# Meningitis, Encephalitis,

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Definition of meningitis

Epidemiology

Causes (organisms)

pathophysiology

Clinical features and diagnosis

CSF findings

Approach and investigations

Differential diagnosis

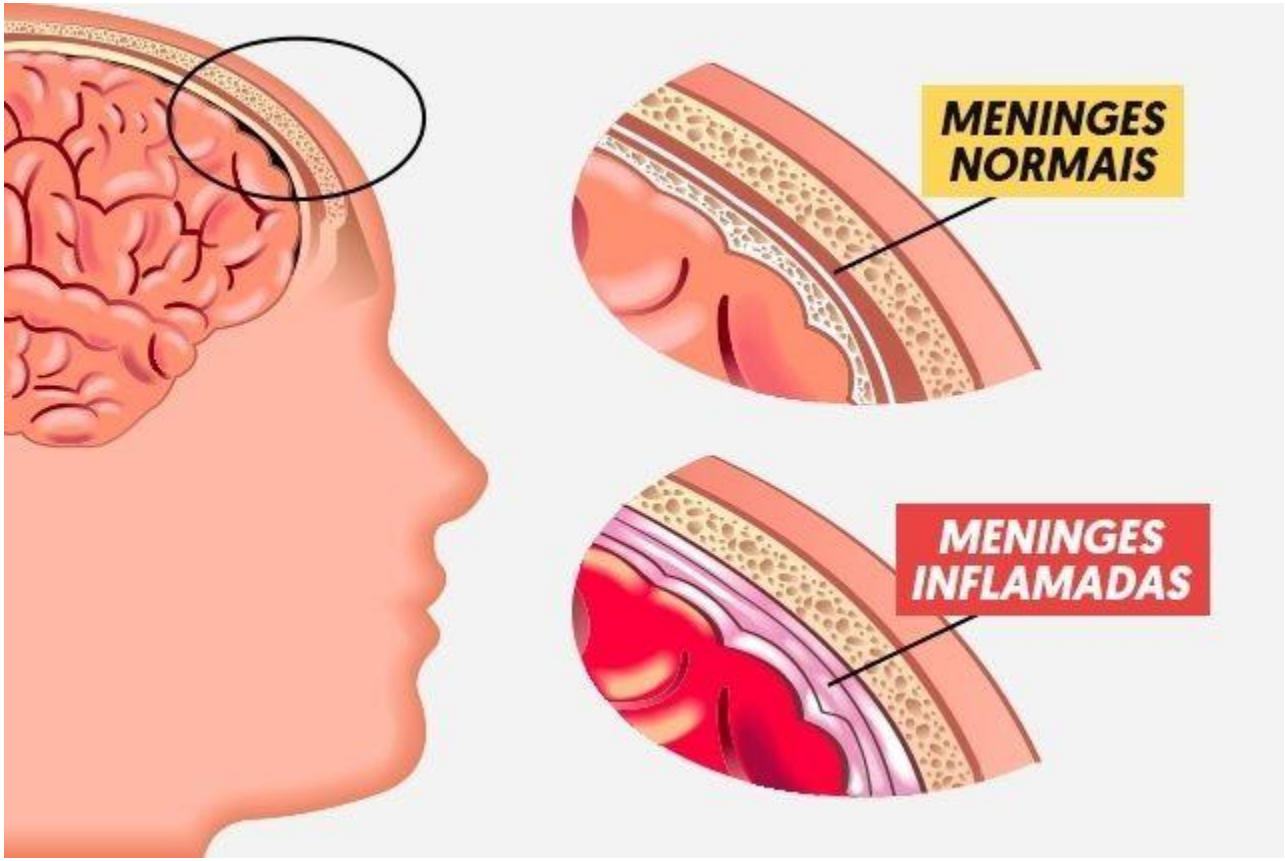
Viral meningitis

treatment

infections of the nervous system include:

1) acute bacterial meningitis
2) viral meningitis
3) Encephalitis
4) brain abscess
5) subdural empyema
6) infectious thrombophlebitis

