

Meningitis

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Objectives

- Pathogenesis & pathophysiology
- Epidemiology
- Microbiology
- Clinical presentation
- Laboratory work up
- Management
- Complications
- Outcomes

Pathogenesis & Pathophysiology

- Complex interplay between virulence factors of the pathogens and the host immune response
- Much of the damage is from cytokines released within the CSF and host inflammatory response
- Colonization of respiratory, gastrointestinal, or lower genital tract (fimbriae or pili which adhere via various receptors)
- Invasion of the bloodstream
- Survival in the bloodstream (polysaccharide capsule of the pathogens)
- Entry into the subarachnoid space

Pathogenesis & Pathophysiology

Direct entry

- Contiguous infection (sinusitis, mastoiditis, preorbital cellulitis)
- Trauma, neurosurgery, or cerebrospinal fluid (CSF) leak
- Medical devices (CSF shunts, cochlear implants)

Pathogenesis & Pathophysiology

Predisposing Factors

- Congenital or acquired immunodeficiency
 - asplenia
 - complement deficiency
 - hypogammaglobulinemia
 - HIV infection
 - glucocorticoid use
 - diabetes mellitus
- Anatomic defects of the spinal cord (dermal sinus , brain, or inner ear)
- Recent infection (especially respiratory and ear infections)
- Recent exposure to someone with meningitis
- Recent travel to an area with endemic meningococcal disease, such as sub-Saharan Africa

Pathogenesis & Pathophysiology

Predisposing Factors

- The CSF has no neutrophils, no immunoglobulins
- The integrity of the Blood brain barrier is one of the most protective mechanisms
- In the newborn the BBB is poorly developed.
Meningitis
- 20% of sepsis cases may be associated with meningitis due to poor BBB in the newborn

Incidence

(USA 2006)

- <2 months – 81 per 100,000 population
- 2 months to 2 years – 7 per 100,000 population
- 2 through 10 years – 0.6 per 100,000 population
- 11 through 17 years – 0.4 per 100,000 population

Microbiology

- **Infants <3 months**
 - Group B streptococcus (GBS)
 - *Escherichia coli*
 - *Listeria monocytogenes*
- **Older infants and children**
 - *S. pneumoniae*
 - *N. meningitidis*
 - *H. influenzae*, and other gram-negative organisms.
- **Adolescents**
 - *N. meningitidis*

