

# CNS Infections

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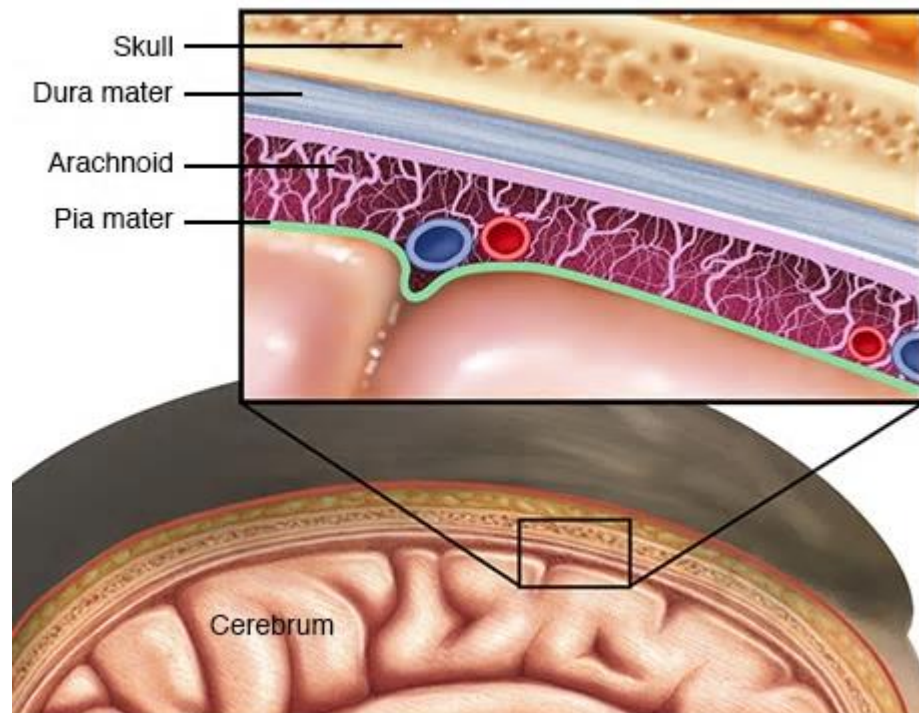


# Objectives

- Definition
- Clinical features of suspected CNS infection.
- Appreciate different causative organisms.
- CSF analysis.
- Approach to management.
- Utilization of antimicrobial therapy
- Role of steroids.
- Prevention.

# Meningitis

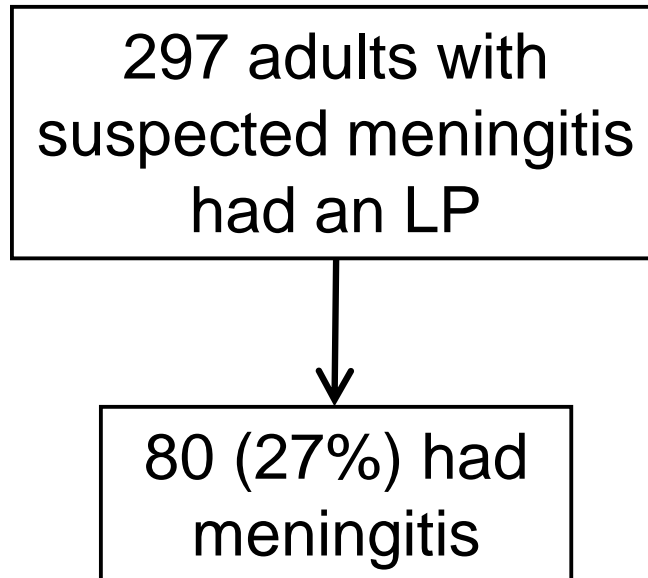
- Meningitis: is an inflammation of the membranes (meninges) surrounding your brain and spinal cord.



# Clinical evaluation of adults with suspected meningitis

Clin Inf Diseases 2002; 35:46–52

# Results



Headache was the most common presenting symptom, followed by fever, n&v, photophobia and stiff neck. The majority (81%) of patients had  $\geq 2$  of these symptoms.