# What is meningitis?



1) *Meningitis*: involves the subarachnoid space
2) *Encephalitis:* brain tissue is directly injured by a bacterial or viral infection

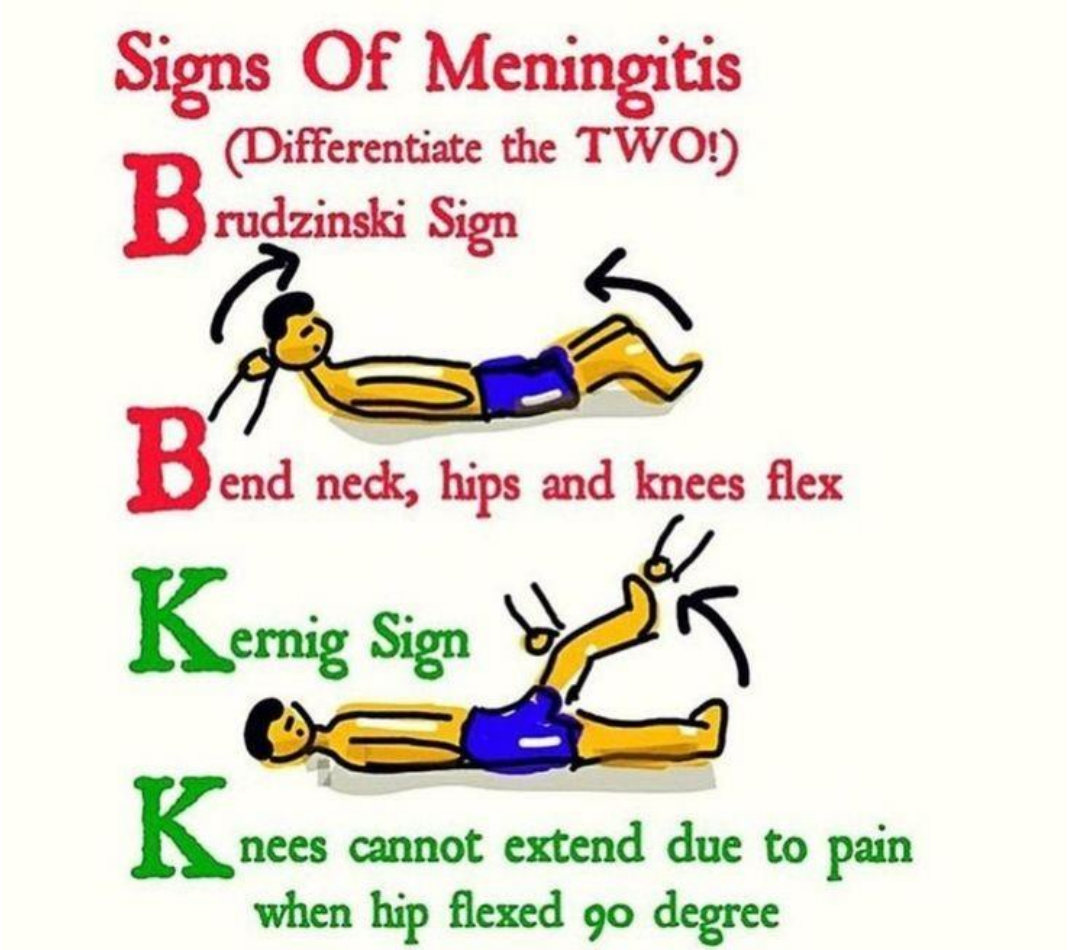
Nuchal rigidity ("stiff neck"): neck resists passive flexion

*Kernig's sign:* The thigh is flexed on the abdomen, with the knee flexed; attempts to passively extend the knee elicit pain when meningeal irritation is present.

