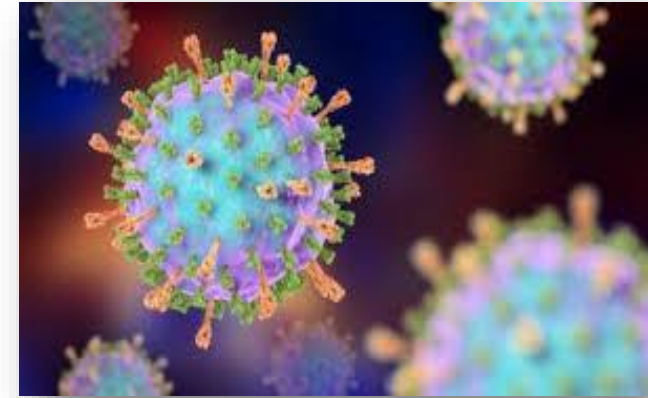
Enteroviruses

- RNA viruses
- Almost all serotypes can cause meningitis
- They are among the smallest viruses discovered
- They are transmitted feco-oral and by droplets
- Acid-resistant viruses
- They are excreted from the digestive tract for a much longer time
- Infection is prevalent during the summer months



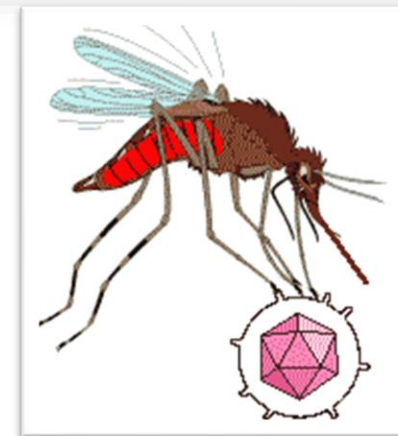
Mumps virus

- RNA virus
- There is only one serotype of the virus
- Highly neurotropic
- 40-50% of patients do not have any manifestations of mumps
- Droplet transmission
- Winter, early spring



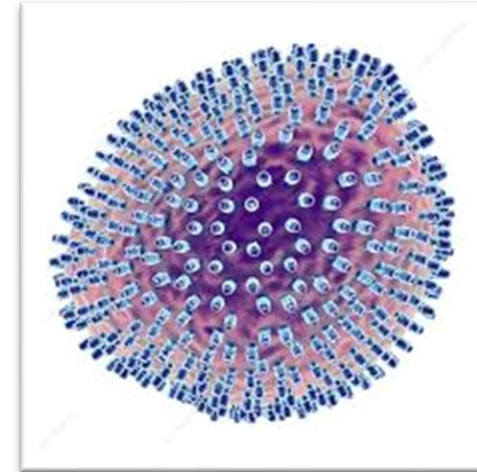
Arboviruses

- RNA virus
- A group of over 500 viruses from different families West Nile virus, St. Louis virus, TBEV..
- Most often cause encephalitis
- Domestic animals are the reservoir of the virus
- Transmission of infection is most often through a tick or mosquito bite



Lymphocytic choriomeningitis (LCMV virus)

- ARENA viruses
- RNA viruses
- Reservoir of infection: rodents, mainly house mice
- Aseptic meningitis, prolonged course
- Winter and early spring
- Elderly, rural environment



Herpes viruses

- HSV₁, HSV₂, VZV, HHV 6, HHV 7, EBV
- DNA viruses
- HSV₂ more often causes meningitis
- HHV 6 in children after a three-day fever
- EBV – meningitis is rarely the only manifestation
- Other viruses: HIV, Influenza A, B, adenoviruses, measles...



Pathogenetic mechanisms of viral meningitis

Viral entry site (skin, respiratory tract, fecooral...)

Viral colonization

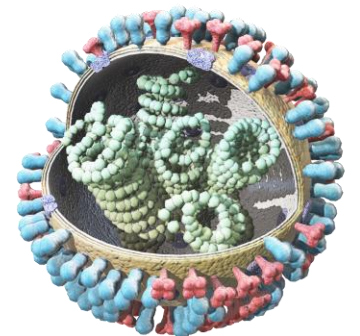
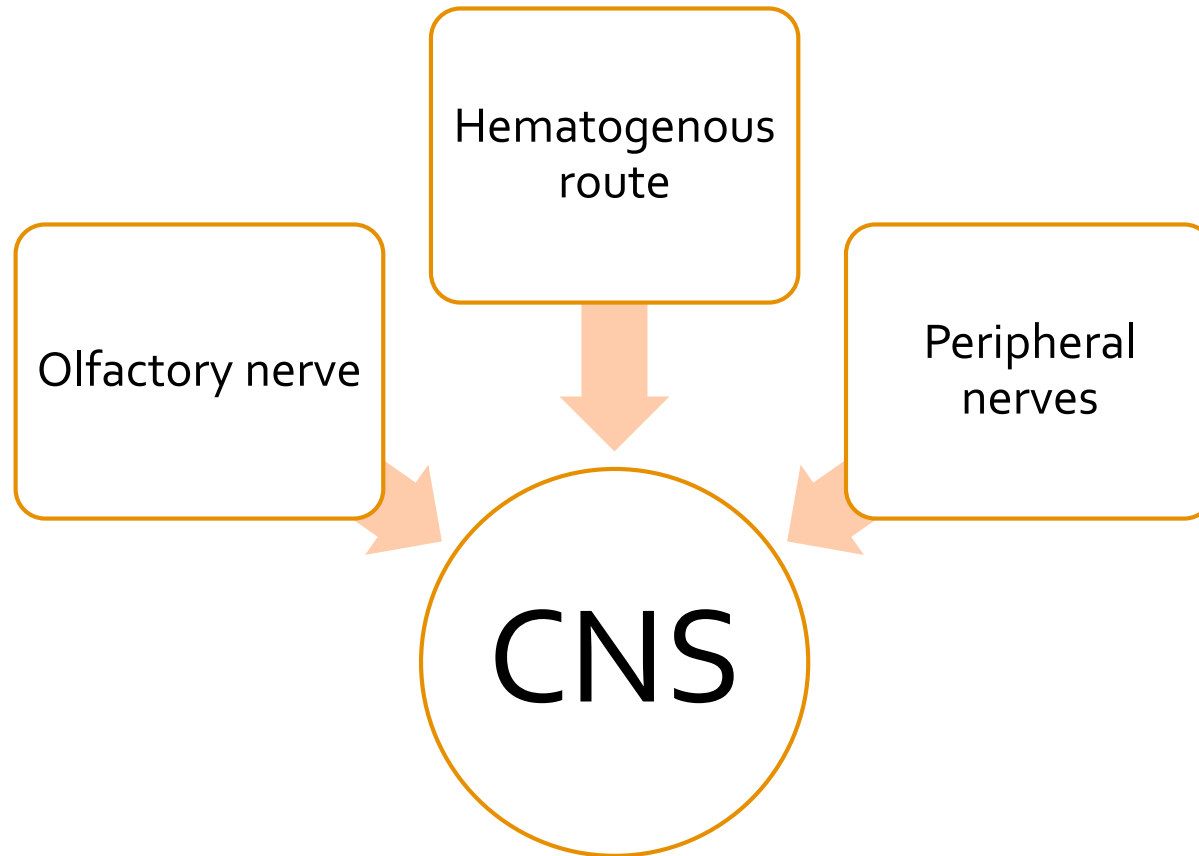
Host defense mechanisms

Secondary viremia

CNS entry

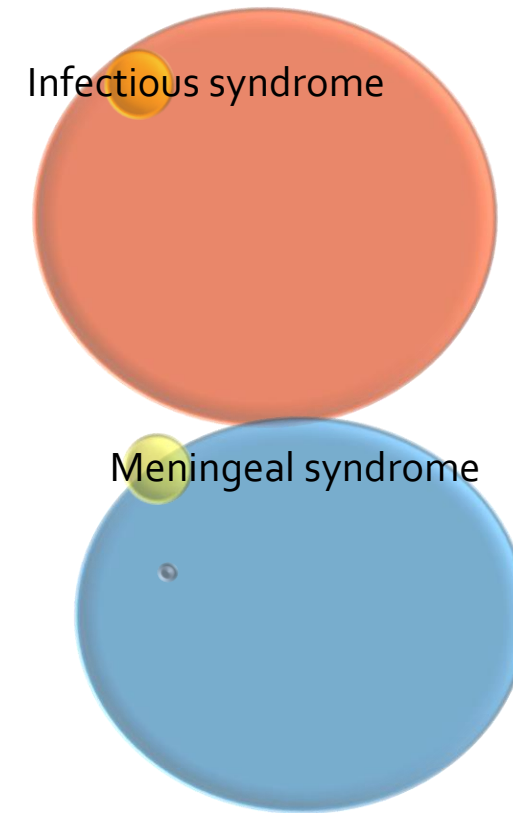
CNS inflammation

Virus entry into the CNS



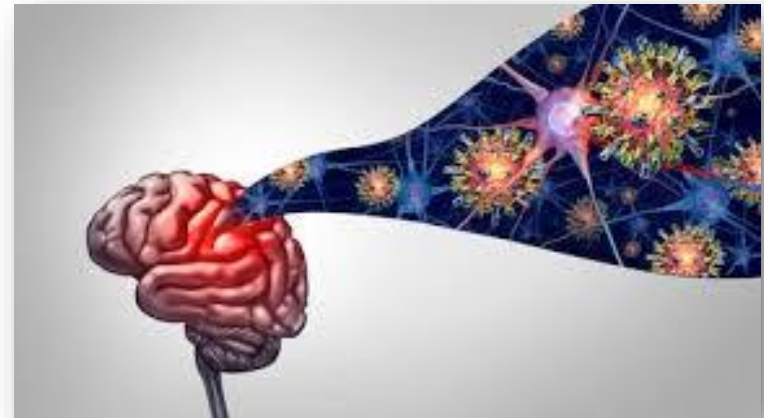
Clinical picture of viral meningitis

- Sudden onset
- Fever
- Headache
- Photophobia
- Vomiting
- Neck stiffness
- Short clinical course
- Good prognosis



Complications of viral meningitis

- Complications are rare because the disease has a good prognosis and resolves without sequelae
- However, they are possible depending on the age of the patient and the host's immune system
- Severe sequelae occur in the neonatal period
- Severe clinical picture in immunodeficient individuals (congenital or acquired)

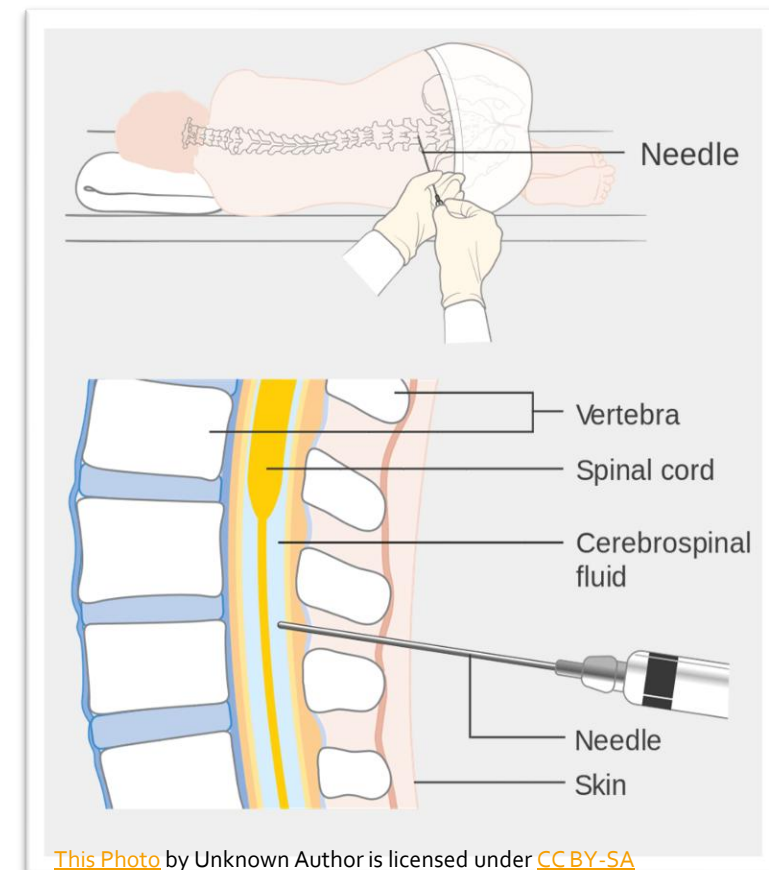


Diagnosis of viral meningitis

- Clinical picture
- Cerebrospinal fluid examination (cytobiochemical findings)
- Etiological diagnosis:
 - ✓Molecular diagnostics (Polymerase chain reaction-PCR CSF)
 - ✓Serological diagnostics (ELISA, Ag detection)
 - ✓Viral cultivation

