

TEAM443
MICROBIOLOGY

Microbiology of acute pyogenic meningitis

LECTURE 2



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 microbiology of common causative agents including the morphology, Identification, pathogenesis and complications of meningitis



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

Any future corrections will be in the editing file, so please check it frequently

Special thanks to Aroub Almahmoud ♥

Color Index:

Main text

Important

Notes

Boys slides

Girls slides

Extra



Acute Pyogenic Meningitis

Pyogenic Meningitis {1}

It is a serious infection that leads to **inflammation of the meninges, affecting pia, arachnoid, and subarachnoid space**. It is associated with marked inflammatory exudation.

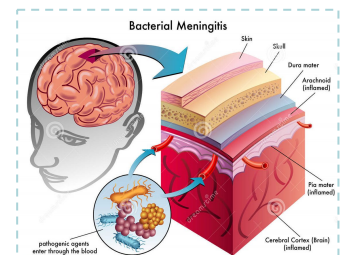
Its characteristics include:

Acute In onset

Usually caused by bacterial infections

May be preceded by URTI

Can be fatal if untreated



Common Etiologic Agents

There are three main bacterial pathogens:

- ✦ *Neisseria Meningitidis*
- ✦ *Streptococcus Pneumoniae*
- ✦ *Hemophilus Influenzae*

Epidemiology of Meningitis

A A worldwide disease, there are 1.2 million cases annually and about 135,000 deaths.

B Bacterial meningitis is one of the top ten infections which **causes death** worldwide.

C Half of the survivals suffer **neurological damage**, and/or permanent side effects.



Acute Pyogenic Meningitis

Causes according to the age ★

Age Group {2}	Pathogens		
Newborns {4}	<ul style="list-style-type: none"> ◦ Group B Streptococcus ◦ Listeria Monocytogenes 	<ul style="list-style-type: none"> ◦ E.coli (and other gram negative bacilli) 	
Infants / Children	<ul style="list-style-type: none"> ◦ S.pneumoniae ◦ H.influenzae 	<ul style="list-style-type: none"> ◦ N.meningitidis 	
Adults	<ul style="list-style-type: none"> ◦ S.pneumoniae ◦ N.meningitidis 	<ul style="list-style-type: none"> ◦ Listeria Monocytogenes if the patient > 50y 	
Special Circumstances {3}	<ul style="list-style-type: none"> ◦ S.aureus ◦ P.aeruginosa 	<ul style="list-style-type: none"> ◦ S.pneumoniae ◦ S.epidermidis 	<ul style="list-style-type: none"> ◦ Anaerobes

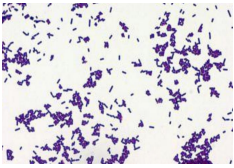
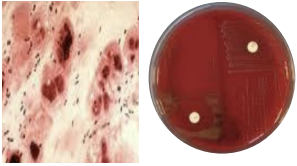
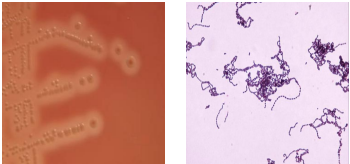
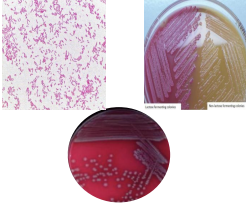
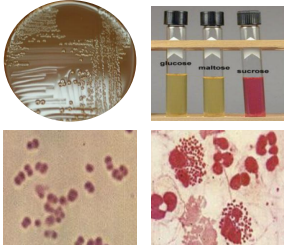
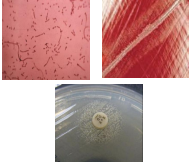
Signs / Symptoms of Acute Meningitis

