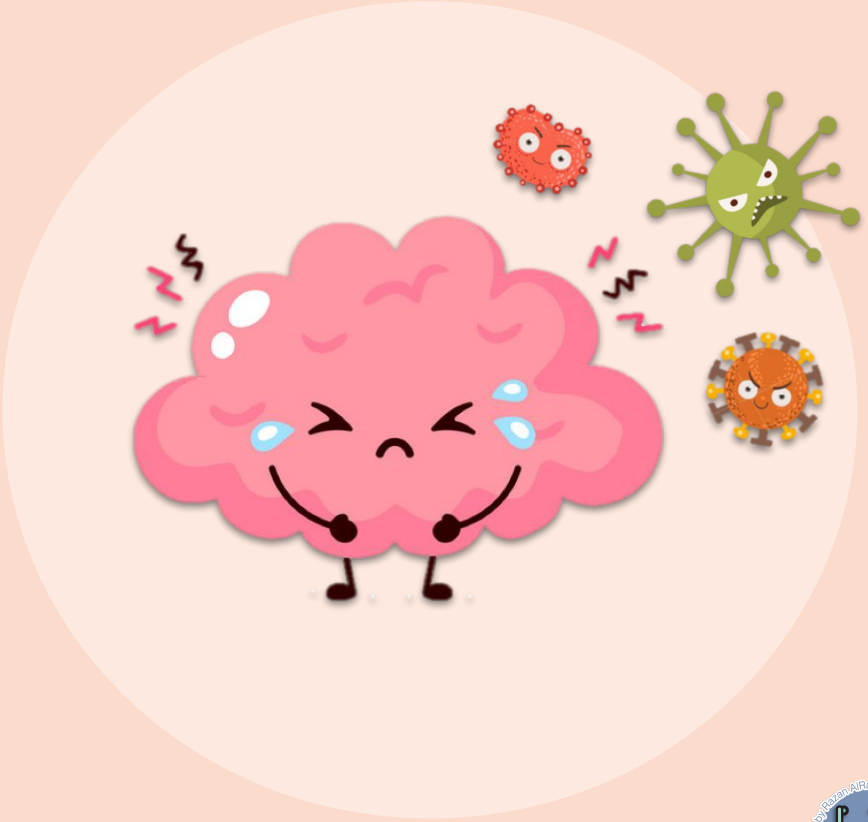
MICROBIOLOGY
TEAM 438

MED438

Acute pyogenic meningitis



Reviewed by: Jazan AlRabah & Ibrahim AlDakhil

Objectives

- ★ Define acute pyogenic meningitis.
- ★ Recall the epidemiology of acute pyogenic meningitis.
- ★ Recall the etiologic agents according to the age and common serotypes of the main causative pathogens.
- ★ Describe the clinical presentation of acute meningitis.
- ★ Identify the microbiology of common causative agents including the morphology, pathogenesis, identification and complications.
- ★ Discuss approaches to the clinical diagnosis of acute meningitis case with emphasis on lab diagnosis and comparison between normal and abnormal CSF analysis.
- ★ Recall the management of acute meningitis with emphasis on rapid diagnosis and selection of empirical antimicrobial therapy for the common pathogens.
- ★ Recall preventative strategies (vaccination and prophylaxis) used against common pathogens.

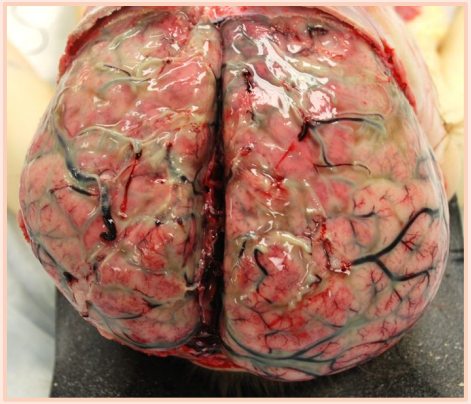
Color index:
- Important
- Doctors note
- Extra