Cerebrospinal fluid examination in viral meningitis

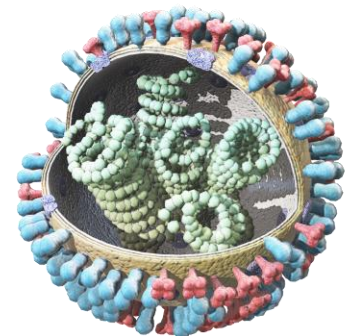
- INCREASED PRESSURE
- CLEAR COLORLESS LIQUID
- CONTAINS 10 TO 500 LYMPHOCYTES IN 1 mm³
- PROTEIN 0.40 g/L TO 1.0 g/L (SLIGHTLY INCREASED)
- CSF glucose IS NOT REDUCED (1/2 TO – 2/3 OF SERUM GLYCEMIA)



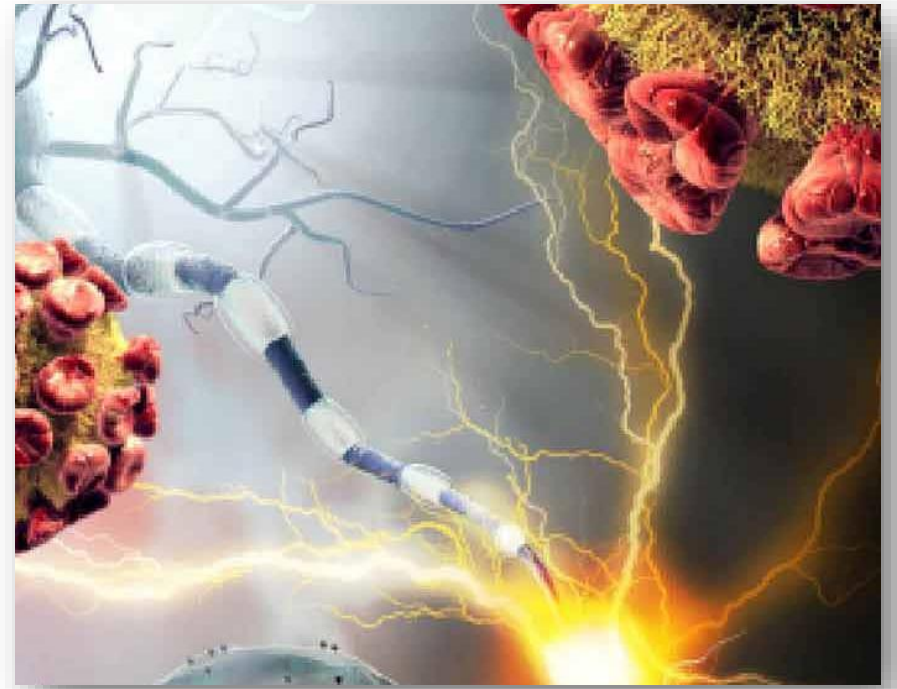
Therapy of viral meningitis

- Therapy is **primarily** symptomatic
- Rehydration
- Analgesics
- Antipyretics
- Correction of electrolyte imbalance
- Antiedematous therapy (furosemide, mannitol)
- **Anti-inflammatory therapy (corticosteroids) rarely indicated**

❖ Specific antiviral therapy is applied in case of detection of the etiological agent (Acyclovir, Preconaril...)



Acute viral encephalitis



Acute viral encephalitis

- Acute viral encephalitis is an inflammatory disease of the brain parenchyma caused by viruses
- Damage to the brain parenchyma can occur directly by the virus or indirectly by immune mechanisms
- Characteristics of encephalitis are sudden onset, progressive course, high risk of disruption of vital functions and uncertain outcome with possible complications and consequences



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Etiology of viral encephalitis

- Any virus can cause encephalitis
- However, there are viruses that have a greater tropism for the CNS than some other viruses

The most common causative agents of acute viral encephalitis

Herpes simplex viruses type I

Herpes simplex viruses type II

Varicella zoster virus

Enteroviruses

Human immunodeficiency virus (HIV)

Influenza A and B viruses

Rubella virus

Morbilli virus

Cytomegalovirus

Lymphocytic choriomeningitis (LCM) virus

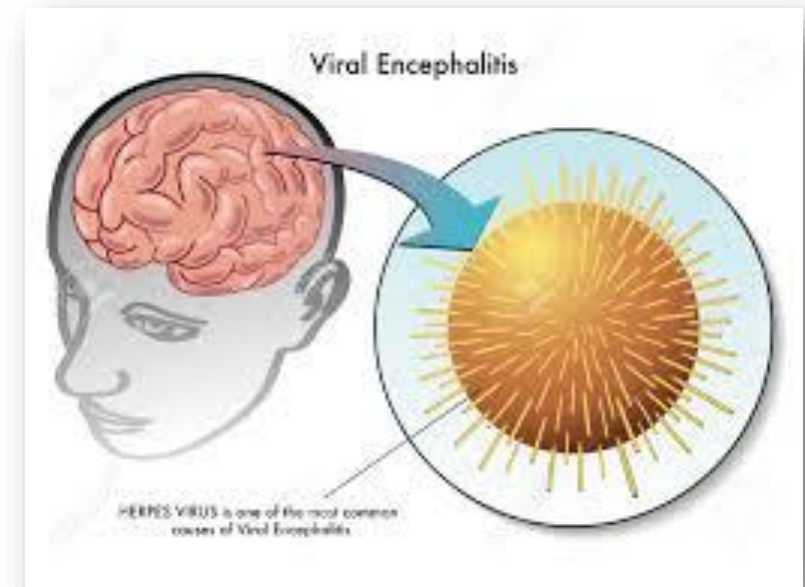
Epstein-Barr virus

Rabies virus

Arboviruses

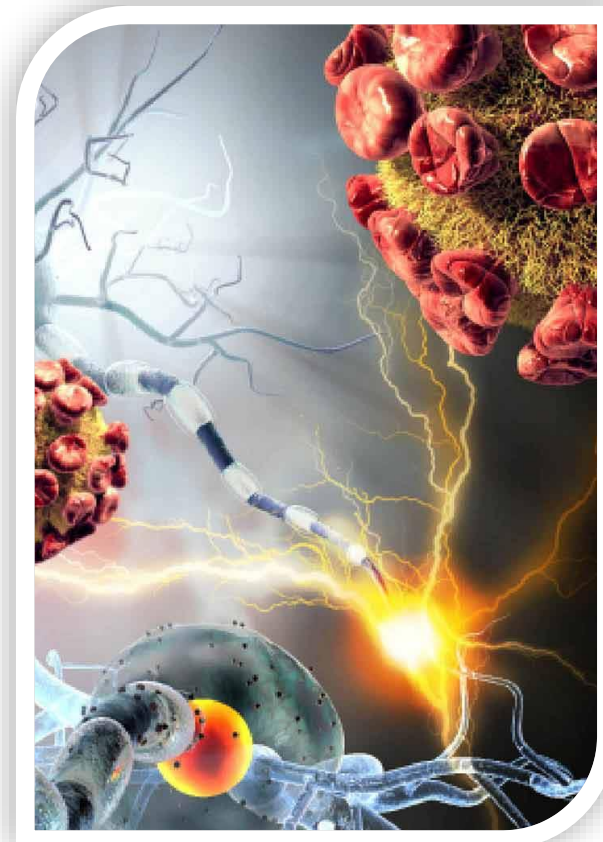
Epidemiology of viral encephalitis

- They can occur sporadically or epidemically
- In Europe, encephalitis mostly occurs sporadically (HSV, VZV, CMV, HIV, EBV...)
- Smaller epidemic encephalitis occurs with enteroviruses
- Since 2012, West Nile virus (mosquitoes) has been occurring in Serbia in smaller epidemics
- In the world, epidemic encephalitis occurs with arbovirus infections, which is directly related to vectors



Modes of transmission of viruses to the CNS

Hematogenous pathway	Neural pathway	Olfactory pathway
<ul style="list-style-type: none">• Coxsackie virusi• HIV• CMV• VZV• EBV• Arbo virusi• LCM• Morbilli	<ul style="list-style-type: none">• HSV₁• HSV₂• VZV• Rabies virus	<ul style="list-style-type: none">• HSV₁