# Presenting symptoms

## Patients without meningitis

- Headache (81%)
- Fever (67%)
- n&v (53%)
- Photophobia (51%)
- Stiff neck (45%)
- Focal symptoms/seizure (21%)

## Patients with meningitis

- Headache (92%)
- Fever (71%)
- n&v (70%)
- Photophobia (57%)
- Stiff neck (48%)
- Focal symptoms/seizure (18%)

# Presenting signs

## Patients without meningitis

- Temperature  $>38^{\circ}\text{C}$  (52%)
- Neck stiffness (32%)
- Kernig's sign (5%)
- Brudzinski's sign (5%)
- GCS  $<13$  (7%)
  
- Mean wbc in CSF 1

## Patients with meningitis

- Temperature  $>38^{\circ}\text{C}$  (43%)
- Neck stiffness (30%)
- Kernig's sign (5%)
- Brudzinski's sign (5%)
- GCS  $<13$  (10%)
  
- Mean wbc in CSF 359

# Presenting signs

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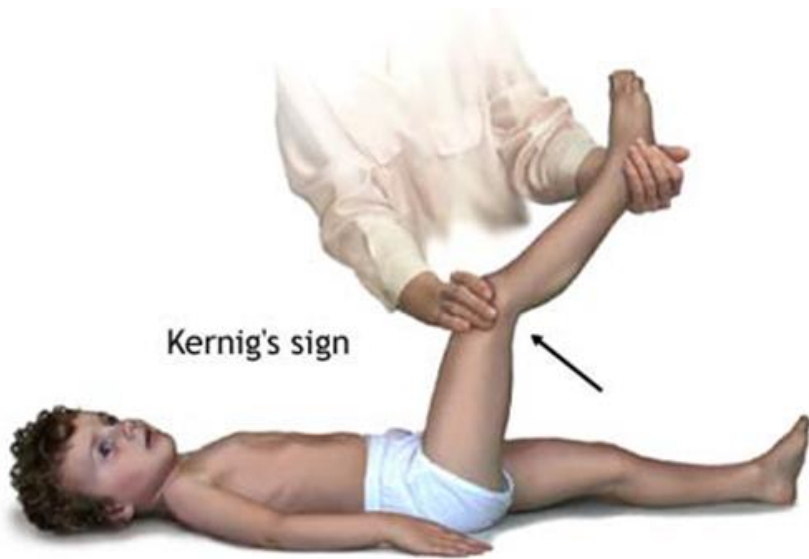
# Symptoms

- Early meningitis symptoms may mimic the flu (influenza). Symptoms may develop over several hours or over a few days.
- Possible signs and symptoms:
  - Sudden high fever
  - Stiff neck
  - Severe headache that seems different than normal
  - Headache with nausea or vomiting
  - Confusion or difficulty concentrating
  - Seizures
  - Sleepiness or difficulty waking
  - Sensitivity to light
  - No appetite or thirst
  - Skin rash (sometimes, such as in meningococcal meningitis)

# Importance of early recognize CNS infection

- High mortality
- Permanent disability
- Features of both meningeal and brain involvement to various degrees
- Common features in presentation and sequelae
  - Bacterial meningitis
  - Tuberculous meningitis
  - Viral meningoencephalitis
  - Brain abscess
  - Fungal
  - polio

# Important meningeal signs



ADAM.



ADAM.

# Differential Diagnosis

- Infectious encephalopathies
  - Cerebral malaria
  - Enteric encephalopathy
  - Shigella encephalopathy
  - Sepsis
- Structural lesions with fever eg stroke/ tumour
- Non infectious encephalopathy with fever eg Reye's, electrolyte encephalopathy

# Acute bacterial Meningitis (ABM)

- Very common & serious
- Medical emergency
- 100% curable if treated adequately or 100% fatal
- High index of suspicion important
- Dx by CSF examination

# ABM : Etiology

- **Streptococcus pneumoniae (pneumococcus)**. This bacterium is the most common cause of bacterial meningitis in infants, young children and adults in the United States. It more commonly causes pneumonia or ear or sinus infections. A vaccine can help prevent this infection.
- **Neisseria meningitidis (meningococcus)**. This bacterium is another leading cause of bacterial meningitis. These bacteria commonly cause an upper respiratory infection but can cause meningococcal meningitis when they enter the bloodstream. This is a highly contagious infection that affects mainly teenagers and young adults. It may cause local epidemics in college dormitories, boarding schools and military bases. A vaccine can help prevent infection.

