CNS INFECTIONS – 1
Acute meningitis

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Definition

- Bacterial meningitis is a medical emergency.
- Meningitis is an acute infection within the subarachnoid space.
- usually secondary bacteremia or viremia illness, or
- direct spread from an adjacent focus of infection in ear, skull fracture, sinus, or respiratory tract.

? meningeal or parenchymal CNS infection : if one or more is present

- Fever, headache;
- nausea and vomiting;
- confusion, obtundation, or uncharacteristic behavior;
- stiff neck;
- focal neurological dysfunction.

Etiology

Acute meningitis is most often caused by bacteria that have

- *Streptococcus pneumoniae* (~50%)
- *Neisseria meningitidis* (~25%)
- *Haemophilus influenzae* (<10%)

mode of transmission: droplet spread or mucosa to mucosa spread during close contacts.

- ***S. pneumoniae:*** is the most common cause in *adults*. Predisposing conditions: *pneumococcal pneumonia* coexisting *acute or chronic otitis media, alcoholism, diabetes*.
- ***N. meningitidis*** : ~ 60% of bacterial meningitis cases in *children and young adults between the ages of 2-20*.

- ***Enteric gram-negative bacilli*** : is associated with chronic and debilitating diseases such as *diabetes, cirrhosis or alcoholism*, and *chronic urinary tract infections* and *following neurosurgical procedures*, particularly *craniotomy or craniectomy.*

- ***Staphylococcus aureus*** and **–ve staphylococci:** esp after *invasive neurosurgical procedures.*
- Some yeasts (e.g., Cryptococcus): more often in cell mediated immunity compromised pts (e.g. lymphoma; AIDS; steroids).

Table 1. Value of locale of acquisition and age to predict the most likely organism of meningitis

locale	*Age group*	*Most likely organism*
Community acquired meningitis	<1 month	Streptococci-B; S. pneumoniae; L. monocytogenes
	1-23 months	S. pneumoniae; N. meningitidis; Streptococci-B; H. influenzae
	2-18 years	N. meningitidis; S. pneumoniae; H. influnzae
	19-59 years	S. pneumoniae; N. meningitidis; H. influnzae
	>60 years	S. pneumoniae; L. monocytogenes

Table 1. Value of locale of acquisition and age to predict the most likely organism of meningitis contd.

locale	*Age group*	*Most likely organism*
Hospital acquired or trauma-related meningitis	Any age	<10 d post trauma – S. pneumoniae; H. influnzae (patients flora) >10d post trauma - K. pneumoniae, P. aeruginosa, E. coli; other hospital flora

Table 2 Value of P.E. in predicting the most likely organism to be causing meningitis

Physical signs	Most likely organism
Otitis media	S. pneumoniae
Sacral pilonidal sinus	Stool flora probably E. coli
Petechiae (depends on age)	Young: N. meningitidis; children: H. influenzae
Purpura fulminans	N. meningitidis
Ecthyma gangrenosum	P. aeruginosa > candida > other fungi; other gram –ve bacilli

Pathophysiology

- *S. pneumoniae* and *N. meningitidis* initially colonize the nasopharynx (epithelial cells).
- Bloodstream ---- bacteria reach the intraventricular choroid plexus--- infection of choroid plexus epithelial cells----direct access to the CSF.
- Bacteria are able to multiply rapidly within CSF because of the absence of effective host immune defenses.

- Many of the neurologic manifestations and complications of bacterial meningitis: immune response to the invading pathogen rather than from direct bacteria-induced tissue injury.
- Neurologic injury can progress even after the CSF has been sterilized by antibiotic therapy.

Clinical presentation

- in a few hours or
- subacute infection that progressively worsens over several days.

- The classic clinical triad: **nuchal rigidity ("stiff neck") :** occurs in 90% of cases.
- Alteration in mental status: occurs in >75% of patients and can vary from lethargy to coma.
- Nausea, vomiting, and photophobia are also common complaints.

- Nuchal rigidity: indicates meningeal irritation and is present when the neck resists passive flexion. Kernig's and Brudzinski's signs
- Seizures: occur as part of the initial presentation of bacterial meningitis or during the course of the illness in up to 40% of patients.

- The rash of meningococcemia: diffuse erythematous maculopapular rash rapidly become petechial esp on the trunk and lower extremities, mucous membranes and conjunctiva.
- Raised ICP: is an expected complication.
  1. a deteriorating of consciousness level
  2. papilledema
  3. dilated poorly reactive pupils,
  4. sixth nerve palsies,
  5. decerebrate posturing, and
  6. the Cushing reflex (bradycardia, hypertension, and irregular respirations).

Diagnosis

- clinical presentation: ?bacterial meningitis, blood cultures and LP should be immediately obtained
- empirical antimicrobial therapy: If LP is delayed, can be started after blood cultures/ CBC
- The presence of papilledema, localizing signs, or lateralizing signs mandates an imaging study (CT or MRI) before the lumber puncture.
- Antibiotic therapy prior to lumbar puncture: < 8-9 h, not significantly alter the CSF WBC / GLU / not sterilize

classic CSF abnormalities

(1) polymorphonuclear leukocytosis (>100/ l in 90%),
(2) decreased GLU (<40 mg/dL) and/or CSF/ serum glucose ratio of <0.4 in ~60%]
(3) increased protein concentration (>45 mg/dL) in 90%],
(4) increased opening pressure (>180 mmH2O in 90%).
(5) CSF bacterial cultures are positive in >80% of patients, and CSF Gram's stain demonstrates organisms in >60%.