Pathogenetic mechanisms of viral encephalitis

Hematogenous route of transmission



VIRUS ENTRY INTO THE HOST ORGANISM



PRIMARY REPLICATION

respiratory tract, gastrointestinal tract, skin, lymph nodes



SECONDARY REPLICATION

endothelium of blood vessels, reticuloendothelial system, muscle



VIREMIA

general infection-febrile

CHORIOID PLEXUS

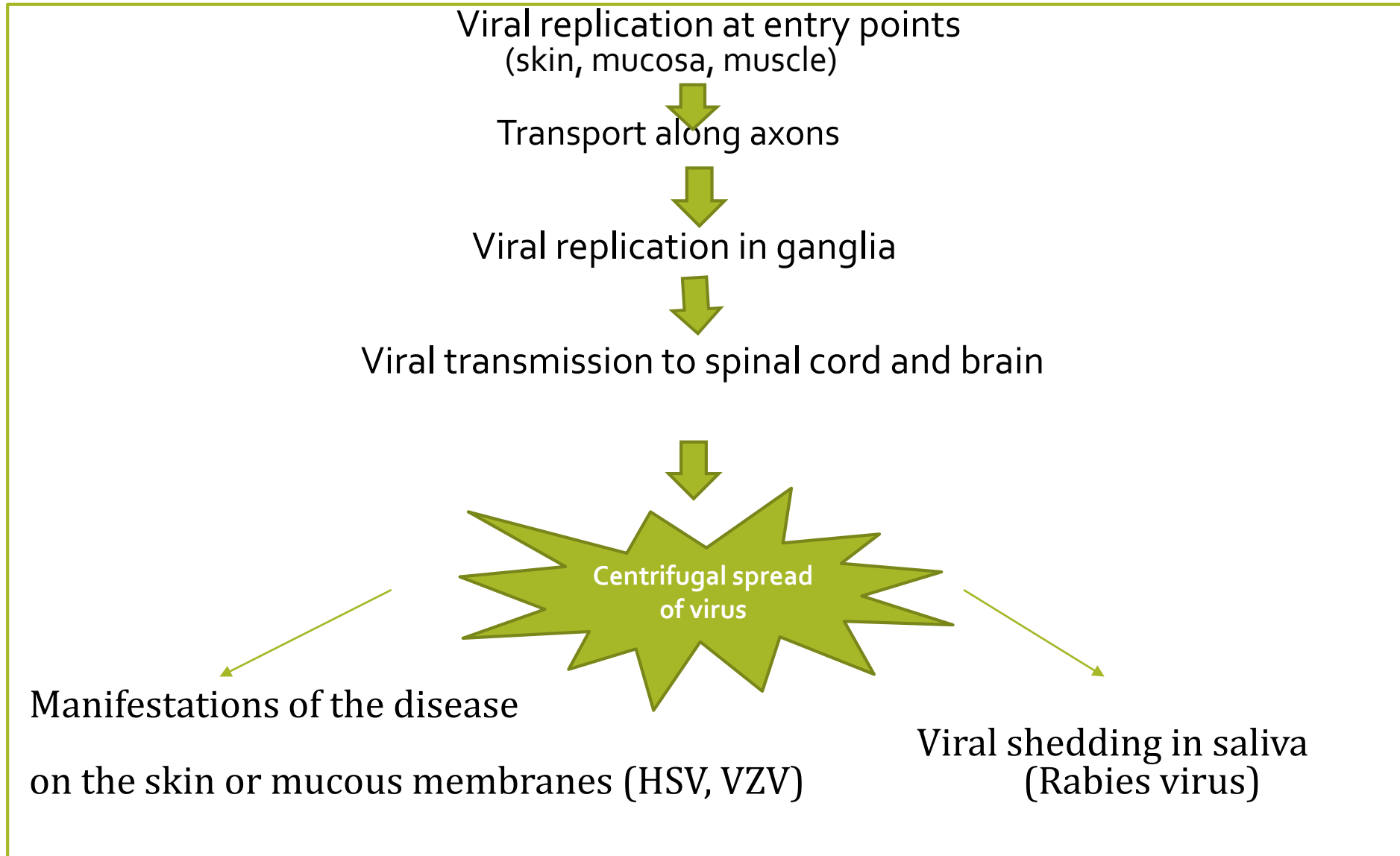


CEREBROSPINAL FLUID

Brain
parenchyma
(encephalitis)

Pathogenetic mechanisms of viral encephalitis

Neural pathway of virus transmission



Clinical picture of acute viral encephalitis

INCUBATION - differs in etiological agents

PRODROME- gradual, difficulty concentrating, hypersensitivity to stimuli....

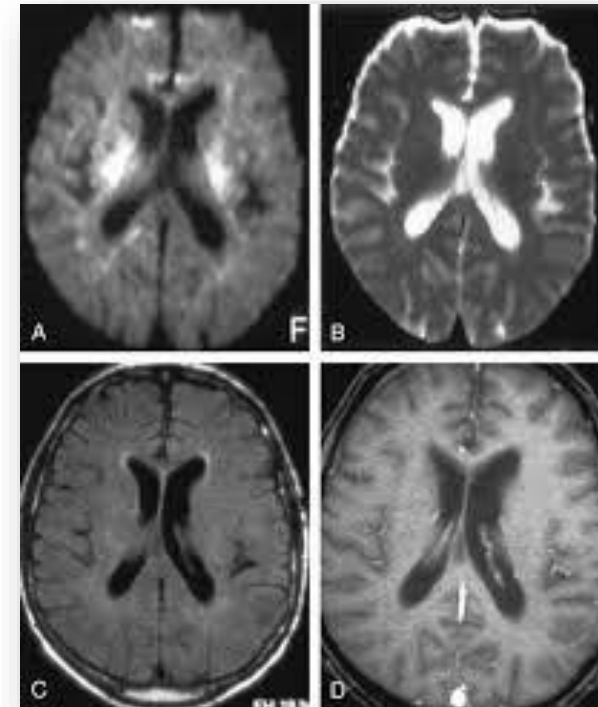
ACUTE NEUROLOGICAL DISEASE

OUTCOME

PERIOD OF STRUCTURAL AND FUNCTIONAL RECOVERY

Acute neurological disease

- Infectious syndrome
- Headache, severe diffuse
- Vomiting and painful neck stiffness occur in up to 50% of patients
- A large number of patients have dysarthria and dysphasia
- One of the most common clinical manifestations is impaired consciousness (quantitative and qualitative)
- Confusions are very common, sometimes as an initial manifestation
- Cranial nerve lesions
- Hemiparesis and hemiplegia



- COMPLICATIONS: status epilepticus, ARI, pneumonia, hyper/hypothermia, hypo/hypertension, shock, erosive gastritis, secondary infections, sepsis, psychosis, decubitus ulcers, contractures
- OUTCOME-mortality is 3-30%, sequelae 3-70%
- Sequelae directly related to the patient's age and the severity of the neurological disorder



DIAGNOSIS

EPIDEMIOLOGY

CLINICAL PICTURE

CSF EXAMINATION

CSF is clear

9-100 lymphomonocytes in mm³

Proteins in CSF is above 0.5 gr/l

Glucose in CSF is normal or slightly elevated

VIROLOGICAL TESTS:

polymerase chain reaction (PCR) - the most reliable method

Serological diagnostics (ELISA) - detection of intrathecally synthesized antibodies to viral antigens

Detection of viral antigens - immunofluorescence, immunoperoxidase, radioimmunoassay

Virus isolation from tissue culture - of limited importance in acute infections

OTHER TESTS: EEG, CT, MR, ECG, X-rays

Therapy of acute viral encephalitis

Patients are treated in Intensive Care Units

ASSESSMENT OF VITAL FUNCTIONS:

consciousness,

breathing,

heart rate and circulation,

diuresis

TREATMENT OF PSYCHOMOTOR RESTLESSNESS: **Diazepam** 0.15-0.25 mg/kg body weight, **Midazolam** i.v./i.m.

TREATMENT OF CONVULSIONS: Diazepam i.v. 0.15 mg/kg body weight, Phenobarbitone 100-200 mg i.v.

Therapy of acute viral encephalitis

ANTI-EDEMA THERAPY:

patient position,

oxygenation,

reduction of fluid intake, Mannitol 20% 0.5-2.0 gr/kg bw per 24h,

Furosemide 0.25 mg/kg bw, human 20% albumin 1-2 ml/kg

ANTIVIRAL THERAPY:

Include Acyclovir in all patients with suspected viral encephalitis until etiological confirmation

In the case of an etiological diagnosis of viral encephalitis, include causal therapy, if available

Immunomodulatory therapy: corticosteroids?

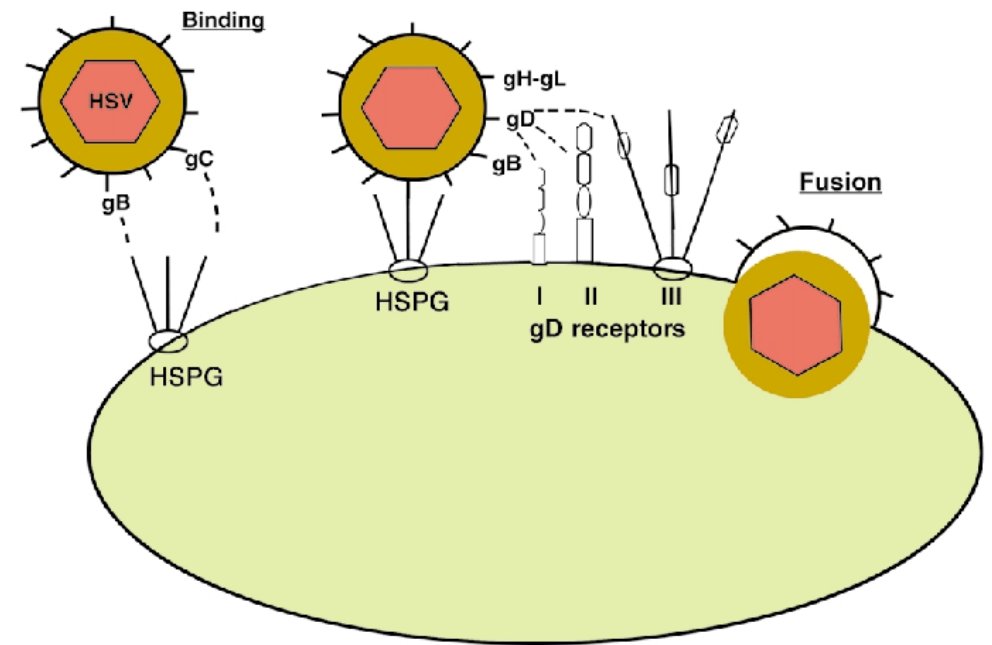
Prevention of secondary infections

Prevention of erosive gastritis

Physical therapy

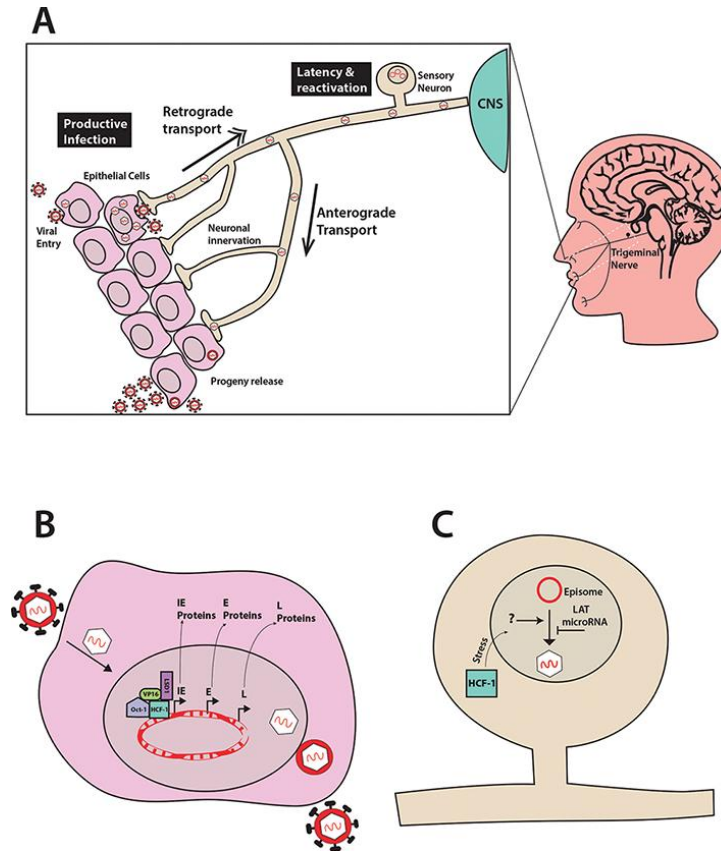
HERPES SIMPLEX ENCEPHALITIS

- The most common sporadic form of encephalitis
- It represents acute inflammation, congestion or hemorrhage that is most often localized in the temporal lobe in adults
- The causative agent is HSV-1, and much less often HSV-2
- Double-stranded DNA
- Homology between HSV-1 and HSV-2 about 50%
- HSV binds to the host cell with the help of glycoproteins B and S, as well as glycoprotein D, which plays a role in the tropism of HSV for certain tissues