Case	Symptoms			
Most Common Children & Adults	<ul style="list-style-type: none"> ◦ Fever ◦ Headache 	<ul style="list-style-type: none"> ◦ Stiff neck {5} ◦ Confusion 	<ul style="list-style-type: none"> ◦ Sensitivity to light ◦ Nausea & vomiting 	
Infants {6}	<ul style="list-style-type: none"> ◦ Inactivity 	<ul style="list-style-type: none"> ◦ Vomiting 	<ul style="list-style-type: none"> ◦ Poor feeding 	<ul style="list-style-type: none"> ◦ Irritability
Advanced Cases	<ul style="list-style-type: none"> ◦ Bruises under skin (bleeding under the skin) that rapidly spread^[3] 			
Advanced Disease (Rare)	<ul style="list-style-type: none"> ◦ Brain damage 	<ul style="list-style-type: none"> ◦ Coma 	<ul style="list-style-type: none"> ◦ Death 	

Physically Demonstrable Symptoms of Meningitis {7}	<p>Brudzinski's Sign</p>	<p>Severe neck stiffness. It causes a patient's hips and knees to flex when the neck is flexed.</p>
	<p>Kernig's Sign</p>	<p>Severe stiffness of the hamstrings. It causes an inability to straighten the leg when the hip is flexed to 90 degrees.</p>



Etiologic Agents

Pathogens in This Lecture (Extra 438)	Gram Positive	1- Listeria Monocytogenes {12}	<ul style="list-style-type: none"> ○ Small Rods (bacilli) ○ Aerobes ○ Tumbling motility ○ Facultative intracellular ○ Beta hemolytic ○ Catalase + 	
		2- S. Pneumonia	<ul style="list-style-type: none"> ○ Diplococci ○ Alpha-hemolytic ○ Optochin sensitive ○ Catalase -ve ○ Coagulase -ve 	
		3- Group B Streptococcus (streptococcus agalactiae)	<ul style="list-style-type: none"> ○ Cocci in chains ○ Beta hemolytic ○ Catalase -ve ○ Coagulase -ve ○ Bacitracin Resistant 	
	Gram Negative	4- E. Coli	<ul style="list-style-type: none"> ○ Rods ○ Lactose fermenter ○ Oxidase -ve 	
		5- Neisseria Meningitidis {10}	<ul style="list-style-type: none"> ○ Kidney bean shaped diplococci ○ Latex particle agglutination ○ Utilises maltose and glucose ○ Grows on thayer-martin agar ○ Catalase and Oxidase +ve ○ Grows on chocolate agar 	
		6- H. Influenzae {13}	<ul style="list-style-type: none"> ○ Requires growth factor: X (Hemin) and V (NAD) ○ Coccobacilli 	



Etiologic Agents

N.
Meningitidis

S.
pneumoniae

H. influenzae

Group B
streptococcus

E. coli

Listeria
monocytogenes

N.
Meningitidis

S.
pneumoniae

H.
influenzae

Group B
streptococcus

E. coli

Listeria
monocytogenes

Morphology	A Gram negative diplococci present in the nasopharynx of 10 % of people
Risk factors	Susceptible individuals
Transmission	Transmitted by inhalation of aerosolized droplets & by close contact {8}
Prevalence	Common in children < 6 years
Pathogenesis	<ul style="list-style-type: none"> Colonization of nasopharynx → Septicemia → blood brain barrier → Widespread endothelial damage → (in sever case) Activation of coagulation → Thrombosis and platelets aggregation → Bleeding : skin rash, adrenal hemorrhage In carriers; it stimulates antibody production
Virulence factors	<ul style="list-style-type: none"> Pili attach to microvilli of nasopharynx , invasion, then bacteremia, endotoxin (LPS) produced which spreads to the meninges. Capsule resists phagocytosis.
Serotypes	<ul style="list-style-type: none"> Serotypes: B,C,Y,W135 cause isolated ,sporadic small epidemics in close population. Serotype A has an epidemic potential in sub-Saharan Africa (meningitis belt) {9}
Prognosis	<ul style="list-style-type: none"> 11-20 % of recovered patients suffer permanent hearing loss, mental retardation. 10-14 % of cases are fatal.