Editing File

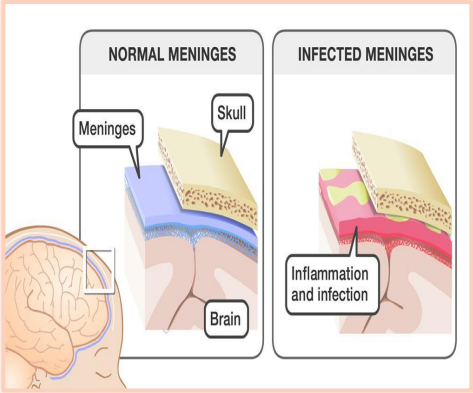
Definition

What is Acute Pyogenic Meningitis?

- A serious infection that causes the inflammation of the meninges (coverings of the brains) affecting the **pia**, **arachnoid** and **subarachnoid space**, and is associated with marked inflammatory exudation.
- Has an **acute** onset.
- Usually caused by bacterial infections. (viral are less severe & self limiting)
- May be preceded by URTI.
- Can be fatal if left untreated.
- Why is it important?
    - Severe, & life-threatening condition.
    - High morbidity & mortality.
- Meningitis can be a complication of untreated otitis media or sinusitis.



Meningitis - gross



Common Etiologic Agents

Three main bacterial pathogens: ★

- Neisseria meningitidis
- Streptococcus pneumoniae
- Haemophilus influenzae (less important these days than the 2 above)

- Prof. Ali Somily's note:
Sometimes meningitis can be misdiagnosed with OM, it will be treated as OM, but meningitis will be partially treated, by time the patient/child will die, this is called "partially treated meningitis".

Causes according to the age

Age	Pathogen
Newborns caused by the normal flora in the birth canal → more common in vaginal deliveries	Group B Streptococcus, E. coli (and other gram negative bacilli), Listeria monocytogenes.
Infants / Children 1 month and above	S. pneumoniae, N. meningitidis, H. influenzae.
Adults [1]	S. pneumoniae, N. meningitidis.
Special circumstances [2]	S. aureus, S. epidermidis, S. pneumoniae, anaerobes, P. aeruginosa.

Epidemiology of Meningitis

- A worldwide disease, about 1.2 million cases annually and 135,000 deaths.
- Bacterial meningitis is one of the top ten infections that causes death worldwide.
- Half of the survivors suffer neurological damage, and/or permanent side effects afterwards.

Note:
1. H. influenzae is not common in adults because they are vaccinated against it.
2. Special cases such as surgery, tumors, devices or severe trauma enhance organisms that usually do not cause meningitis to infect, not important ;)

Signs & Symptoms of Acute Meningitis

more severe in bacterial meningitis than viral

Most common (children & adults)

- Fever
- severe Headache
- Stiff neck
- Nausea & vomiting
- Sensitivity to light
- Confusion

In infant

- Inactivity
- Irritability
- Vomiting
- Poor feeding

Advanced cases

- Bruises under skin (rapidly spread)
  - Seen in S. Pneumoniae & N. Meningitidis infections due to alteration in coagulation pathways.

Advanced disease

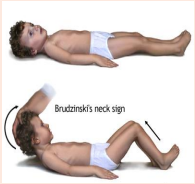
- Brain damage
- Coma
- Death

Physically demonstrable symptoms of meningitis

Both are non-specific signs.

Brudzinski's sign:

Severe neck stiffness (due to the inflammation of the meninges) causes the patient's hips and knees to flex when the neck is flexed.



Kernig's sign:

Severe stiffness of the hamstrings cause an inability to straighten leg when the hip is flexed to 90 degrees.