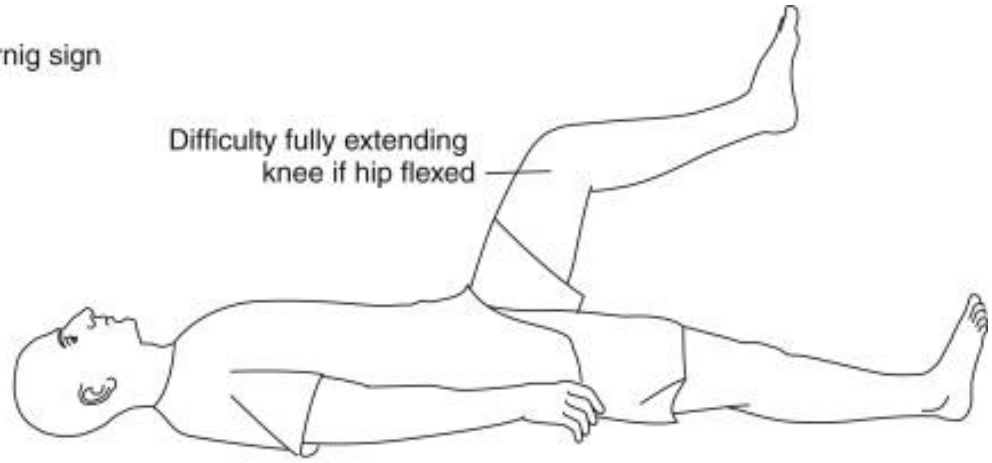
*Brudzinski's sign:* passive flexion of the neck results in spontaneous flexion of the hips and knees.