HERPES SIMPLEX ENCEPHALITIS

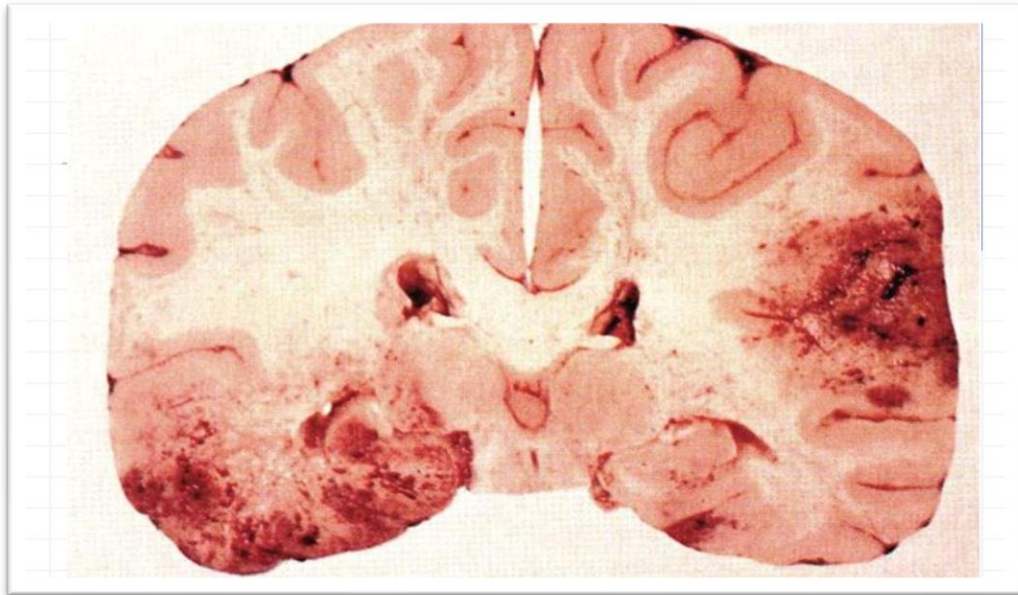
- Modes of transmission of the virus to the central nervous system:
- Primary infection with HSV-1 virus
- Reactivation of HSV-1 virus from the trigeminal ganglion and autonomic ganglia
- Reinfection with another type of HSV-1 virus



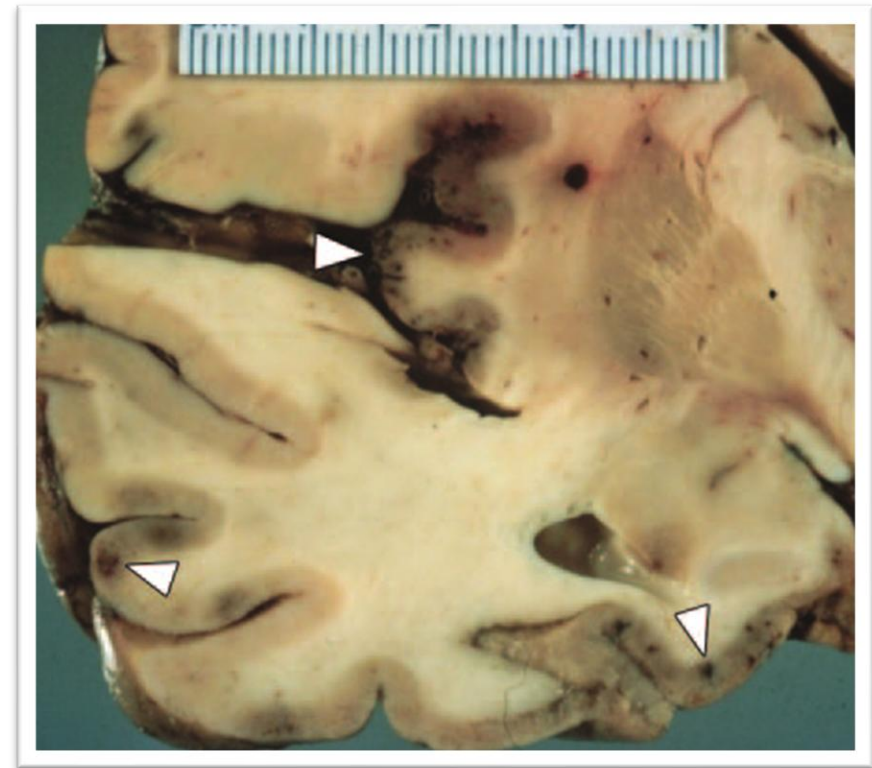
Clinical picture of herpetic encephalitis

- Infectious syndrome
- Confusion
- Psychomotor restlessness
- Focal neurological findings
- (convulsions, cranial nerve lesions, hemiparesis, hemiplegia)
- Consciousness disturbance (somnolence, stupor, coma)

Pathohistological findings of acute herpetic encephalitis



In the early stage of the disease, the changes are nonspecific and include capillary congestion, and petechiae are possible. Later, hemorrhagic necrosis develops, with subsequent gliosis.



Uploaded by [James George Smirniotopoulos](#)

- ✓ Multiple petechial hemorrhages and granular atrophy of the cortex and medial temporal lobe

Diagnostic procedures

Cerebrospinal fluid examination - clear cerebrospinal fluid, mild pleocytosis (lymphocytes, rarely erythrocytes), elevated protein level, normal glycorragic values

Polymerization chain reaction (PCR), detection of HSV-1 genome in cerebrospinal fluid - the most reliable method

Serological diagnostics (ELISA) - detection of intrathecally synthesized antibodies in the IgM class

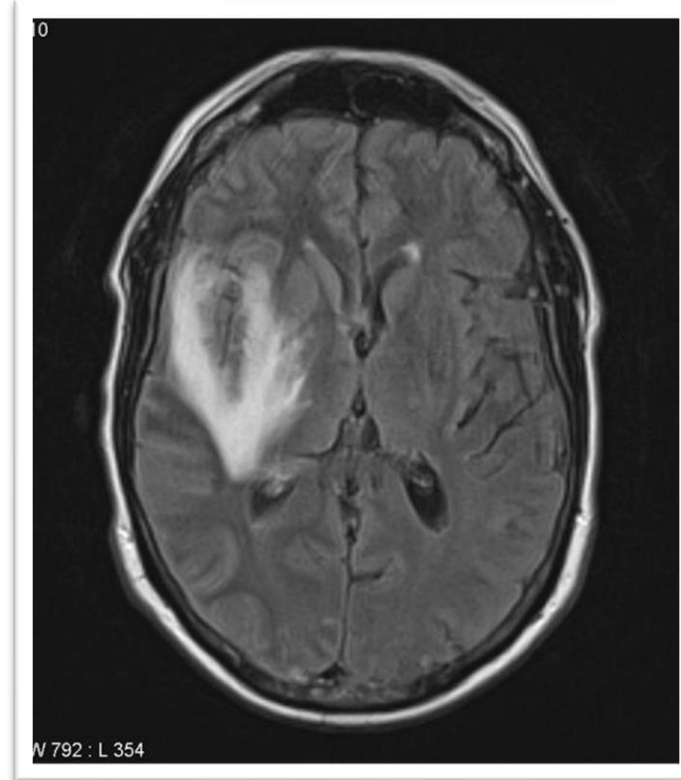
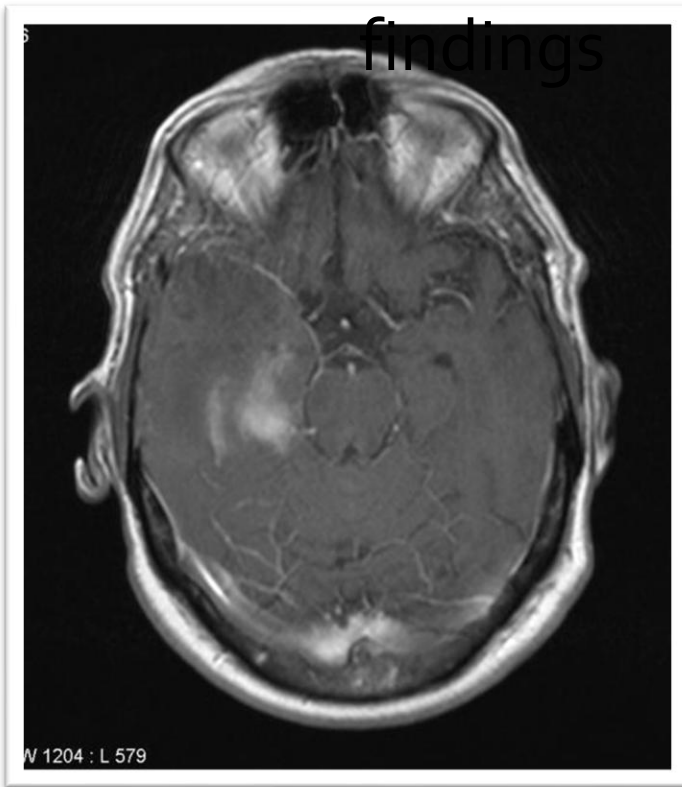
Electroencephalogram (EEG) - most often shows focal slowing and epileptic activity

Computed tomography (CT) - less sensitive than MRI, changes in the form of local ischemia, edema or necrosis can be registered after 3-4 days


Nuclear magnetic resonance imaging (MRI)

Herpetic encephalitis - MRI

findings

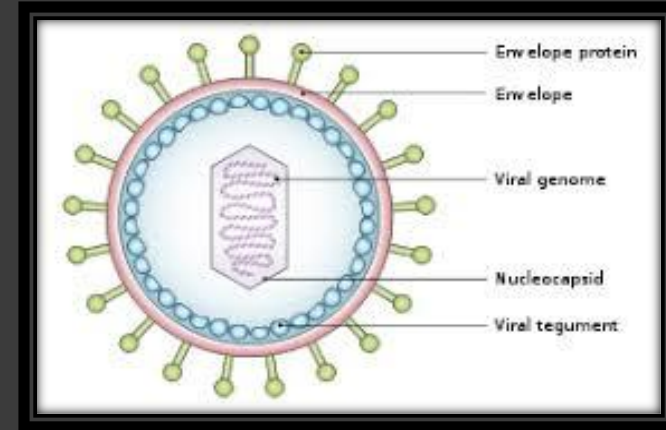


MRI is 80%-90% sensitive in detecting pathological changes in herpes simplex encephalitis. MRI is most sensitive with diffuse images and FLARE sequences. The temporal lobe is usually involved, while inferomedial changes in this lobe are seen in the cingulate gyrus. The basal ganglia are usually spared

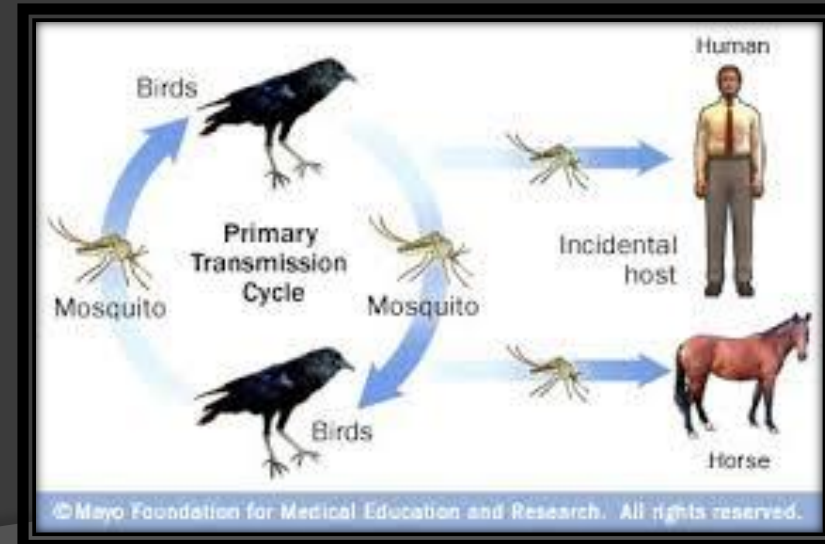
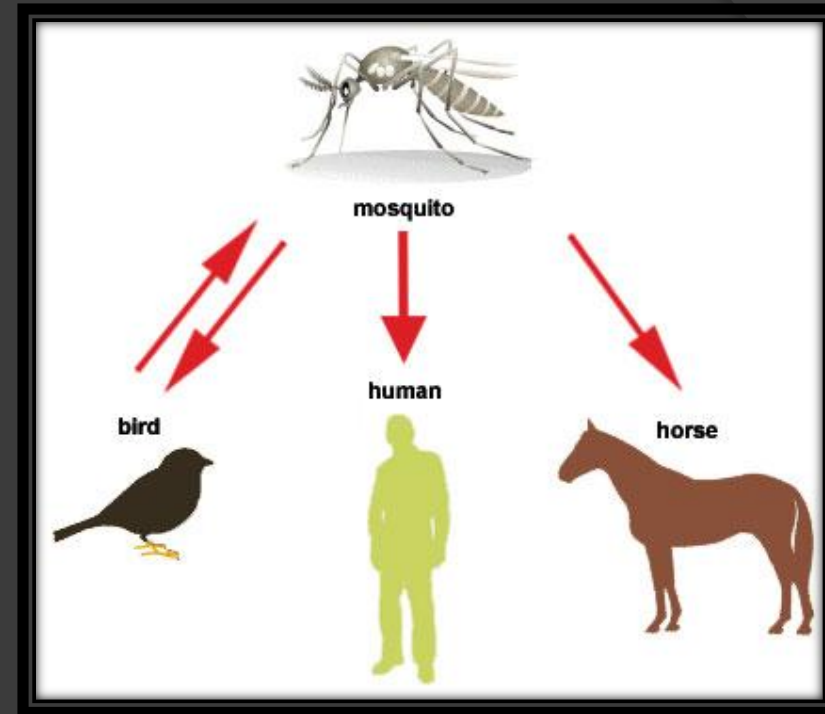
- 
- Treatment in intensive care units
 - Patients with HSV encephalitis are treated with parenteral administration of Acyclovir at a dose of 10mg/kg every 8 hours (total daily dose 30mg/kg)
 - In newborns, it is administered at a dose of 20 mg/kg every 8 hours (total daily dose 60mg/kg)
 - The duration of antiviral therapy is at least 14 days, in children 21 days
 - In the case of resistance to Acyclovir, we can give Foscarnet or Cidofovir
 - Antiedema therapy involves the use of Mannitol and Furosemide
 - The use of corticosteroids is controversial
 - Epi seizures are treated with drugs from the benzodiazepine group