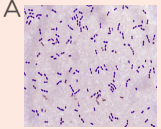
Only the pictures were in the doctors slides

About the bacteria in this lecture (EXTRA)

Gram +ve

Strept. Pneumoniae

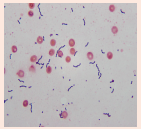
- Diplococci [A]
- Catalase -ve
- Coagulase -ve
- ***α*** hemolytic
- Bile soluble
- Optochin sensitive [B]

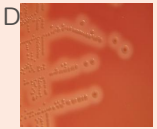
A 

B 

Strept. Agalactiae (group B)

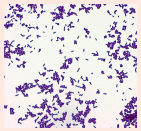
- Cocci in chains [C]
- **β** hemolytic [D]
- Catalase -ve
- Coagulase -ve
- Bacitracin resistant

C 

D 

Listeria Monocytogenes

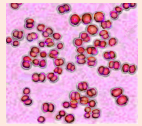
- Small rods [E]
- Aerobes
- Tumbling motility
- Facultative intracellular

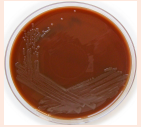
E 

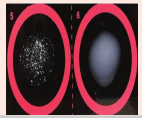
Gram -ve

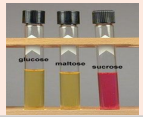
N. Meningitidis:

- Kidney bean-shaped diplococci [F]
- Oxidase +ve
- Latex particle agglutination [G]
- Grows on thayer-martin agar [H]
- Grows on chocolate agar.
- Utilities maltose & glucose [I]

F 

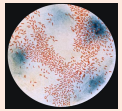
H 

G 

I 

H. Influenzae:

- Coccobacilli [J]
- Requires growth factor x (hemin) and v (NAD) [K]
- Satellitism test [L]:
  Most strains of *Haemophilus* spp does not grow on 5% Sheep Blood Agar, which contains hemin (factor X) but lacks NAD (factor V). *Staphylococcus aureus* produce NAD as a metabolic byproduct when grow in a culture media containing blood.

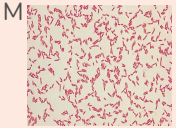
J 

K 

L 

E. coli:

- Rods [M]
- Facultative anaerobic
- Oxidase -ve
- Ferments lactose [N]

M 

N 

- Neisseria Species don't cause RTIs.
- N. Meningitidis → causes meningitis.
- N. Gonorrhoeae → causes gonorrhea.

N. Meningitidis

Morphology	A Gram negative diplococci present in the nasopharynx of 10% of people potential pathogen.
Transmission	By the inhalation of aerosolized droplets, close contact, & sharing drinks or cigarettes.
Prevalence	Common in children < 6 years old, And young adults.
Risk Factor	Susceptible individuals (unvaccinated).
Serotypes	• Serotypes B, C, Y, and W135 cause isolated, sporadic small epidemics in close population, schools and prisons. • Serotype A has an epidemic potential in the sub-Saharan Africa (meningitis belt). 
Pathogenesis	• Colonization of nasopharynx → Septicemia blood brain barrier → Widespread endothelial damage → Activation of coagulation → Thrombosis and platelets aggregation → Bleeding: skin rash, adrenal hemorrhage, followed by death. • It stimulates antibody production in carriers (Neisseria is normal flora in some people). • Pili attach to microvilli of nasopharynx → Invasion → Bacteremia → production of endotoxin (LPS) → endotoxin is spread to the meninges. • **Capsule** resists phagocytosis. Postexposure prophylaxis to close contact.
Prognosis	• 11-20 % of recovered patients suffer permanent hearing loss/mental retardation. • 10-14 % of cases are fatal.

Most common adult cause

S. Pneumoniae

Morphology	A Gram positive diplococci.
Risk factors	• May develop after trauma to the skull. • Non vaccinated patient (infection rate decreases with vaccination).
Pathogenesis	• Meningitis may follow pneumococcal pneumonia, OM, sinusitis, or any other infections caused by this bacteria. • Pneumolysin toxin decreases inflammatory immune response and leads to severe infection. • **Capsule** is a polysaccharide polymer.
Prognosis	• High mortality rate > 30% due to invasiveness of disease. • Recovered cases develop sustained learning disabilities.

H. Influenzae

Morphology	• A small Gram negative coccobacilli. (pleomorphic) • H. Influenzae type B has a **polysaccharide capsule**, others species of H. Influenzae don't. • Need blood for optimal growth, Hematin (factor X) and NAD (factor V). (or chocolate agar) • Found in the nasopharynx normal flora. • Major cause of lower RTI, occasionally invades deeper tissues and causes bacteremia Infection rate is decreased since the routine use of Hib vaccine. • Bacteremia: bacteria spread to the CNS, bones, or other organs.