Brudzinski sign

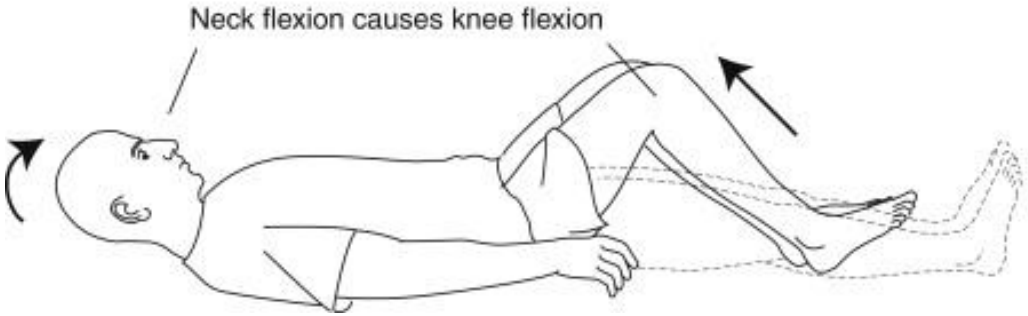
Kernig sign



Kernig sign



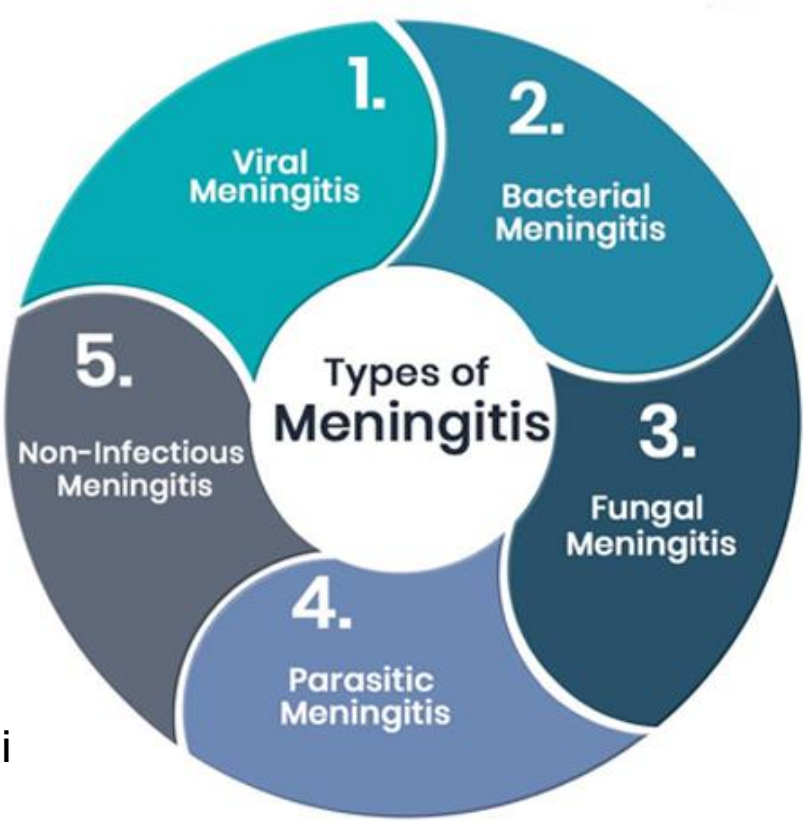

Brudzinski sign



1) Kernig's and Brudzinski's may be absent or reduced in:
    1) very young or elderly patient
    2) immunocompromised individuals
    3) severely depressed mental status

# Meningitis types

Enteroviruses
Mumps / HIV
HSV / VZV




Streptococcus pneumoniae

Haemophilus influenzae

Neisseria meningitides
Listeria monocytogene

Malignancy
Autoimmune
Drugs

Cryptococcus
Histoplasma

Naegleria fowleri

# ACUTE BACTERIAL MENINGITIS

Definition: acute purulent infection within the subarachnoid space

1) CNS inflammatory reaction that may result
   1) decreased consciousness
   2) Seizures
   3) raised intracranial pressure (ICP)
   4) Stroke

2) The organisms most often responsible meningitis:
   1) *Streptococcus pneumoniae*(~50%)
   2) *Neisseria meningitidis* (~25%)
   3) group B streptococci(~15%)
   4) *Listeria monocytogenes* (~10%)
   5) *Haemophilus influenzae*

## risk of pneumococcal meningitis:

1) acute or chronic pneumococcal sinusitis
2) otitis media
3) Alcoholism
4) Diabetes
5) Splenectomy
6) Hypogammaglobulinemia
7) complement deficiency
8) head trauma with basilar skull fracture
9) CSF rhinorrhea

## meningitis due to *N. meningitides*

1) decreased with the routine immunization quadrivalent (serogroups A, C, W-135, and Y)

2) petechial or purpuric skin lesions is an important clue to the diagnosis

3) Sometimes disease is fulminant, progressing to death within hours of symptom onset.

4) Individuals with deficiencies of complement, are highly susceptible to meningococcal infections.

# Gram-negative bacilli

1) Diabetes
2) Cirrhosis
3) alcoholism
4) chronic urinary tract infections.
5) neurosurgical procedures

1) Group B *Streptococcus*, or *Streptococcus agalactiae*
   1) Neonates
   2) individuals >50 years of age+ underlying diseases

2) *L. monocytogenes* cause meningitis in:
   1) neonates (<1 month of age)
   2) pregnant women
   3) >60 years
   4) immunocompromised of all age