Etiologic Agents

N.
Meningitidis

**S.
pneumoniae**

H.
influenzae

Group B
streptococcus

E. coli

Listeria
monocytogenes

Morphology	A Gram positive diplococci.
Risk factors	May develop after trauma to the skull.
Pathogenesis	Meningitis may follow pneumococcal pneumonia, or other infections with the bacteria. {11}
Virulence factors	<ul style="list-style-type: none"> ○ Capsule is a polysaccharide polymer ○ Pneumolysin toxin decreases inflammatory immune response and leads to severe infection.
Prognosis	<ul style="list-style-type: none"> ○ High mortality rate >30% due to invasive disease. ○ Infection rate decreased due to vaccination . ○ Recovered cases develop sustained learning disabilities .

N.
Meningitidis

S.
pneumoniae

**H.
influenzae**

Group B
streptococcus

E. coli

Listeria
monocytogenes

Overview	<ul style="list-style-type: none"> ○ Major cause of lower RTI , occasionally invade deeper tissues and cause bacteremia. ○ Bacteremia: bacteria spread to the CNS ,bones or other organs.
Morphology	<ul style="list-style-type: none"> ○ A small Gram negative coccobacilli ○ Need blood for optimal growth, Hematin (factor X) and NAD (factor V) ○ Found in the nasopharynx normal flora
Virulence factors	H. Influenza Has polysaccharide capsule , other species has no capsule. {14}
Prognosis	<ul style="list-style-type: none"> ○ 3-6% mortality rate (the neurological complication difference according to age and severity some people have seizures and other have hearing impairments) ○ 1/3 of survivals have significant neurological sequelae ○ Infection rate decreased since the routine use of <i>Hib</i>vaccine .
Serotypes {15}	Many serotypes a-f H.influenzae type b has a capsule made of a polymer of PRP (Polyribosyl Ribitol Phosphate) causes acute life threatening invasive infections .



Etiologic Agents

N.
Meningitidis

S.
pneumoniae

H.
influenzae

**Group B
streptococcus**

E. coli

Listeria
monocytogenes

Morphology

- Gram positive cocci in chains
- Resident bacteria in GIT & vagina {16} (10 - 30 %)

Risk factors

premature rupture of membrane, prematurity, low infant innate immunity .

Pathogenesis

- Gain 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 and after 4 weeks.

N.
Meningitidis

S.
pneumoniae

H.
influenzae

Group B
streptococcus

E. coli

Listeria
monocytogenes

Morphology

A Gram negative bacilli

Prevalence

Most common cause of neonatal meningitis

Pathogenesis

- Many features similar to GBS .
- Vaginal *E.coli* colonize infant via rupture of amniotic membrane or during birth.
- Failure of preterm maternal IgM to cross placenta & special susceptibility of newborn.

Virulence factors

K1 sialic acid capsule of some strains invade brain microvascular endothelial cells.

N.
Meningitidis

S.
pneumoniae

H.
influenzae

Group B
streptococcus

E. coli

**Listeria
monocytogenes**

Morphology

- Gram positive rods (*diphtheroids like*)
- Widespread among animals in nature including those associated with certain foods (cheese and meat) {17}

Risk Factor

Causes meningitis in newborns and immunosuppressed patients.

Pathogenesis

- Human intestinal colonization (2-12%)
- Spread to fetus following hematogenous spread in mother or from birth canal.
- Has tropism to the CNS



Diagnosis of Meningitis

Diagnosis {19}

Clinically: **Signs & Symptoms, age**

Specimens: **CSF** analysis acquired through lumbar puncture and **blood** specimen for culture

CSF is analyzed for: cells, **proteins, glucose and chloride** in addition to culture and antimicrobial susceptibility testing.

CNS PARAMETERS

Normal CSF		Pyogenic Meningitis {18}	
Adults	<ul style="list-style-type: none"> ○ WBC = 0-5 /mm³ ○ PMN^[1] = 0 % ○ glucose = > 60 % of blood ○ protein = < 30 mg/dl ○ chloride = 115-130 mmol/l 	<ul style="list-style-type: none"> ○ ↑WBC = 5 - 5000/mm³ ○ ↑PMN^[1] = > 60% ○ ↓Glucose = < 45 % of blood ○ ↑Protein = > 60 mg/dl ○ ↓Chloride = 110 mmol/l <p>^[1]Polymorphonuclear leukocytes</p>	
Neonates	<table border="0"> <tr> <td>Term (mature): WBC = 0-32 /mm³ PMN=> 60 % glucose = > 60 % of blood protein = 20-170 mg/dl</td> <td>Preterm (premature): WBC = 0-29/mm³ PMN = < 60 % glucose = > 60 % of blood protein = 60-150 mg/dl</td> </tr> </table>		Term (mature): WBC = 0-32 /mm ³ PMN=> 60 % glucose = > 60 % of blood protein = 20-170 mg/dl
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CSF Evaluation {18}