# ABM : Etiology

- **Haemophilus influenzae (haemophilus)**. Haemophilus influenzae type b (Hib) bacterium was once the leading cause of bacterial meningitis in children. But new Hib vaccines have greatly reduced the number of cases of this type of meningitis.
- **Listeria monocytogenes (listeria)**. These bacteria can be found in unpasteurized cheeses, hot dogs and lunchmeats. Pregnant women, newborns, older adults and people with weakened immune systems are most susceptible. Listeria can cross the placental barrier, and infections in late pregnancy may be fatal to the baby.
- Anatomic defects (# base of skull, pilonidal sinus), immunodeficiency □ others

# ABM: Epidemiology

- Max in 1<sup>st</sup> 5 yrs
- Risk Factors:
  - Colonization
  - Crowding: person to person droplet infection
  - Poverty
  - Male
  - Absence of breast feeding



# ABM: Pathology

- Bacterial colonization of nasopharynx → bacteremia → choroid plexus → meninges
- Meningeal exudates, ventriculitis, perivascular inflammatory exudates, venous occlusion, infarction, necrosis, ↑ICT
- Role of cytokines

# ABM: Clinical Features

- Sudden onset
- **high fever, headache**, anorexia, myalgia, **photophobia**, meningeal signs, convulsions, stupor, coma
- ↑ICP: hypertension, bradycardia, bulging AF, 3rd/6th cranial nerve palsy, posturing, breathing abnormalities.
- Papilledema
- Purpuric rash s/o meningococcus
- Septic foci



# Other things that cause a petechial rash

- Strep and staph bacteraemias
- Haemorrhagic viral fevers e.g. Dengue
- Low platelets
- Vasculitis (e.g. Henoch-Schönlein purpura)
- Spotted fevers (e.g. Mediterranean Spotted Fever)
- Trauma (e.g. violent coughing/vomiting especially around the eyes)

# ABM

- DDx
  - TBM
  - Viral meningoencephalitis
  - Aseptic meningitis
  - Other

# ABM

- Diagnosis
  - High index of suspicion very important
  - Confirm by CSF examination
  - LP deferred if there is contraindication
  - Start empirical antibiotics on suspicion
- CSF: ↑Pressure, turbid, ↑cells (mostly polys), ↑protein, ↓sugar to < 40% of blood sugar
- Gram stain, culture
- Latex
- Imaging

# CSF

Table 1 | Typical cerebrospinal fluid (CSF) findings in infectious meningitis<sup>1 3 14</sup>

Cause of meningitis	White blood cell count (cells/mm <sup>3</sup> /10 <sup>6</sup> cells/l)	Predominant cell type	CSF: serum glucose (normal $\geq 0.5$ )	Protein (g/l) (normal 0.2-0.4)
Viral	50-1000	Mononuclear (may be neutrophilic early in course)	$>0.5$	0.4-0.8
Bacterial	100-5000	Neutrophilic (mononuclear after antibiotics)	$<0.5$	0.5-2.0
Tuberculous	50-300	Mononuclear	$<0.3$	0.5-3.0
Cryptococcal	20-500	Mononuclear	$<0.5$	0.5-3.0

# ABM

- **Complications**
  - Subdural effusion
  - Subdural empyema
  - Ventriculitis
  - Abscess
  - SIADH
  - Hydrocephalus
  - Infarcts
- **Sequelae**
  - Neurological deficits
  - Deafness
  - MR
  - Epilepsy
  - hydrocephalus



# Treatment for bacterial meningitis

- IV ceftriaxone 2g BD (or cefotaxime 2g QDS)
- Vancomycin 500-750 mg q6hrs ( highly penicillin resistant pneumococcus)
- Dexamethasone 0.15mg QDS for 4 days started with first dose of antibiotics (especially if pneumococcal meningitis is suspected); stop if non-bacterial cause is identified
- **Plus** IV ampicillin 2g 4 hourly if **Listeria** suspected (age >55 yrs, immunosuppressed)
- Consult with Microbiology if returning traveller (?penicillin resistance) or immunocompromised host

# Treatment

- Subsequent therapy according to sensitivity
- Repeat LP/ imaging indicated if poor response
- Supportive Rx
  - IV Fluids ? Restrict
  - Management of  $\uparrow$ ICT : mannitol, glycerine, acetazolamide
  - Tt of Seizures, pyrexia
  - Dexamethasone
  - Treat shock, DIC if present
  - Nutrition
  - Nursing

# Advice for relatives

- Prophylaxis is only indicated for meningococcal cases
- The risk for a contact is low and highest in the first 7 days
- Regardless of immunisation status, household contacts, people exposed to droplets when the person got ill (e.g. healthcare workers) and the patient should be treated
- The guidelines have changed ...
- All ages including pregnant women should receive a single dose of ciprofloxacin
- Adults and children over 12 yrs 500mg PO



# ABM: Prevention

- Vaccines
  - Hib
  - Pneumococcal vaccine
  - Meningococcal vaccine during outbreaks
- Chemoprophylaxis for contacts: rifampicin 10 mg/kg/d every 12 hrs x 2 days
- Wash your hands.
- Practice good hygiene.
- Cover your mouth.