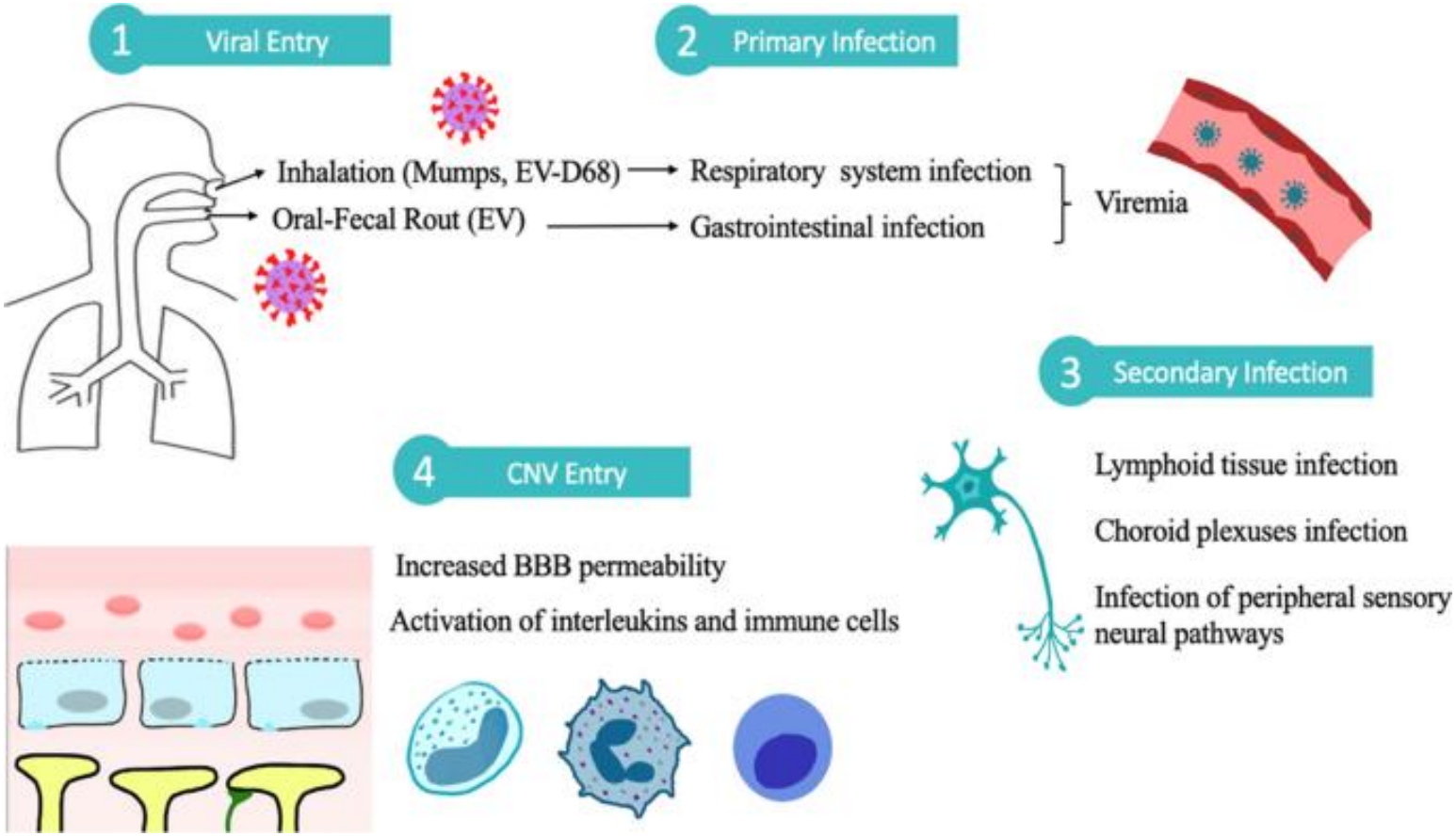
3) *S. aureus* and coagulase-negative staphylococci
   1) invasive neurosurgical procedures
   2) shunting procedures for hydrocephalus,
   3) subcutaneous reservoirs intrathecal chemotherapy

# PATHOPHYSIOLOGY

1) *S. pneumoniae* and *N. meningitidis*, initially colonize the nasopharynx by attaching to nasopharyngeal epithelial cells.

2) Bacteria are transported across epithelial cells in intravascular.

3) Bloodborne bacteria can reach the intraventricular choroid plexus, directly infect choroid plexus epithelial cells.