Meningococcal Rash



Meningococcal Rash



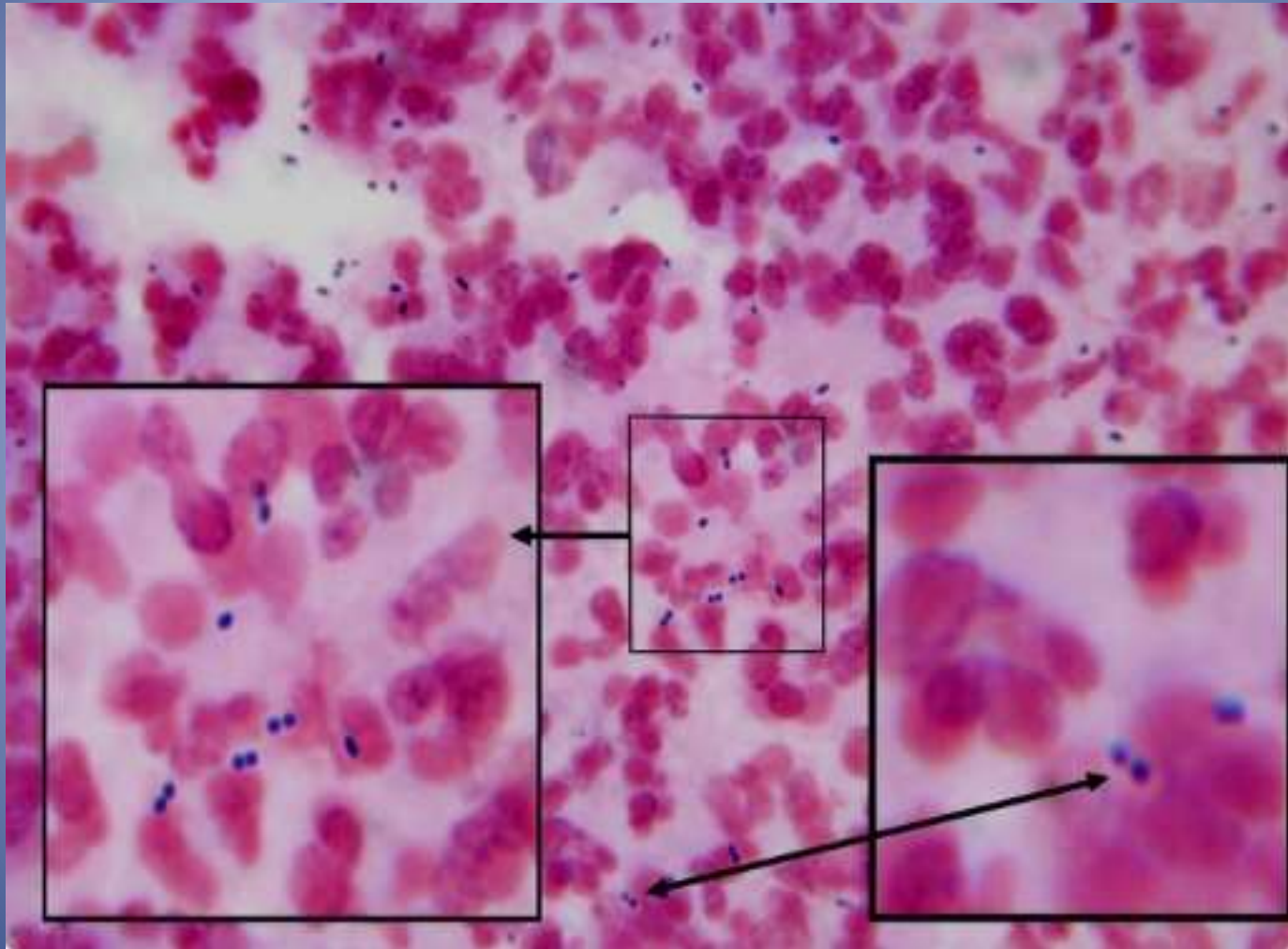
HSV



Enteroviruses



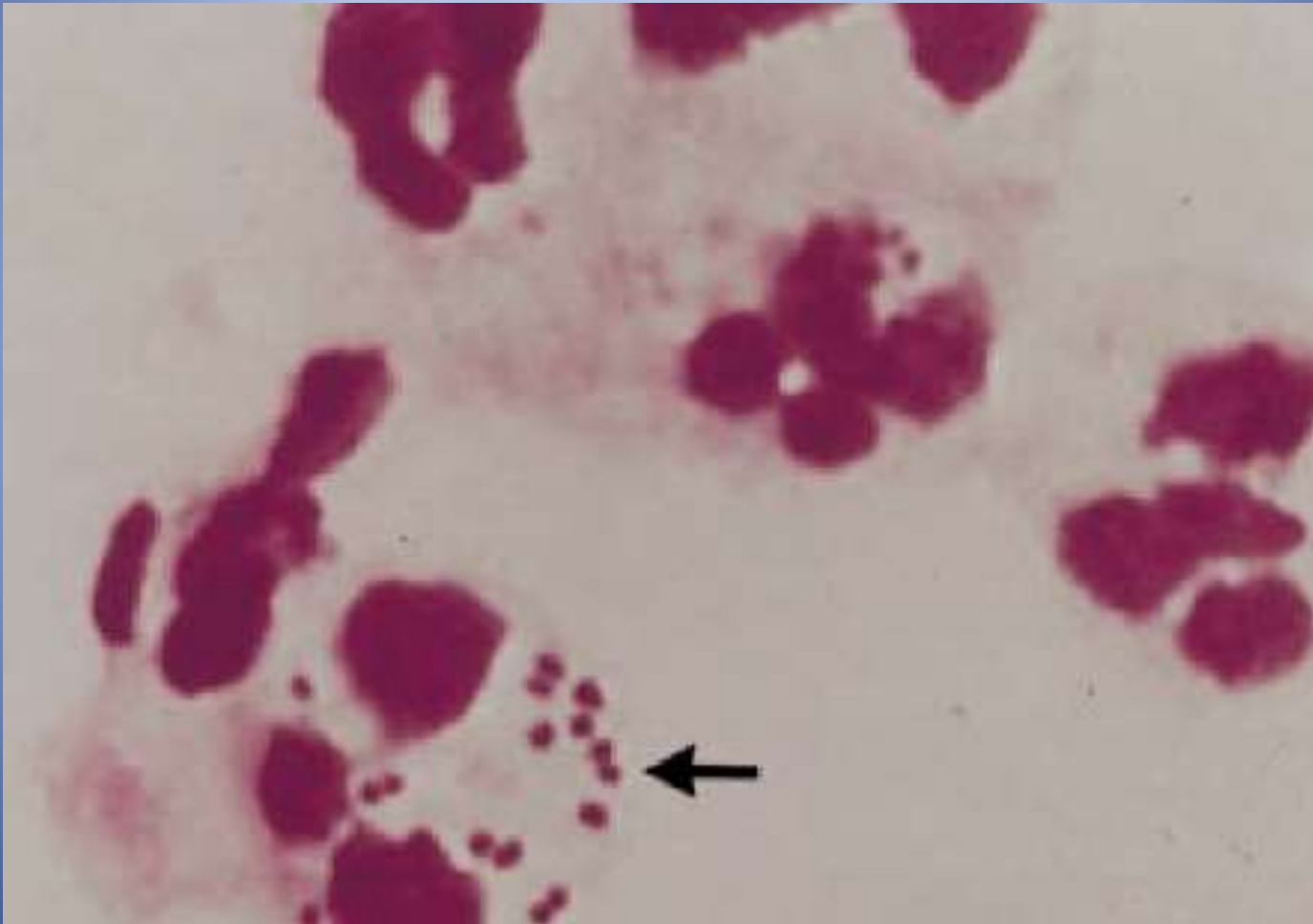
Streptococcus Pneumoniae



Haemophilus Influenzae B



Nisseria Meningitidis



Clinical presentation

Infants :

- Fever, hypothermia
- Bulging fontanel
- lethargy, irritability
- Seizures
- Respiratory distress
- Poor feeding, vomiting

Clinical presentation

Children:

- Fever
- Headache
- Photophobia
- Meningismus
- Nausea/vomiting
- Confusion, lethargy, irritability

Laboratory testing

- Blood culture.
- CBC with differential and platelet count.
- Inflammatory markers (CRP, procalcitonin).
- Serum electrolytes, BUN, creatinine, glucose.
- PT, INR, and PTT

Laboratory testing

Lumbar puncture

- cell count and differential
- glucose
- protein concentration
- Gram stain
- Culture
- PCR (Strep pneumoniae ,MRSA , HSV, Enteroviruses)

Contraindications to LP

- cardiopulmonary compromise,
- clinical signs of increased intracranial pressure,
- papilledema,
- focal neurologic signs, and
- skin infection over the site for LP.

CSF in Meningitis

Opening pressure 200-500 mm H₂O

White blood cell count 1000-5000/mm³

Percentage of neutrophils >80%

Protein 100-500 mg/dL

Glucose <40 mg/dL

CSF : serum glucose <0.4

Typical cerebrospinal fluid findings in central nervous system infections*

	Glucose (mg/dL)		Protein (mg/dL)		Total white blood cell count (cells/microl.)		
	<10 [†]	10 to 40 ^Δ	100 to 500 [◊]	50 to 300 [♢]	>1000	100 to 1000	5 to 100
More common	Bacterial meningitis	Bacterial meningitis	Bacterial meningitis	Viral meningitis Nervous system Lyme disease (neuroborreliosis) Encephalitis Neurosyphilis TB meningitis [‡]	Bacterial meningitis	Bacterial or viral meningitis TB meningitis	Early bacterial meningitis Viral meningitis Neurosyphilis TB meningitis
Less common	TB meningitis Fungal meningitis	Neurosyphilis Some viral infections (such as mumps and LCMV)		Early bacterial meningitis	Some cases of mumps and LCMV	Encephalitis	Encephalitis