West Nile virus

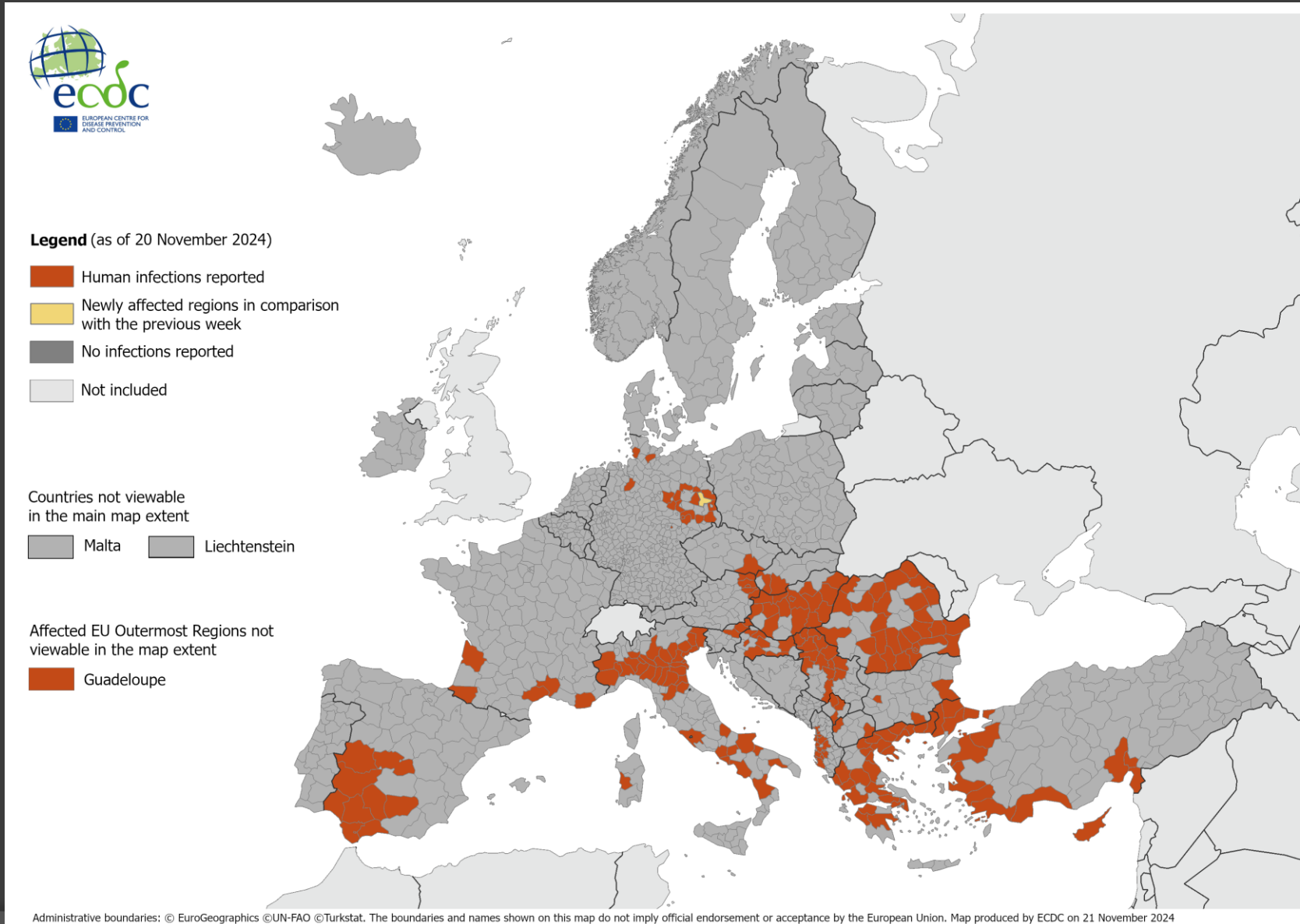
- West Nile virus, the causative agent of West Nile fever
- A single-stranded RNA virus, belongs to the family Flaviviridae, genus Flavivirus
- The capsid is of icosahedral symmetry, and the envelope consists of matrix protein M and glycoprotein E.
- It forms an antigenic complex with other viruses of the genus Flavivirus



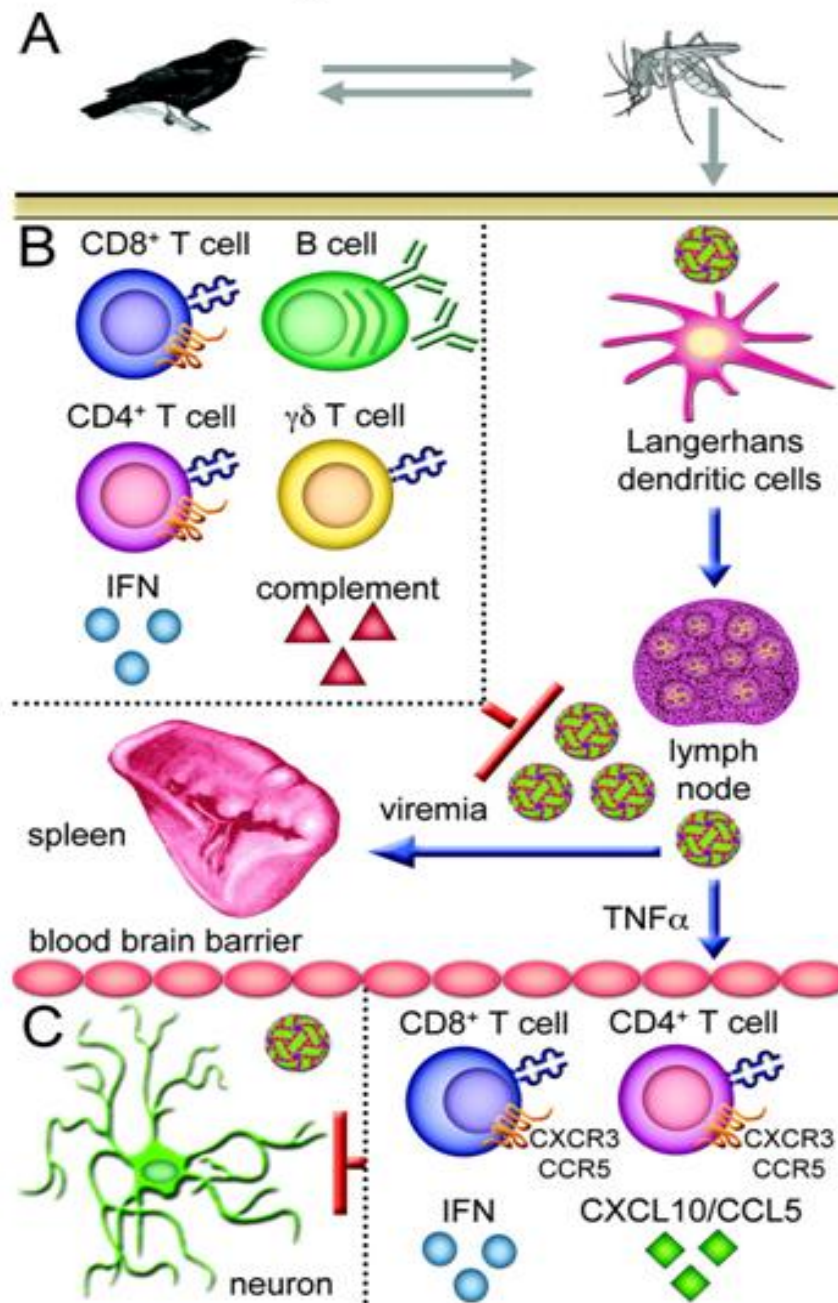
- Virus first isolated in 1937 in Uganda
- First cases with severe CNS manifestations in the USA in 1999
- Transmitters of infection are mosquitoes of the genus Culex
- A reservoir of infection is birds



Distribution of West Nile fever in Europe and the Mediterranean region in 2024



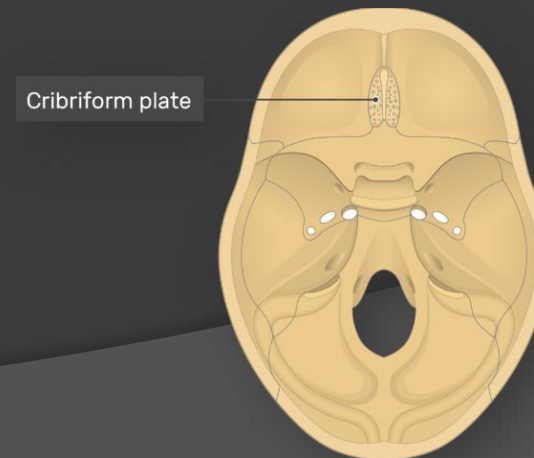
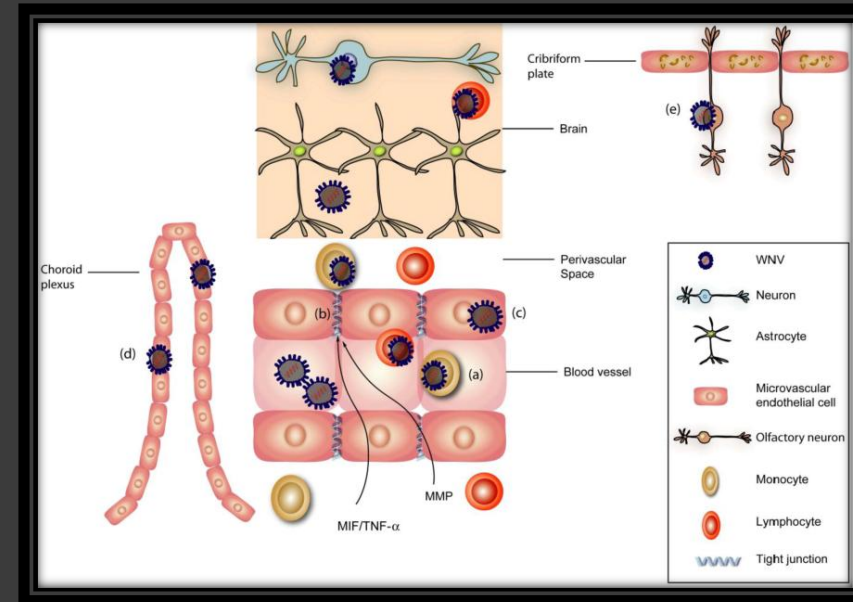
Since the beginning of 2024, and as of 20 November 2024, 19 countries in Europe reported human cases of West Nile virus infection: Albania, Austria, Bulgaria, Croatia, Cyprus, Czechia, France, Germany, Greece, Hungary, Italy, North Macedonia, Romania, Serbia, Slovakia, Slovenia, Spain and Türkiye.