1 Viral Entry
2 Primary Infection
Inhalation (Mumps, EV-D68)
Respiratory system infection
Oral-Fecal Rout (EV)
Gastrointestinal infection
Viremia
3 Secondary Infection
Lymphoid tissue infection
Choroid plexuses infection
Infection of peripheral sensory neural pathways
4 CNV Entry
Increased BBB permeability
Activation of interleukins and immune cells

# CLINICAL PRESENTATION

1) The classic clinical triad of meningitis is fever, headache, and nuchal rigidity.
2) decreased level of consciousness occurs in >75% of patients and can vary from lethargy to coma
3) Nausea, vomiting, and photophobia are common complaints
4) Seizures is a presentation of bacterial meningitis in 20–40% of patients(focal or status)
5) Raised ICP in More than 90% of patients will >180 mmH2O
    1) deteriorating or reduced level of consciousness
    2) Papilledema
    3) dilated poorly reactive pupils
    4) sixth nerve palsies
    5) decerebrate posturing
    6) Cushing reflex (bradycardia, hypertension, and irregular respirations)

# DIAGNOSIS

1. When bacterial meningitis is suspected, blood cultures should be immediately obtained and empirical antimicrobial and adjunctive dexamethasone therapy initiated without delay.

2. Patients should undergo CT or MRI prior to LP:
    1. recent head trauma
    2. Immunocompromised
    3. focal neurologic findings
    4. papilledema
    5. depressed level of consciousness

1) CSF/serum glucose ratio <0.4 is highly suggestive of bacterial meningitis but may also be seen in other conditions, including fungal, tuberculous, and carcinomatous meningitis.

2) Antibiotic therapy initiated a few hours prior to LP will not significantly alter the CSF WBC count or glucose concentration, nor is it likely to prevent visualization of organisms by Gram's stain or detection of bacterial nucleic acid by polymerase chain reaction (PCR) assay.

# DIFFERENTIAL DIAGNOSIS

1) Viral meningoencephalitis
2) Rickettsial disease
3) Focal suppurative CNS infections
4) noninfectious CNS disorders such as Subarachnoid hemorrhage
5) Subacute meningitis such as TB

# EMPIRICAL ANTIMICROBIAL THERAPY

Bacterial meningitis is a medical emergency.
The goal is to begin antibiotic therapy within 60 min of a patient's arrival in the emergency room.

**TABLE 164-1 ANTIBIOTICS USED IN EMPIRICAL THERAPY OF BACTERIAL MENINGITIS AND FOCAL CENTRAL NERVOUS SYSTEM INFECTIONS[a]**

| Indication | Antibiotic |
|---|---|
| Preterm infants to infants <1 month | Ampicillin + cefotaxime |
| Infants 1–3 months | Ampicillin + cefotaxime or ceftriaxone |
| Immunocompetent children >3 months and adults <55 | Cefotaxime, ceftriaxone, or cefepime + vancomycin |
| Adults >55 and adults of any age with alcoholism or other debilitating illnesses | Ampicillin + cefotaxime, ceftriaxone or cefepime + vancomycin |
| Hospital-acquired meningitis, posttraumatic or postneurosurgery meningitis, neutropenic patients, or patients with impaired cell-mediated immunity | Ampicillin + ceftazidime or meropenem + vancomycin |

# ADJUNCTIVE THERAPY

Dexamethasone (10 mg intravenously) was administered 15–20 min before the first dose of an antimicrobial agent, and the same dose was repeated every 6 h for 4 days.

1) It is unlikely to be of significant benefit if started >6 h after antimicrobial therapy has been initiated.

2) its efficacy in decreasing meningeal inflammation and neurologic sequelae such as the incidence of sensorineural hearing loss.

## risk of death from bacterial meningitis increases with:

- decreased level of consciousness on admission
- onset of seizures within 24 h of admission
- signs of increased ICP
- young age (infancy) and age >50
- the presence of comorbid conditions including shock and/or the need for mechanical Ventilation
- delay in the initiation of treatment

# ACUTE VIRAL MENINGITIS

## CLINICAL MANIFESTATIONS

1) Headache+ fever+signs of meningeal irritation
2) Nuchal rigidity is present in most cases but may be mild
3) Constitutional signs can include malaise, myalgia, anorexia, nausea and vomiting, abdominal pain, and/or diarrhea
4) Depressed level of consciousness (e.g., somnolence, coma), seizures, or focal neurologic deficits do not occur in viral meningitis