H. Influenzae

Serotype	• Many serotypes (a-f) • H. Influenzae type b has a capsule made of a polymer of PRP (Polyribosyl Ribitol Phosphate) that causes acute life threatening invasive infections.
Prevalence	Epidemic in unvaccinated children ages 3 months to 2 years, after maternal antibody has diminished and before immune response of child is adequate.
Prognosis	• 3-6% mortality rate. • 1/3 of survivals have significant neurological sequelae.

Group B Streptococcus (GBS)

Morphology	• Gram positive cocci in chains. • Resident bacteria in GIT & vagina (10-30%) (colonizes the body during delivery through vagina).
Risk factors	• Premature rupture of membrane (baby becomes highly susceptible for colonization). • Prematurity. • Low infant innate immunity.
Pathogenesis	• Gains access to amniotic fluid during delivery or colonize newborn during passage through birth canal. • Causes sepsis and meningitis in the first few days of life up to after 4 weeks.

E. Coli

Morphology	• A Gram negative bacilli. • Most common cause of neonatal meningitis. • Many of its features are similar to GBS.
Pathogenesis	• Vaginal E. Coli colonize the infant via rupture of amniotic membrane or during birth. • Failure of preterm maternal IgM to cross placenta & special susceptibility of newborn. • **K1 sialic acid capsule of some strains invade brain microvascular endothelial cells**. (this makes it more broad to produce meningitis).

Listeria Monocytogenes

Morphology	• Gram positive rods (diphtheroids like). • Human intestinal colonization (2-12%).
Risk factors	Causes meningitis in newborns and immunosuppressed patients, & in elderly. (may cause gastroenteritis in adults)
Pathogenesis	• Widespread among animals in nature especially those associated with certain foods (**soft cheese and cold meat**), Can also affect adults by consuming bad food. • Spreads to fetus following hematogenous spread in mother or from birth canal. • Has **tropism to the CNS**. • Has cold tolerance (can growth in foods even if it in refrigerator).

Diagnosis of Meningitis

Clinically:
- Signs & symptoms.

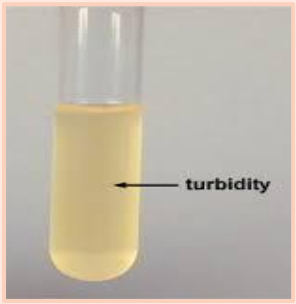
Specimens:
- CSF analysis acquired through lumbar puncture and blood specimen for culture. Sometimes CSF is -ve but there is septicemia
- CSF is analyzed for cells, proteins, glucose and chloride in addition to culture and antimicrobial susceptibility testing.

CNS Parameters

	Normal CSF		Pyogenic Meningitis
Adults	• WBC = 0-5 /cmm3 • PMN = 0 % • Glucose = > 60 % of blood • Protein = < 30 mg/dl • Chloride = 115-130 mmol/l		• WBC = 5 - 5000/cmm3 • PMN = > 60% • Glucose[1] = < 45 % of blood • Protein[2] = > 60 mg/dl • Chloride = 110 mmol/l
Neonates	• Term (mature): - WBC = 0-32 /cmm3 - PMN = > 60 % - Glucose = > 60 % of blood - Protein = 20-170 mg/dl	• Preterm (premature): - WBC = 0-29/cmm3 - PMN = < 60 % - Glucose = > 60 % of blood - Protein = 60-150 mg/dl	

1. It's decreased because it is used up by bacteria
2. Increased due to inflammation and destruction of the tissue

CSF Evaluation



Condition	WBC	Protein (mg/dL)	Glucose (mg/dL)
Normal	<5, ≥75% lymphos	20-45	>50 (or 75% serum glucose)
Bacterial, acute	100-10,000 or more; usually 300-2,000; Neutros predominate	Usually 100-500	Decreased, usually <40 (or <50% serum glucose)
Bacterial, partially treated	5-10,000	Usually 100-500	Low to normal
TB	10-500 Lymph not as high as acute pyogenic	100-3000	<50
Viral or Meningoencephalitis	Rarely > 1000 Lymph	Usually 50-200	Generally normal; may be decreased