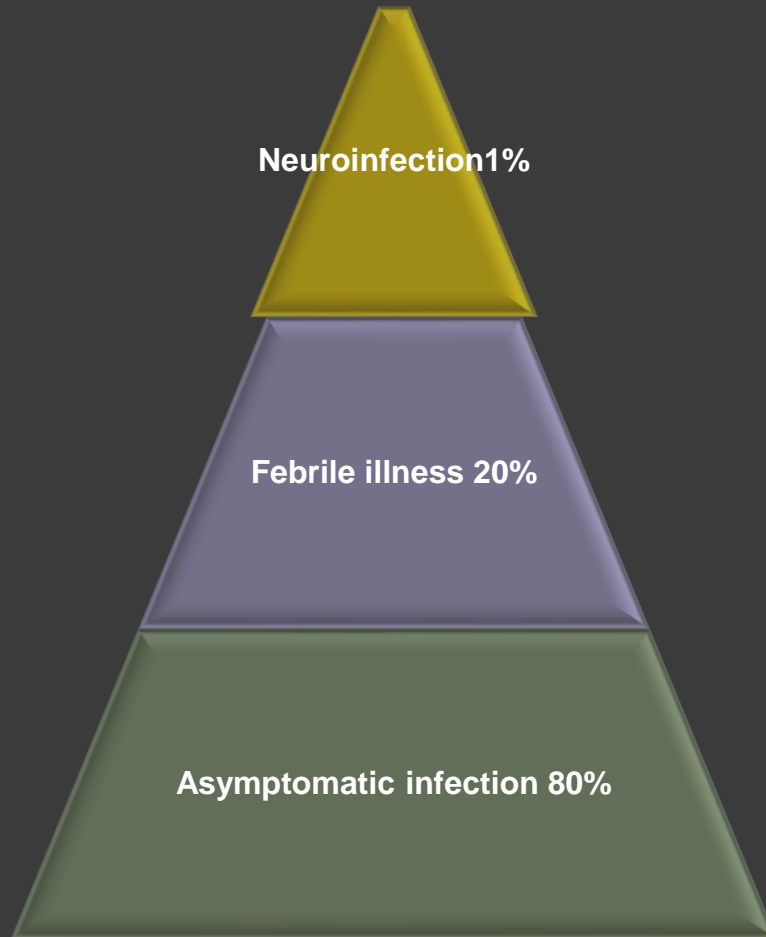
Melanie A. Samuel, and Michael S. Diamond J. Virol.
2006;80:9349-9360

Penetration of WNV into the central nervous system

- ✓ Trojan Horse Model
- ✓ Loss of barrier integrity involving destruction of intracellular junctions and basement membrane
- ✓ Direct infection of brain endothelial cells
- ✓ Infection of choroid plexus epithelial cells
- ✓ Direct infection of olfactory neurons via the cribriform plate

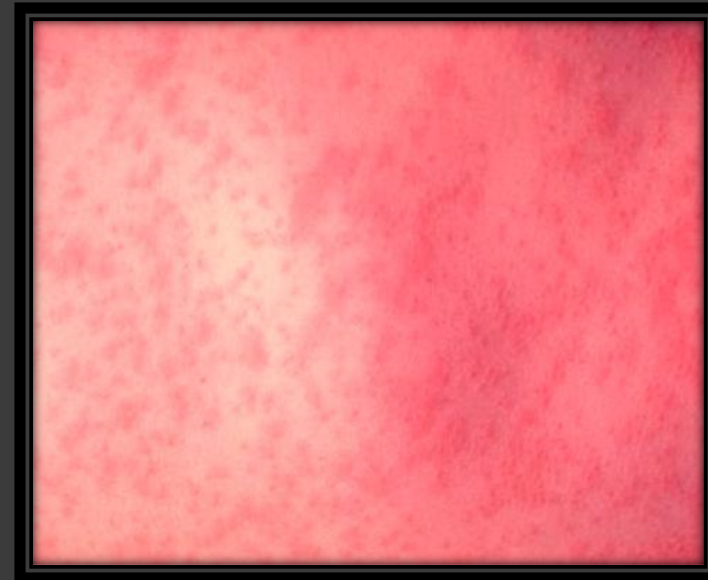
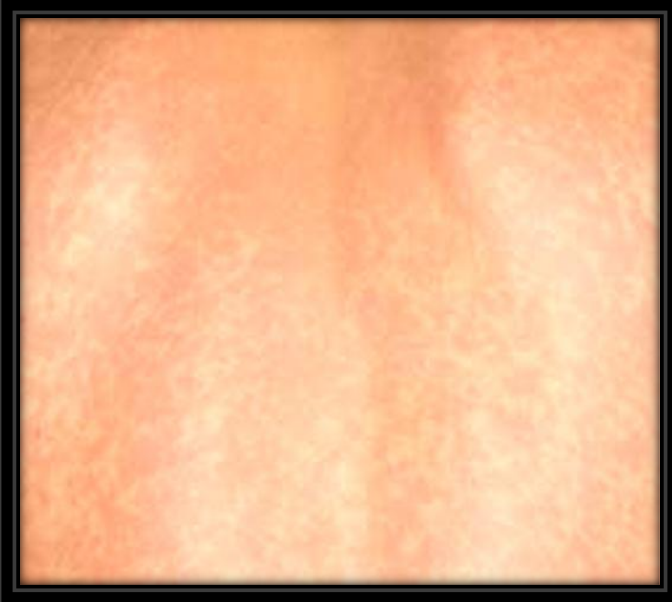


Clinical picture WNV

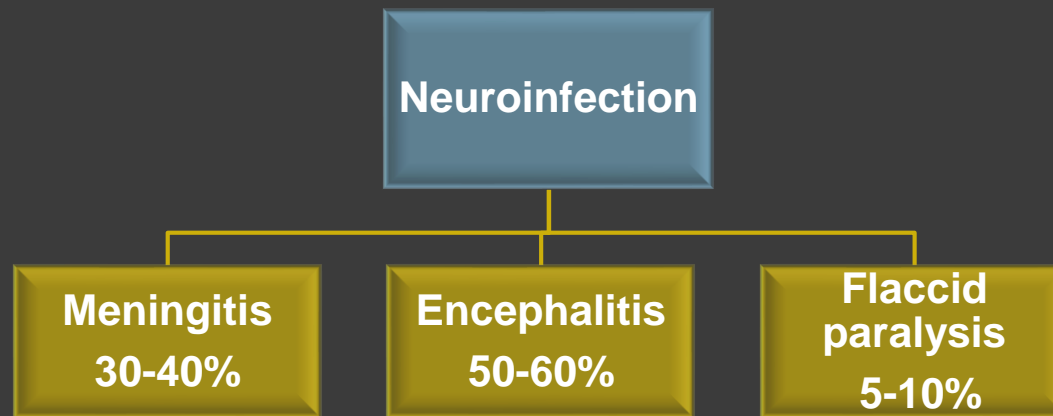


- Risk factors - older age, comorbidities (HTA, DM, previous CVI)
- Febrile illness - headache, sore throat, joint and muscle pain, nausea, vomiting, rash
- Rash - in 20%, erythematous, maculopapular, morbilliform...

Rash in febrile WNV



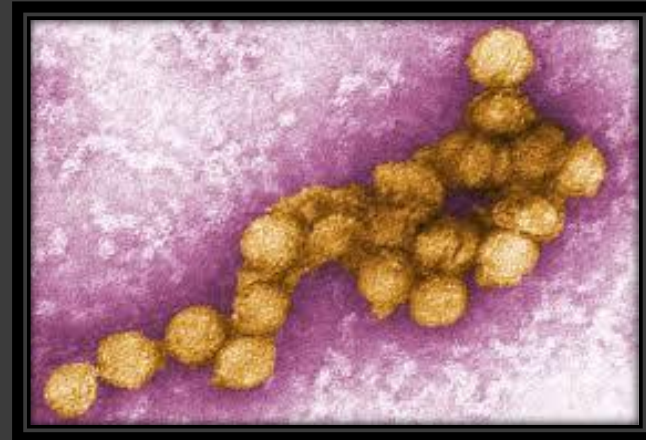
Neuroinfection WNV



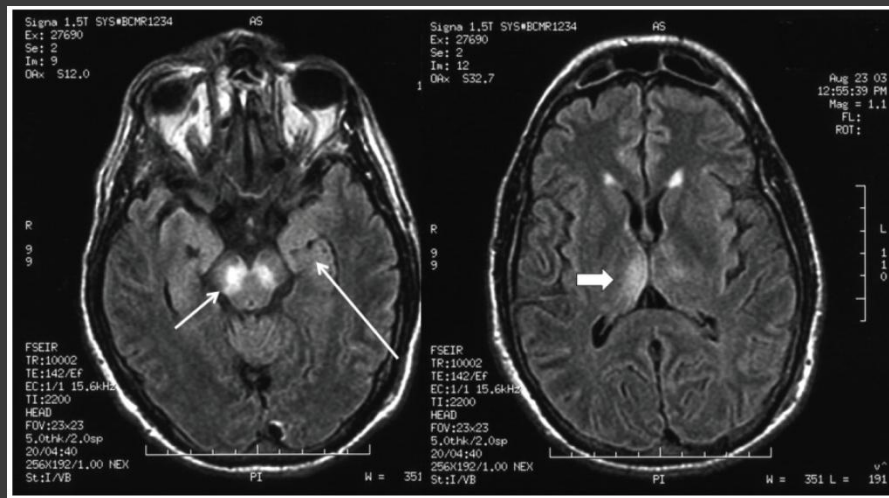
- CSF findings in WNV
- 200-400 cellular elements
- Neutrophils predominate in 50% of cases
- Moderately elevated proteins
- Normal glycorrhagia

Diagnosis of WNV infection

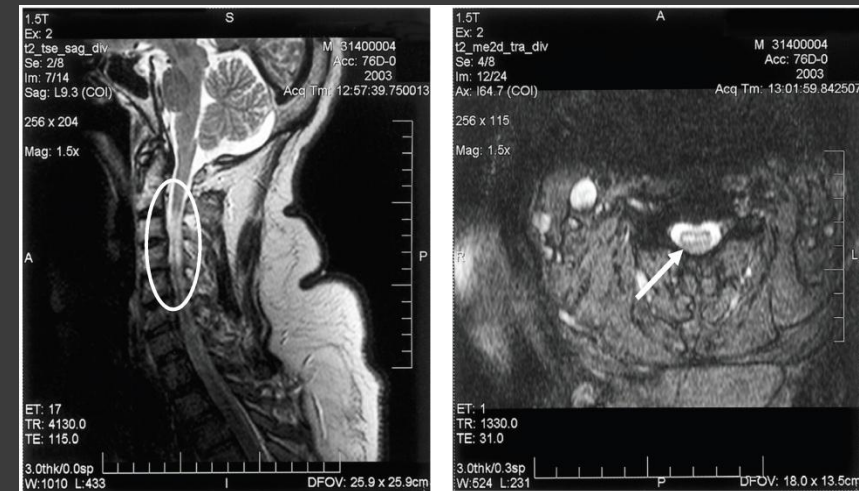
- Serological tests (blood, cerebrospinal fluid...)
- IgM antibodies to WNV positive already in the first week
- WNV RNA PCR
- Virus isolation in cell culture
- CT of the endocranium (Computed tomography)
- NMR of the endocranium (Nuclear magnetic resonance)