# ETIOLOGY

| Acute Meningitis | |
|---|---|
| **Common** | **Less Common** |
| Enteroviruses (coxsackieviruses, echoviruses, and human enteroviruses 68–71) | Herpes simplex virus 1 |
| Varicella-zoster virus | Human herpesvirus 6 |
| Herpes simplex virus 2 | Cytomegalovirus |
| Epstein-Barr virus | Lymphocytic choriomeningitis virus |
| Arthropod-borne viruses | Mumps |
| HIV | |

# CSF Examination:

1) The total CSF cell count in viral meningitis is typically 25–500/µL
2) normal or slightly elevated protein(20–80 mg/dL)
3) normal glucose concentration
4) normal or mildly elevated opening pressure (100–350 mmH2O).
5) Organisms are *not* seen on Gram's stain of CSF
6) Polymerase Chain Reaction
7) Viral Culture
8) Serologic Studies

## TREATMENT Acute Viral Meningitis

1) Treatment of almost all cases of viral meningitis is primarily symptomatic and includes use of analgesics, antipyretics, and antiemetics.

2) Hospitalization may not be required in immunocompetent patients.

3) Seriously ill patient should probably receive intravenous acyclovir (15–30 mg/kg per day in three divided doses), which can be followed by an oral drug such as acyclovir (800 mg five times daily), famciclovir (500 mg tid), or valacyclovir (1000 mg tid) for a total course of 7–14 days

# VIRAL ENCEPHALITIS

## Definition:

In encephalitis the brain parenchyma is also involved. Many patients with encephalitis also have evidence of associated meningitis (meningoencephalitis)

## CLINICAL MANIFESTATIONS

1) altered level of consciousness (confusion, behavioral abnormalities)
2) depressed level of consciousness (mild lethargy to coma)
3) focal or diffuse neurologic signs and symptoms
4) Hallucinations
5) Agitation
6) personality change
7) behavioral disorder
8) frankly psychotic state
9) Focal or generalized seizures

# ETIOLOGY

| Acute Encephalitis | |
|---|---|
| **Common** | **Less Common** |
| Herpesviruses | Rabies |
| Cytomegalovirus[a] | Eastern equine encephalitis virus |
| **Herpes simplex virus 1[b]** | |
| Herpes simplex virus 2 | |
| Human herpesvirus 6 | |
| Varicella-zoster virus | Powassan virus |
| Epstein-Barr virus | Cytomegalovirus[a] |
| Arthropod-borne viruses | Colorado tick fever virus |
| La Crosse virus | Mumps |
| **West Nile virus[c]** | |
| St. Louis encephalitis virus | |
| Enteroviruses | |

# CSF Examination

1) lymphocytic pleocytosis( PMN pleocytosis in WNV, CMV myeloradiculitis, EEE virus, echovirus9)

2) Mildly elevated protein concentration

3) normal glucose concentration(Rare patients with mumps, LCMV, or advanced HSV encephalitis and many patients with CMV myeloradiculitis have low CSF glucose concentrations.)

4) A CSF pleocytosis (>5 cells/μL) >95%

5) 20% of patients will have a significant number of RBC(>500/μL)

6) CSF PCR(sensitivity (~96%) and specificity (~99%) of HSV CSF PCR)
7) CSF Culture
8) Serologic Studies and Antigen Detection

# MRI, CT, and EEG in encephalitis

Focal findings in a patient with encephalitis should always raise the possibility of HSV encephalitis:

1) areas of increased signal intensity in the frontotemporal, cingulate, or insular regions of the brain on T2-weighted, FLAIR, or diffusion-weighted MRI

2) focal areas of low absorption, mass effect, and contrast enhancement on CT

3) periodic focal temporal lobe spikes on a background of slow or low-amplitude ("flattened") activity on EEG.