# Chronic meningitis

- Slow-growing organisms (such as fungi and *Mycobacterium tuberculosis*) that invade the membranes and fluid surrounding your brain cause chronic meningitis.
- Chronic meningitis develops over two weeks or more.
- The signs and symptoms of chronic meningitis — headaches, fever, vomiting and mental cloudiness — are similar to those of acute meningitis.

# Tuberculous meningitis (TBM)

- Most dreaded and dangerous form of TB
- Risk Factors:
  - Young age
  - Household contact
  - Recent infection
  - Measles
- Pathophysiology
  - Primary infection → bacillemia → hematogenous seeding of meninges (Rich's foci) → rupture
  - Thick exudates in basal cisterns
  - Arteritis

# TBM: Clinical Features

- 3 stages
  - Stage 1: prodromal stage with nonspecific symptoms 1-4 weeks
  - Stage 2: neurological manifestations – seizures, deficits, meningeal signs
  - Stage 3: coma
- Decerebrate posturing, cranial nerve palsies, optic atrophy, extrapyramidal signs, hydrocephalus (communicating or obstructive) more common

# TBM

- DDx
  - Partially treated bacterial meningitis
  - Other CNS infections
- Dx
  - CSF examination - ↑pressure, cells upto 500 /cu mm, mostly lymphos, ↑protein, sugar ↓upto ½ of concomitant blood sugar
  - AFB
  - Culture
  - CXR
  - Skin test
  - Newer Tests:
    - Tuberculostearic acid
    - Adenosine deaminase test
    - Bromide partition test
    - NBT
    - ELISA for antibody/antigen
    - PCR
    - Intrereferon gamma release assays



# TBM

- Complications & sequelae:
  - Hydrocephalus
  - Optic neuritis
  - Focal deficits
  - Epilepsy
  - MR
  - Spinal block/ arachnoiditis
  - Endocrine
- Treatment
  - 4 anti TB drugs for initial 2 months + 3 drugs for 6-7 months
  - DOTS ??
  - Steroids initially for 6 weeks
  - Shunt surgery for hydrocephalus

# Viral meningitis

- Viral meningitis is usually mild and often clears on its own.
- Most cases in the United States are caused by a group of viruses known as enteroviruses, which are most common in late summer and early fall.
- Viruses such as herpes simplex virus, HIV, mumps, West Nile virus and others also can cause viral meningitis.

# VIRAL MENINGOENCEPHALITIS

- Encephalitis and meningitis are 2 ends of the spectrum
- Neurotropic & non neurotropic viruses can cause VME
  - Arbo: JE/ west nile/ dengue
  - Entero
  - Herpes: HSV1, EBV, CMV, HHV-6, Varicella zoster
  - Myxo
  - Paramyxo
  - Adeno
  - Rhabdo

# VME: Clinical features

- 3 stages
  - Prodromal: fever, vomiting, diarrhea, anorexia, malaise
  - Acute encephalitic stage: convulsion. Coma, neurodeficits, raised ICT, death
  - Convalescent stage: improving coma, extrapyramidal

# VME

- Neutrophilia +/-
- CSF clear, pleocytosis +/- . Normal or ↑protein, normal sugar
- Specific Dx by PCR
- Imaging: normal/ edema/ patchy hypodensity/ specific changes
- EEG: nonspecific diffuse slowing

# VME

- DDX: very wide
  - Other CNS infections
  - Enteric encephalopathy
  - Reye's
  - Cerebral malaria
  - Vascular
  - Abscess
  - Metabolic