NMR examinations in WNV infections

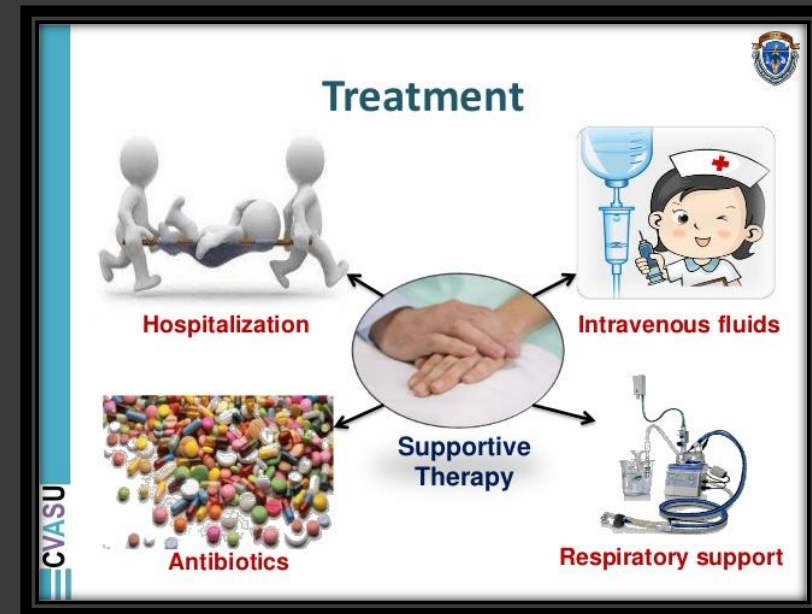


Endocranial MRI in a patient with West Nile virus encephalitis associated with parkinsonism and tremor shows pathological signal in the substantia nigra (short arrow), middle temporal lobe (long arrow), and right posterior thalamus (thicker arrow).



Sagittal (A) and axillary (B) T2-weighted magnetic resonance imaging of the cervical spinal cord in a patient with bilateral paralysis and respiratory failure due to West Nile virus poliomyelitis, showing increased signals in the anterior spinal horns.

- **Treatment** of WNV infections
 - There is currently no causal therapy.
 - Symptomatic and supportive therapy in patients treated in intensive care units
-
- **Prevention** of WNV infections
 - Protection from mosquitoes
 - Killing mosquitoes
 - Vaccine development is underway.



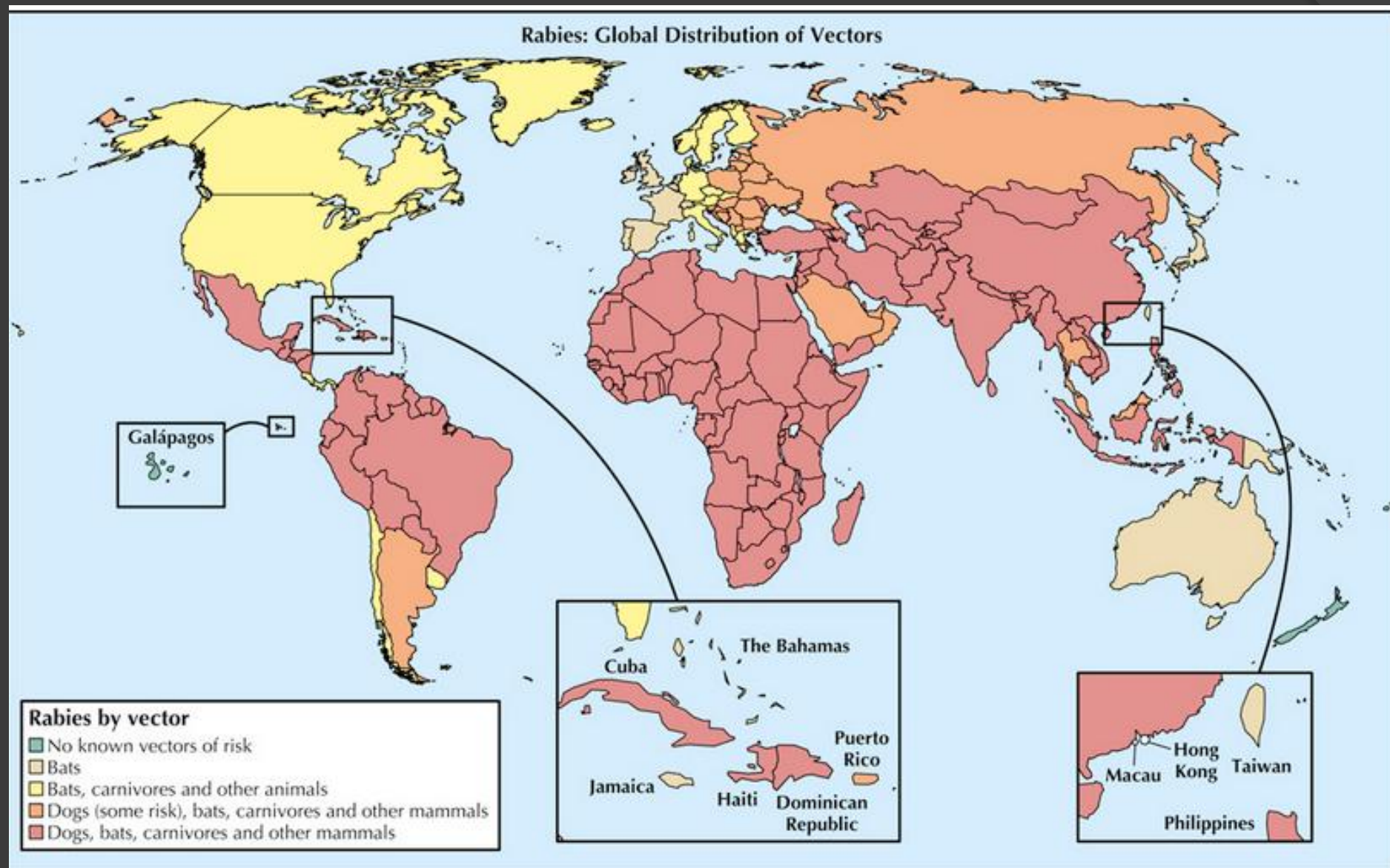
Rabies

- ◉ Rabies has been recognized as a source of great human suffering and fear since ancient times
- ◉ Characterized by a near 100% case fatality rate, it is among the deadliest infectious diseases known to humanity



- The rabies virus (RABV) is present in the saliva of clinically ill mammals and is typically transmitted to humans through a bite
- The incubation period is usually 1 to 3 months
- After entering the central nervous system (CNS), the virus causes an acute, progressive encephalomyelitis
- Although treatment options for rabies are currently limited, the disease is highly preventable by receipt of preexposure prophylaxis (PrEP) with rabies vaccine among persons at possible or known risk or by proper administration of rabies postexposure prophylaxis (PEP) after a possible high-risk rabies exposure





The World Health Organization (WHO) estimates that rabies is responsible for 59,000 deaths every year, of which more than 99% occur as a result of dog bites in the countries of Africa and Asia. Exposure risk is highest in rural areas, where free-roaming dogs are commonplace.

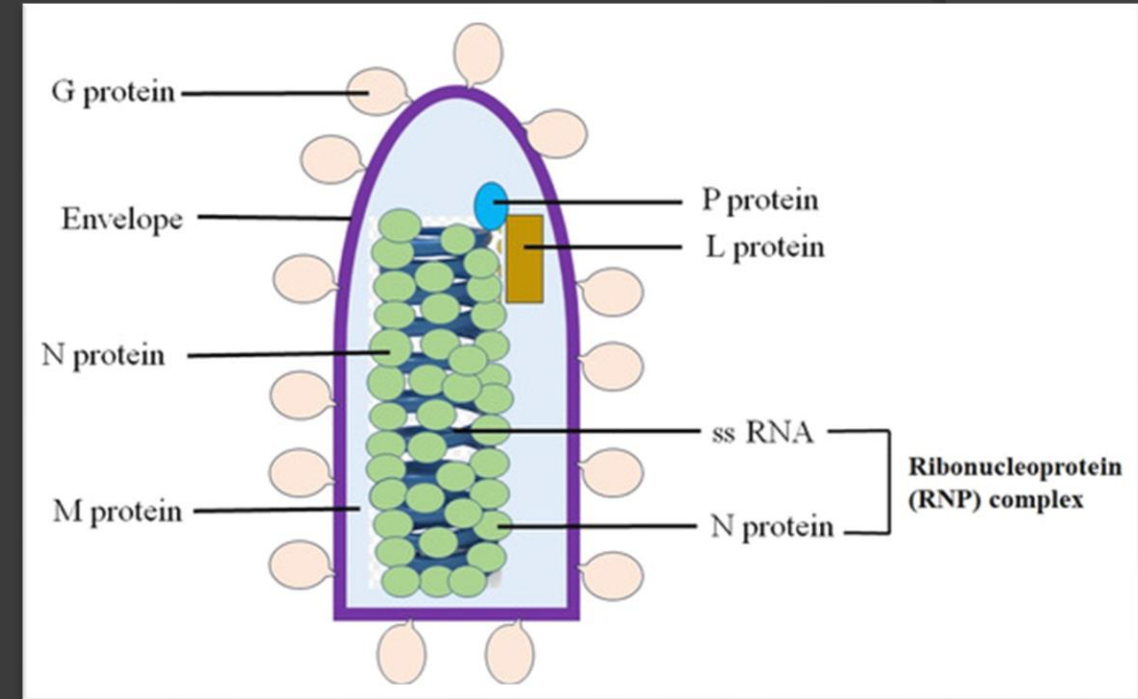
Recommendation for pre-exposure immunization for travelers

Recommendations for Pre-Exposure Immunization for Travelers

Exposure	Vaccine recommended for:
No known risk	No recommendation
<ul style="list-style-type: none">• Bats	<ul style="list-style-type: none">• Travelers with high occupational risks such as wildlife professionals, researchers, veterinarians• Adventure travelers visiting areas where vectors commonly found
<ul style="list-style-type: none">• Bats• Carnivores and other mammals	
<ul style="list-style-type: none">• Bats• Dogs (some risk)• Carnivores and other mammals	<ul style="list-style-type: none">• All of the above, plus• Long-term travelers• Expatriates
<ul style="list-style-type: none">• Bats• Dogs• Carnivores and other mammals• High-risk activities explicitly identified	<ul style="list-style-type: none">• All of the above, plus• Travelers spending a lot of time outdoors• Travelers to rural areas• Travelers involved in activities like bicycling, camping, hiking• Children

Etiology

- The rabies and rabies-related viruses belong to the Rhabdoviridae family as members of the Lyssavirus genus
- Lyssaviruses are neurotropic single-stranded ribonucleic acid (RNA) viruses characterized by a bullet-shaped morphology, and five structural proteins
- Eleven recognized lyssaviruses cause rabies, but only one species is formally called the rabies virus
- Humans are poor conduits of disease transmission (naturally occurring human-to-human transmission has yet to be definitively established); thus they are considered dead-end hosts