Abnormal findings of CSF in some pathological conditions ★

Parameter	Confition			
	Bacterial Meningitis	Tuberculous Meningitis	Viral Meningitis	Brain Tumor
Protein	↑↑	↑↑	Normal	↑
Glucose	↓↓	↓↓	Normal or slightly ↓	↓
Chlorides	↓↓	↓↓	Normal or ↓	Normal or ↓

Management

- A medical emergency.
- Antibiotics given after taking specimens for lab diagnosis.
- Parenteral administration.

Children & Adults [1]	• Ceftriaxone (or Cefotaxime)[2] + Vancomycin [3] (covers the main 3 pathogens, N. meningitidis, S. pneumoniae, H. influenzae). • Add ampicillin if > 50 or at risk for Listeria.
Neonates [1] (1 month or less)	• Ampicillin + Gentamicin + Cefotaxime (to cover gram +ve group B, Listeria Monocytogenes & E.coli) ○ We don't give Ceftriaxone in this case (contraindication) because it'll effect the biliary tract (cause biliary sludge and jaundice), so we use Cefotaxime instead of it because it has less side effects. • Modify treatment after lab results (as needed).
Duration	10-14 days (or more) according to the medical condition.
Prevention	• Vaccination • Prophylactic antimicrobial agent for contacts (Hib & N. meningitidis)

1- It's empiric therapy given immediately after taking specimens, after identifying the organism we choose a specific antibiotic.
2- Ceftriaxone or cefotaxime covers S.pneumoniae, N.meningitidis, & H.influenzae. 3- we use vancomycin because there is a risk of resistance S.pneumoniae.

Quiz :

Q1/ A 7 days-old patient, diagnosed with acute bacterial meningitis, which Antibiotic that can't be use as empiric therapy in this case?

A. Ampicillin
B. Ceftriaxone
C. Cefotaxime
D. Gentamicin

Q2/ Which one is elevated in case of meningitis caused by S.pneumoniae?

A. Lymphocytes
B. Glucose
C. Protein
D. Chlorides

Q3/ A 3 years old child from sudan was diagnosed with N.Meningitidis what is the most likely serotype?

A. serotype B
B. serotype W135
C. serotype A
D. serotype C

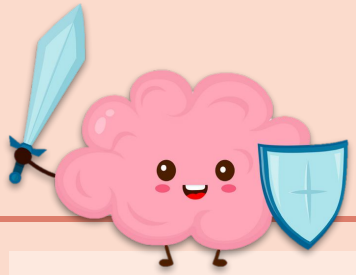
Q4/ A 34 years women delivered her baby 3 months prior to her due date , after 2 days she noticed stiffness in the baby's neck , vomiting and fever. The doctor diagnosed him with meningitis caused by a gram +ve β hemolytic cocci in chains , what is the organism?

A. S.pneumoniae
B. N.meningitidis.
C. H. Influenzae
D. Group B Streptococcus

SAQ/ A 28 years-old college student, has 1 day history of fever & severe headache, was brought to emergency department, in examination he had severe neck stiffness, CSF analysis showed: neutrophilia, ↑ protein, ↓ Glucose. Culture showed: gram +ve, diplococci, alpha hemolytic. [1] what is the diagnosis? [2] what is the most common causes in this age? [3] what is the most common cause in this case? [4] what is the empiric therapy for this case? [5] which antibiotic can we add if the patient was 59 years-old?

1/ Acute bacterial meningitis.
2/ S.pneumoniae & N.meningitidis.
3/ S.pneumoniae.
4/ Ceftriaxone (or Cefotaxime) + Vancomycin.
5/ Ampicillin.

Q1/B
Q2/C
Q3/C
Q4/D



THANK YOU

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