## TREATMENT Viral Encephalitis

1) supportive therapy
    1) monitoring of ICP
    2) fluid restriction
    3) avoidance of hypotonic IV solutions
    4) suppression of fever
    5) Seizures should be treated
    6) prophylactic therapy for seizure

2) Adults should receive a dose of 10 mg/kg of acyclovir intravenously every 8 h (30 mg/kg per day total dose) for 14–21 days.

# SUBACUTE MENINGITIS

## CLINICAL MANIFESTATIONS

1) headache, stiff neck, low-grade fever, and lethargy for days to several weeks

## ETIOLOGY

1) *M. tuberculosis*
2) *C. neoformans*
3) *H. capsulatum*
4) *T. pallidum*

## LABORATORY DIAGNOSIS

1) elevated opening pressure
2) lymphocytic pleocytosis (10–500cells/μL)
3) elevated protein concentration in the range of 1–5g/L
4) decreased glucose concentration to 20–40 mg/dL

# BRAIN ABSCESS

## DEFINITION

A brain abscess is a focal, suppurative infection within the brain parenchyma, typically surrounded by a vascularized capsule

## Predisposing conditions

- otitis media
- mastoiditis,
- paranasal sinusitis
- pyogenic infections in the chest or other body sites
- penetrating head trauma
- neurosurgical procedures
- dental infections

## In immunocompetent individuals

- *Streptococcus* spp
- Enterobacteriaceae
- anaerobes
- staphylococci

## In immunocompromised hosts

- *Nocardia* spp
- *Toxoplasma gondii*
- *Aspergillus* spp
- *Candida* spp
- *C. neoformans*.

# ETIOLOGY

- (1) by direct spread from a contiguous cranial site of infection, such as paranasal sinusitis, otitis media, mastoiditis,or dental infection

- (2) following head trauma or a neurosurgical Procedure

- (3) as a result of hematogenous spread from a remote site of infection

## CLINICAL PRESENTATION

classic clinical triad of headache, fever, and a focal neurologic deficit is present in <50% of cases

The clinical presentation of a brain abscess depends on its location:

1) Hemiparesis is sign of a frontal lobe
2) dysphasia or an upper homonymous quadrantanopia is sign of temporal abscess
3) Nystagmus and ataxia are signs of a cerebellar abscess

## DIAGNOSIS

1) Diagnosis is made by neuroimaging studies: MRI is better than CT for demonstrating abscesses in the early (cerebritis) stages and is superior to CT for identifying abscesses in the posterior fossa.

## TREATMENT Brain Abscess

1) Empirical therapy: third- or fourth-generation cephalosporin +metronidazole

# SUPPURATIVE THROMBOPHLEBITIS

## DEFINITION

Suppurative intracranial thrombophlebitis is septic venous thrombosis of cortical veins and sinuses.

This may occur as a complication of:

1) bacterial meningitis
2) SDE
3) epidural abscess
4) infection in the skin of the face
5) paranasal sinusitis
6) middle ear or mastoiditis

## CLINICAL MANIFESTATIONS

1) *Septic thrombosis of the superior sagittal sinus* presents with headache, fever, nausea and vomiting, confusion, and focal or generalized seizures.

2) The symptoms of *septic cavernous sinus thrombosis* are fever, headache, frontal and retroorbital pain, and diplopia. The classic signs are ptosis, proptosis, chemosis, and extraocular dysmotility due to deficits of cranial nerves III, IV, and VI; hyperesthesia of the ophthalmic and maxillary divisions of the fifth cranial nerve and a decreased corneal reflex may be detected

3) transverse sinus thrombosis may also present with otitis media, sixth nerve palsy, and retroorbital or facial pain (*Gradenigo's syndrome*)

4) Sigmoid sinus and internal jugular vein thrombosis may present with neck pain.

## DIAGNOSIS

MRI, MRV, CT angiography

## TREATMENT

1) Antibiotics
2) hydration
3) removal of infected tissue and thrombus in septic lateral or cavernous sinus thrombosis
4) Anticoagulation