Pathophysiology of rabies. CNS, Central nervous system

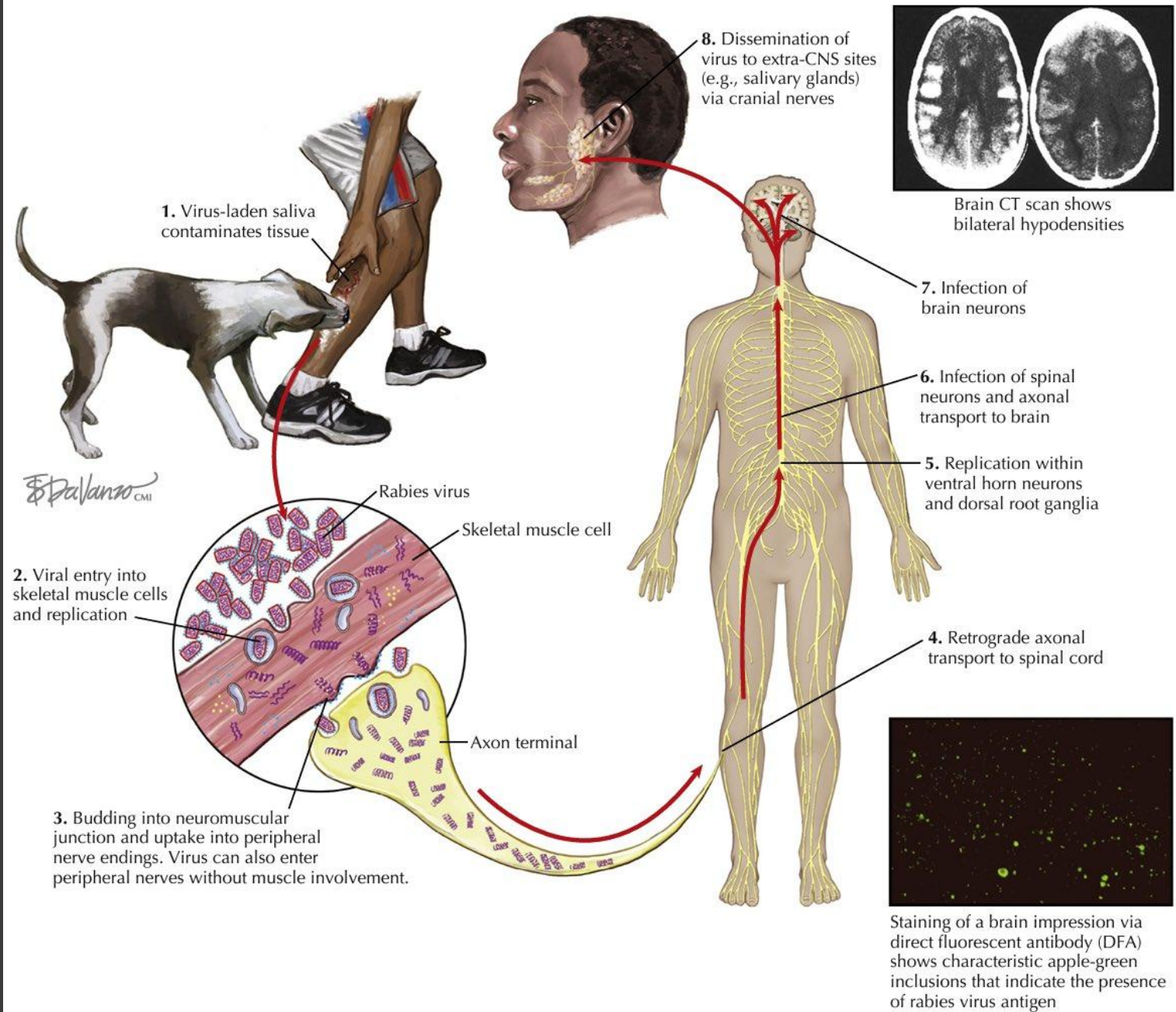


Fig. 69.3 Pathophysiology of rabies. CNS, Central nervous system. (Computed tomography and direct fluorescent antibody courtesy Centers for Disease Control and Prevention.)

Clinical Features

- Onset of symptoms for most rabies patients occurs 3 to 12 weeks postexposure
- Incubation periods of a year or more have been described in a few cases of human infection
- Rabies has two clinical manifestations:

the encephalitic form
(or furious rabies)

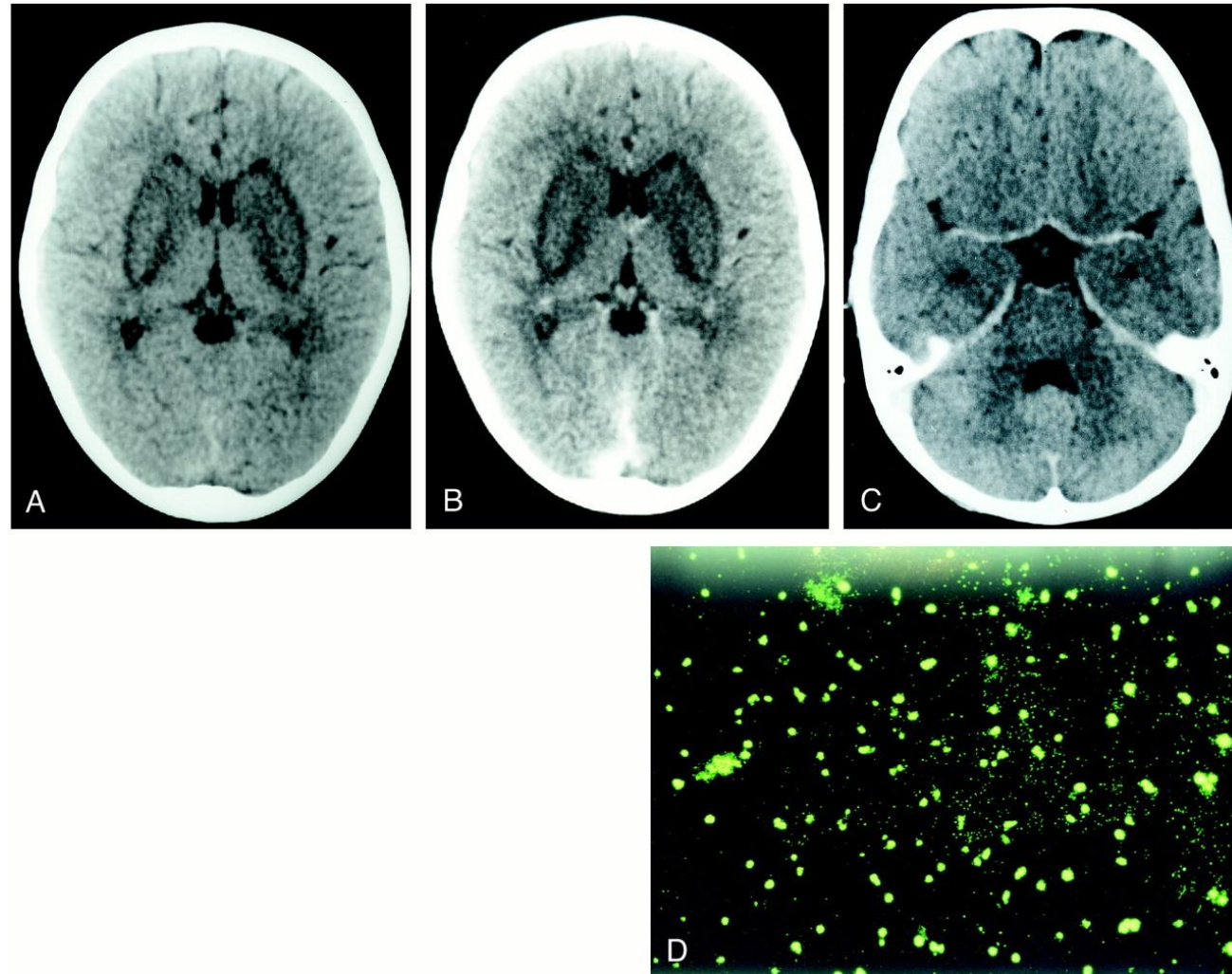
the paralytic form
(or dumb rabies)

- Prodromal signs and symptoms for both are nonspecific and include fever, chills, malaise, and headache
- Paresthesias on the part of the body that received the bite and pain and/or pruritus at the site of the bite wound unrelated to the injury itself are also common features

Encephalitic rabies

- Encephalitic rabies is the most common form overall
- Encephalitic rabies is characterized by altered mental status, agitation, hyperreactivity to sensory stimuli, intermittent consciousness, myoclonus, and muscle tremors
- Also featured are signs indicative of autonomic neuropathy, including hypersalivation, mydriasis, and excessive lacrimation
- Dysphagia and hydrophobia are cardinal sequelae
- Aerophobia is also frequently observed, as reflected by an exaggerated response to air currents passing over the skin (commonly referred to as the “fan test”)
- Paralysis leading to coma usually occurs within 10 to 14 days, with death ensuing shortly thereafter, frequently precipitated by multiple organ failure.

Case 1: 6-year-old boy with generalized seizures and altered consciousness.



Manasi Awasthi et al. AJNR Am J Neuroradiol 2001;22:677-680



Paralytic rabies

- Patients initially develop ascending muscle weakness that rapidly progresses to flaccid paralysis
- Mental status is often unremarkable at the onset, hydrophobic spasms are less likely to be present, and patients may be unable to speak because of laryngeal muscle weakness
- Peripheral neuropathy may be the cause of the muscle weakness seen in this form
- Patients with the paralytic form overall tend to have longer periods of survival than patients exhibiting encephalitic rabies.

Diagnostic Approach

- Epidemiological data
- Clinical picture
- Laboratory testing should be pursued soon after the disease is suspected
- For antemortem diagnosis, specimens used to confirm rabies include serum, cerebrospinal fluid, saliva, and neck skin biopsy
- A brain biopsy specimen may also be used for antemortem diagnosis; however, its collection is not recommended because its diagnostic value is outweighed by associated risks to the patient
- Serum and cerebrospinal fluid are examined for the presence of rabies virus antibody via indirect fluorescent antibody and virus neutralization tests
- Detection of viral antigen in a neck skin biopsy specimen and reverse transcription–polymerase chain reaction (RT-PCR) is used to detect the presence of viral RNA in both saliva and skin

Treatment

- ⦿ There is no standard treatment for rabies besides palliative support, which includes appropriately applied analgesia, sedation, and assisted ventilation
- ⦿ Given the poor prognosis, careful consideration should be given before pursuing aggressive treatment measures
- ⦿ Experimental therapeutic approaches have been used to treat human cases, including one patient in Wisconsin who successfully recovered from the disease
- ⦿ Treatment for this patient included antiviral therapy using ribavirin and coma induction using benzodiazepines and barbiturates, with ketamine and amantadine used to prevent excitotoxicity

Prevention

Preexposure Prophylaxis

- For preexposure immunization, a 1-mL dose of rabies vaccine (either HDCV or PCECV) should be injected intramuscularly (IM) in the deltoid (or outer thigh in children) on days 0, 7, and 21
- After primary immunization, boosters may later be indicated for individuals continuously or frequently at risk for inapparent rabies exposures, such as those encountered by rabies laboratory workers or bat handlers

Prevention

Postexposure Prophylaxis

What To Do If an Animal Bites During International Travel

It is medically urgent to seek healthcare!

Wash wound thoroughly with soap and water

Get an immediate evaluation at a local medical facility. If they are unable to evaluate you, go to the closest modern medical facility as soon as possible. If no satisfactory evaluation is possible, then FLY TO THE NEAREST COUNTRY WITH ADVANCED MEDICAL FACILITIES as soon as possible.

Rabies pre-exposure vaccination received?

Yes

No RIG required
Rabies vaccine (1mL) given IM on days 0 and 3
Start ASAP after the bite

No

Human RIG (20 IU/kg) locally infiltrated
Rabies vaccine (1mL) given IM on days 0, 3, 7, and 14
Start ASAP after the bite

Algorithm for rabies postexposure management of travelers