Clinical and laboratory features of viral and bacterial meningitis in children

Feature	Viral meningitis	Bacterial meningitis
Seasonal pattern	Enteroviral infections (the most common cause of viral meningitis) occur mostly in summer and fall	No characteristic seasonal pattern
Clinical features		
Fever, headache, stiff neck, photophobia	Common	Common
Ill appearance	Uncommon	Common
Petechiae or purpura	Absent	May be present
Other manifestations of enteroviral infection (eg, rash, conjunctivitis, herpangina, pharyngitis)	Common	Uncommon
Symptoms after LP	Often, there is improvement	No improvement
CSF parameters		
WBC count	Typically 10 to 500 cells/microl	Typically >1000 cells/microl, but can be lower, particularly early in the course
Differential	Mononuclear predominance	Neutrophil predominance
Glucose	Normal or slightly reduced Usually ≥40% of serum value	Usually <60% of serum value Often <40 mg/dL
Protein	Normal to slightly elevated Usually <150 mg/dL	Typically 100 to 500 mg/dL

Neuroimaging

Indications for neuroimaging before LP

- severely depressed mental status (coma)
- papilledema
- focal neurologic deficit (with the exception of cranial nerve VI or VII palsy)
- history of hydrocephalus and/or presence of a CSF shunt
- recent history of CNS trauma or neurosurgery

Management

Supportive care

- Ensure adequate oxygenation, ventilation, and circulation
- Obtain venous access
- Cardio-respiratory monitoring while obtaining laboratory studies.
- Keep the head of bed elevated at 15 to 20°.
- Treat hypoglycemia, acidosis, and coagulopathy

Management

Antimicrobial therapy

- Antibiotic therapy should be **initiated immediately** following the LP if the clinical suspicion for meningitis is high

Vancomycin (15 mg/kg IV)

Ceftriaxone (50 mg/kg IV) or cefotaxime (100 mg/kg IV)

Management

- Consider dexamethasone therapy* (0.15 mg/kg IV) in patients with certain risk factors
 - unimmunized patients,
 - young children [age ≥ 6 weeks to ≤ 5 years],
 - children with sickle cell disease,
 - asplenic patients) or
 - if there is known or suspected *Haemophilus influenzae* infection (eg, based on Gram stain results).
- If dexamethasone is given, it should be administered before, or immediately after, the first dose of antibiotic therapy

Dexamethasone

- Neonates (C-I) (not proved)
- Infants and children with Haemophilus influenzae type b meningitis (A-I)
- Infants and children with pneumococcal meningitis (B-I)
- Adults with pneumococcal meningitis (A-1)
- Patients with pneumococcal meningitis caused by highly penicillin- or cephalosporin-resistant strains (B-III) Administer at 0.15 mg/kg every 6 hours for 2-4 days concomitant with or just before first antimicrobial dose

Duration of Therapy

- *N meningitidis* 7 d
- *H influenzae* 7 d
- *S pneumoniae* 10-14 d
- *S agalactiae* (GBS) 14-21 d
- Aerobic gram-negative bacilli 21 days or 2 wks beyond the first sterile culture (whichever is longer)
- *L monocytogenes* 21 d or longer

Contacts

- Prophylaxis should be given to contacts of Hib and Meningococcal infections
- Prophylaxis for Meningococcal meningitis Give to ALL household or very close contact regardless of age
- Risk of secondary case is 1%
- Rifampicin, or ceftriaxone, or ciprofloxacin PLUS meningococcal vaccine

Complications

- Death 3-5%
- Subdural effusion/empyema
- Hearing deficit 7-30%
- Decreased IQ 30-50%
- Seizures
- Hemiparesis
- Other neurological deficit

Outcomes

- Overall mortality for bacterial meningitis is 5-10%
- In neonates, mortality is 15-20%, whereas in older children, it is 3-10%
- *S pneumoniae* meningitis 26.3-30%
- Hib meningitis 7.7-10.3%
- *N meningitidis* has the lowest, at 3.5-10.3%
- **However meningococemia is worse and may be associated with a very high rate unless identified in time**

Summary

- Acute bacterial meningitis remains a major cause of mortality and morbidity despite antibiotics
- Epidemiologic factors depend on availability of vaccination, crowding as well as availability of good health systems
- Host factors play a major role in brain damage need better therapies to modulate this
- Dexamthasone adjunct therapy now recommended for children and adults

Summary

- Outcome may be more guarded with subtle brain damage and decreased IQ
- Prevention is primary, vaccines for all three pathogens are now present
- In Jordan we have only introduced Hib for all children
- N meningitides for pilgrims and the military recruits
- Pneumococcal vaccine needs to be included in the national program