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; Neutrophils predominate highly increased	Usually 100-500 highly increased	Decreased, usually <40 (or <50% serum glucose) highly decreased
Bacterial, partially treated	5-10,000	Usually 100-500	Low to normal
TB	10-500 Lymph	100-3000 highly increased	<50
Viral or meningoencephalitis	Rarely > 1000 Lymph	Usually 50-200 Normal / slightly increased	Generally normal ; may Viral or be decreased





Diagnosis of Meningitis

Abnormal findings of CSF in some pathological conditions

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



Management of Meningitis



A medical emergency {22}



Antibiotics given after taking specimens for lab diagnosis {20}



Parenteral administration. (Non-oral route for administration such as I.V)

Children & Adults {21}	<p>★ Ceftriaxone (or Cefotaxime) + Vancomycin (covers the main 3 pathogens).</p> <ul style="list-style-type: none"> ○ Add ampicillin if the patient age is > 50 or at risk for Listeria.
Neonates {21}	<p>★ Ampicillin + Gentamicin + Cefotaxime,</p> <ul style="list-style-type: none"> ○ Modify treatment after lab results (as needed)
Duration	10-14 days (or more) according to the medical condition
Prevention	<ul style="list-style-type: none"> ○ Vaccination (Hib^[2], N.meningitides, S. Pneumonia) ○ Prophylactic antimicrobial agent (rifampin) for contacts (carrier Patient) (Hib^[2] & N. meningitidis)

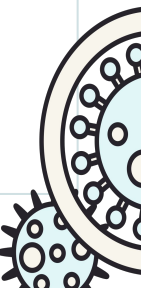
^[2] haemophilus influenzae B





Dr khalifa Notes

- (1) Acute pyogenic meningitis commonly caused by bacteria, virus also can cause acute meningitis as well specially self limiting virus like enterovirus
- (2) Any case come we must have to see sign and symptoms to be able to know the diagnosis, in case meningitis the most important thing to see the age because each group have different organism
- (3) not important focus on our lecture, Just to know the idea there's other organism also causes meningitis, and it's mainly happen after neurosurgical procedures and skull fractures
- (4) newborn are age group from (birth to one month) they gate pathogens due it's transmitted from mother to them during Delivery
- (5) Neck stiffness can be felt when flexing the patient's neck. Flexing becomes difficult & painful.
- (6) In cases of newborns and young infants (<1 year), it is difficult to see the classic signs of meningitis (neck stiffness and headache). Instead, they come with non specific signs such as fever, decreased movement, poor feeding, and irritability.
- (7) Physical examination include Brudzinski's sign and kernig's sign they are specific in meningitis but not sensitive .
- (8) N. Meningitidis is common in college students especially those with European & North American lifestyle. (they are in close proximity and share stuff such as drinks and cigarettes).
- (9) In hajj season, everyone gets vaccinated because we fear the epidemic of N. Meningitidis type A which is highly prevalent in African countries of meningitis belt.
- (10) To differentiate between Neisseria types, we use sugar utilization/fermentation test (bacteria is placed in glucose, maltose, and sucrose mediums then we see how it is reacts). N.Meningitidis is the only type that utilizes glucose and Maltose (other types cannot utilize maltose).
- (11) S.pneumoniae can cause meningitis on its own (in cases of skull trauma/fractures), or through bacteremia after upper/lower respiratory tract infections and sinusitis. S.pneumoniae is more virulent than N.meningitidis and it has a much higher mortality rates. Its main virulence factor is its capsule, pneumolysin(which is toxin e produced by bacteria lead to cell dustraction), and autolysin
- (12) to know the difference between s. pneumoniae and s.viridans we have two test *optochin test* and *solubility test* in optochin test s.pneumoniae are sensitive while the s.viridans is resistant in solubility test the s.pneumoniae is soluble and s.viridans insoluble





Dr khalifa Notes

(13) H.influenzae can only grow on chocolate agar as it needs x & v factors, on blood agar can growth around staph.aureus , it is not growth on McCouny agars.