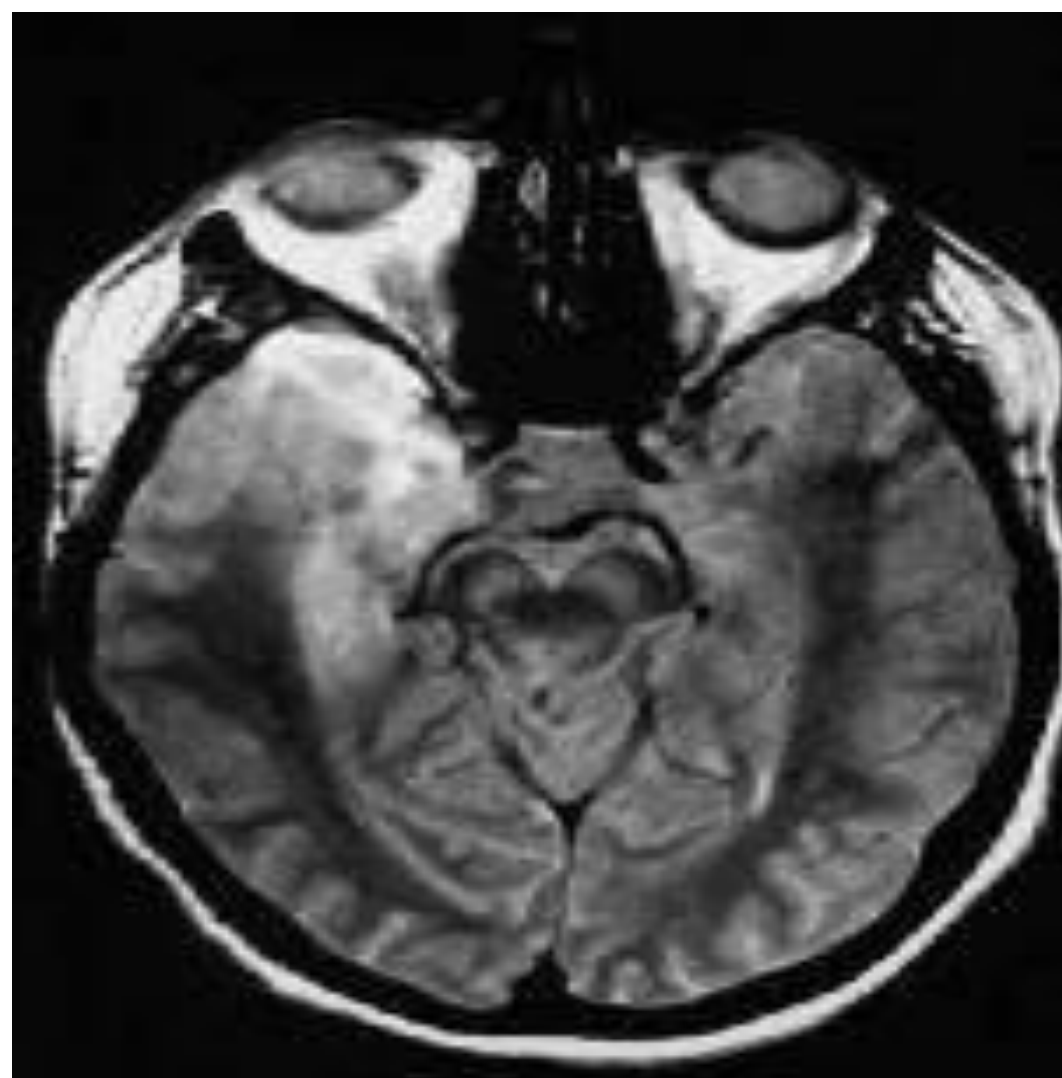
# VME: treatment

- Specific Treatment only for Herpes:HSV1 (HSE)
- Supportive
  - Treat pyrexia
  - Treat seizures
  - Treat ↑ICP:
    - Raise head end
    - Mannitol
    - Diuretics
    - Diamox
    - Glycerine
    - Ventilation
  - Fluids & electrolytes
  - Nutrition
  - Nursing
  - Treatment of movement disorder
  - Physiotherapy & rehabilitation

# Herpes encephalitis

- Commonest sporadic encephalitis in west
- Severe, fulminant course
- Focal deficits
- Focal features on EEG
- Imaging: temporal hypodensities
- Specific antiviral Treatment available: acyclovir 10 mg/kg/d x 14-21 days





# Viral (aseptic) meningitis

- Mild, self limited
- Etiology:
  - Mumps
  - Enterovirus
  - EBV
  - Arbovirus
  - M pneumoniae
- Clinical features:
  - Fever
  - Headache
  - Irritability
  - Vomiting
  - Convulsion (rare)
  - Meningeal signs
- Lab: CSF clear, pleocytosis, ↑protein, normal sugar
- Tx: supportive only

# Brain Abscess

- Predisposing features:
  - Congenital cyanotic heart disease
  - Meningitis
  - Penetrating head injury
  - Local extension from mastoid, otitis, sinusitis, soft tissues of face and scalp
- Etiology:
  - S aureus
  - Micro aerophilic strep
  - Other aerobic & anaerobics
  - Mixed infections in 35%
- Clinical Features:
  - Fever
  - Headache
  - Vomiting
  - Focal deficits
  - ↑ICT
- Lab
  - Blood counts non specific
  - EEG: focal slowing
  - CT scan diagnostic
- Treatment:
  - IV antibiotics – cover anaerobes (CP + Chloro)
  - Surgical drainage

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Im: 11 AC  
EPDV: 22.5cm  
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Thank you