- normal opening pressure:<180 mmH2O,
- normal WBC: <5 mononuclear cells
- Polymorphonuclear neutrophils (PMNs): not present in Normal CSF
- CSF GLU :<40 mg/dL are abnormal, and CSF/serum glucose ratio <0.40:: highly suggestive of bacterial meningitis.

Differential diagnosis

viral meningoencephalitis: Herpes simplex virus (HSV) encephalitis.

- headache, fever, altered consciousness, focal neurologic deficits (e.g., dysphasia, hemiparesis), and focal or generalized seizures.
- CSF studies, neuroimaging,
- The classic CSF profile: a lymphocytic pleocytosis with a normal glucose concentration.

Table 1.Value of CSF findings in predicting the cause of meningitis

Diagnosis	*Cells/µl*	*Glu mg/dl*	*Protein mg/dl*	*Opening pressure mmH_2O*	*Stain and other tests*
Normal	0-5, lym	45-85	15-45	70-80	
Bacterial	200-20000, PMN	<45	>50	↑↑↑	Gram stain, culture
Tubercular	100-1000, lym	<45	>50	↑↑	ZE stain, culture, PCR
Fungal	100-1000, lym	<45	>50	↑↑	India ink, culture, antigen antibody
Viral	25-2000, lym	Normal or low	>50	↑	Culture, PCR
Carcinomatous	Lym, tumor cells	<45	>50	↑↑	cytology

Differential diagnosis

Focal suppurative CNS infections: subdura / epidural empyema and brain abscess, should also be considered.

- The presence of focal features in suspected bacterial meningitis: CT/MRI MRI is preferable to CT and is extremely sensitive and specific for diagnosis.

Differential diagnosis

Subarachnoid hemorrhage (SAH):

- explosive onset of a severe headache
- a sudden transient loss of consciousness then severe headache.
- CT scan is a sensitive indicator for dx
- lumbar puncture: grossly bloody CSF

Treatment

- Begin antibiotic therapy within 60 min of a patient's arrival in ER.
- Empirical antimicrobial therapy: initiated before the results of CSF
- Community-acquired: children and adults should include a third-generation cephalosporin (e.g., ceftriaxone 2 gm Q12h; or cefotaxime 2gm Q4h) and vancomycin 1gm Q12h.
- individuals under three months of age, those over age 55, or those with suspected impaired cell-mediated immunity: Ampicillin 2gm Q4h should be added to coverage *L. monocytogenes.*
- Gentamicin is also often added (2 mg/kg loading dose then 5.1 mg/kg per day given every 8 h and adjusted for serum levels and renal function).

- Hospital-acquired meningitis/ or following neurosurgical procedures, : Staphylococci and gram-ve including *Pseudomonas aeruginosa* are the most common. combination of vancomycin and ceftazidime 2 gm Q8h.
- The duration of therapy: varies on etiology

  H. influnzae 7 days;

  N.meningitidis 7 days;

  S. pneumoniae 10-14 days;

  L monocytogens 14-21 days;

  gram negative bacilli 21 days.

Chemoprophylaxis

- All close contacts with meningococcal meningitis patients
- Close contacts are defined as those individuals who have had contact with oropharyngeal secretions either through kissing or by sharing toys, beverages, or cigarettes.
- 2-day regimen of rifampin (600 mg Q12h)/ or 10 mg/kg Q12h in children >1 year.
- Alternatively, adults can be treated with one dose of ciprofloxacin 750 mg or , azithromycin 500 mg, or ceftriaxone 250 mg Im.

Adjunctive therapy

- The American Academy of Pediatrics recommends the use of dexamethasone for bacterial meningitis

1. infants and children
2. high bacterial load (positive culture),
3. increased ICP, altered mental status.

- 0.6 mg/kg/d in four divided doses given IV for the first 2 days of antibiotic therapy or 0.8 mg/kg/d in two divided doses given for 2 days.
- The first dose of dexamethasone should be administered before or at least with the first dose of antibiotic.

Increased Intracranial Pressure

- intensive care unit.
- elevation of the patient's head to 30 to 45,
- Intubation and hyperventilation (PaCO2 25 to 30 mmHg),
- Mannitol (25-50 gm as bolus)
- Dexamethasone 4mg q4-6hr
- In these patients, accurate ICP measurements are best obtained with an ICP monitoring device.

Complication of septicemia (esp. occurs with meningitis)

- Disseminated intravascular coagulation(DIC).
- Waterhouse-Friderichsen syndrome: hemorrhagic adrenal necrosis.
- Myocarditis with CCF, shock, prolonged fever.
- Damage of cranial nerves.
- Seizures or hydrocephalus.

Prognosis

- Mortality is 3 to 7% for meningitis and depends on
  1) decreased level of consciousness on admission,
  2) onset of seizures within 24 h of admission,
  3) signs of increased ICP,
  4) young age (infancy) and age >50,
  5) the presence of comorbid conditions including shock and/or the need for mechanical ventilation, and
  6) delay in the initiation of treatment.
- Moderate or severe sequelae: occur in ~25% of survivors.
- Common sequelae include decreased intellectual function, memory impairment, seizures, hearing loss and dizziness, and gait disturbances.