(14) H. influenzae classified into non capsulated group which causes URTI and capsulated group which causes meningitis and epiglottitis

(15) H.influenzae type B has a capsule due of that, used to be the main cause of severe invasive diseases, but nowadays, there is a decrease in its significance due to the development of an effective vaccine against type B (the most virulent type).

(16) Routine screening is done for pregnant women and vaginal swab is taken. If colonization with group B streptococcal is found, they will be given prophylaxis (ampicillin) to decrease the risk of transmission to the newborn.

(17) Listeria is associated with certain foods such as cheese and cold meat because it can grow in decreased temperature (refrigerator). For most people, it causes self-limited mild gastroenteritis; however, it causes bacteremia and severe diseases in elderly and immunosuppressed. Pregnant women are recommended to avoid certain foods to decrease the risk of listeria transmission to the newborn. The pregnant women herself will only have mild gastroenteritis, however; it is feared that she will pass it to the fetus hematogenously or during delivery and cause meningitis to the baby.

(18) in CSF evaluation show increase in protein due to the infection which causes to increase blood vessels permeability , and decrease in Glucose due to increased Bacteria consumption, note the CSF evaluation help also to know if the causes of infection virus or bacteria,the increase in the wbc if bacteria causes are extremely high (in thousands) and if viruses causes increase the number (in hundred)

(19)To deal with meningitis patients first we must take specimen before giving him antibiotics,such as a blood specimen for blood cultures and gram stain to know the organism . CSF analysis to show changed occurs in protein and wbc and glucose level * see the table * and molecular test for viruses (may use for bacteria)

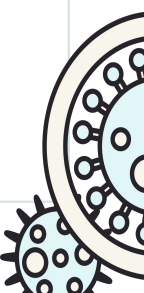
(20) why it is important to take specimen before AB ? For example s. Pneumonia is sensitive and will die after taking the antibiotic, so when the sample is taken I will not find the bacteria and we will not know what is the cause of meningitis.

(21) ceftriaxone and cefotaxime both are 3rd generation of cephalosporin antibiotics so I can use one of them with vancomycin (is add mainly for S. pneumoniae).

to treat adults and children with meningitis the difference between them in dosage and extraction .

ceftriaxone is contraindicated in neonates so we don't use it, use cefotaxime in combination with **Ampicillin** + **Gentamicin**, the duration take three week if they have gram negative

(22) empirical therapy (vancomycin +ceftriaxone) are given to patient who has meningitis and we don't know the caustic organism





MCQs

Q1 - A 4 weeks old baby is suffering from meningitis, and the microbiological tests revealed gram negative bacilli. Which one of the following is the most likely causative organism for this condition?

- | | | | |
|--------------------------|-----------------|-----------|-----------------|
| A) Group B Streptococcus | B) H.influenzae | C) E.coli | D) S.pneumoniae |
|--------------------------|-----------------|-----------|-----------------|

Q2 - Which one of the following is the likely cause of meningitis in a 7 days old newborn baby?

- | | | | |
|-----------------|-------------------|-----------------|-----------------|
| A) H.influenzae | B) N.meningitidis | C) S.pneumoniae | D) S.agalactiae |
|-----------------|-------------------|-----------------|-----------------|

Q3 - After returning from Hajj, a man experienced headache and neck stiffness, leading to suspicion of acute bacterial meningitis. The culture results revealed the presence of gram-negative diplococci. What is the probable causative pathogen in this case?

- | | | | |
|-------------------|-----------------|-----------|-----------------|
| A) N.meningitidis | B) S.pneumoniae | C) E.coli | D) H.influenzae |
|-------------------|-----------------|-----------|-----------------|

Q4 - A 4-year-old child has been unwell for two days, displaying escalating lethargy and increased crying. The child has not received childhood immunizations. An analysis of cerebrospinal fluid (CSF) revealed 97% neutrophils and a glucose level of 2 mmol/L. Additionally, a Gram Stain indicated the presence of Gram-negative coccobacilli. What is the most probable cause of the child's condition?

- | | | | |
|-----------|-----------------|--------------------------|-------------------|
| A) E.coli | B) H.influenzae | C) Klebsiella pneumoniae | D) N.meningitidis |
|-----------|-----------------|--------------------------|-------------------|

Q5 - In the empiric treatment of a patient at risk for Listeria when the suspected organism is Streptococcus pneumoniae, which combination of antibiotics is typically used?

- | | | | |
|--|----------------------------|-----------------------------|------------------------|
| A) Ceftriaxone + vancomycin+ampicillin | B) Ampicillin + vancomycin | C) Ceftriaxone + Gentamicin | D) Paracetamol + Water |
|--|----------------------------|-----------------------------|------------------------|

Q6 - A 3-day-old neonate presented with symptoms of fever, vomiting, poor feeding, and irritability, which were later diagnosed as meningitis. A swab taken from the mother's vagina and examined under the microscope revealed the presence of Gram-positive cocci in chains. What organism is most likely responsible for the infection?

- | | | | |
|--------------------------|-------------------------------|-----------|---|
| A) Group B Streptococcus | B) Mycobacterium Tuberculosis | C) E.coli | - |
|--------------------------|-------------------------------|-----------|---|

Case 1

40 year old Adult/Male presented with DM 2 days history of headache & fever, now starting to have neck stiffness feeling very unwell + vomiting, he was taken to the emergency, on examination found neck stiffness, CSF analysis show the following: (3000 WBC 90% of it Neutrophils, low glucose and High protein, Gram stain & culture was done and showed Gram +ve cocci in pairs.

Q1-What is the most clinical diagnosis in this case ?

Answer : Acute Bacterial (Pyogenic) Meningitis

Q2- what is most likely the organism ?

Answer : Strep. Pneumoniae

Q4-How do you treat this patient ?

Answer : Ceftriaxone (Cefotaxime) & Vancomycin

Case 2

18 year old Male presented with DM, 2 days history of headache & fever, now starting to have neck stiffness feeling very unwell + vomiting, he was taken to the emergency, on examination found neck stiffness, CSF analysis show the following: (3000 WBC 90% of it Neutrophils, low glucose and High protein, Gram stain & culture was done and showed Gram -ve diplococci

Q1-What is the most clinical diagnosis in this case ?

Answer : Acute (Bacterial) Meningitis

Q2- what is most likely the organism ?

Answer : N.Meningitidis (Seen more in young adults)

Case 3

8 Year old unvaccinated child was seen with neck stiffness. Lumbar puncture of CSF was taken and showed the following: (3000 WBC, 90% of it Neutrophils, low glucose and High protein), Gram stain was done and showed Gram -Ve coccobacilli.

Q1-What is the organism ?

Answer : H.influenzae

Q2-How do you treat this patient ?

Answer : Ceftriaxone (or Cefotaxime) & Vancomycin

Dr note if you write ceftriaxone is correct but in neonates are contraindicated

Case 3

1 week old newborn have fever, Irritability and poor feeding, CSF analysis showed elevation (but not like adults), Gram stain culture was done and showed Gram +Ve cocci in chains, B hemolytic, Catalase -ve.

Q1- What is the organism ?

Answer : Group B Streptococcus (GBS)

Q2-What is the source of infection ?

Answer : during delivery.

Q3-What if it shows Gram -Ve Bacilli ?

Answer : E.Coli

Q4-How do you treat this patient ?

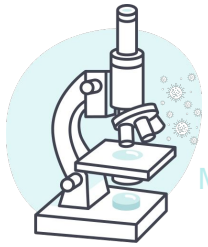
Answer : Ampicillin & Gentamicin & Cefotaxime

Factors to focus on

1-Signs & Symptoms (To know what is the diagnosis)

2-Age (To know the organism)

3-Duration of symptoms (To know if acute or chronic)



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MICROBIOLOGY

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