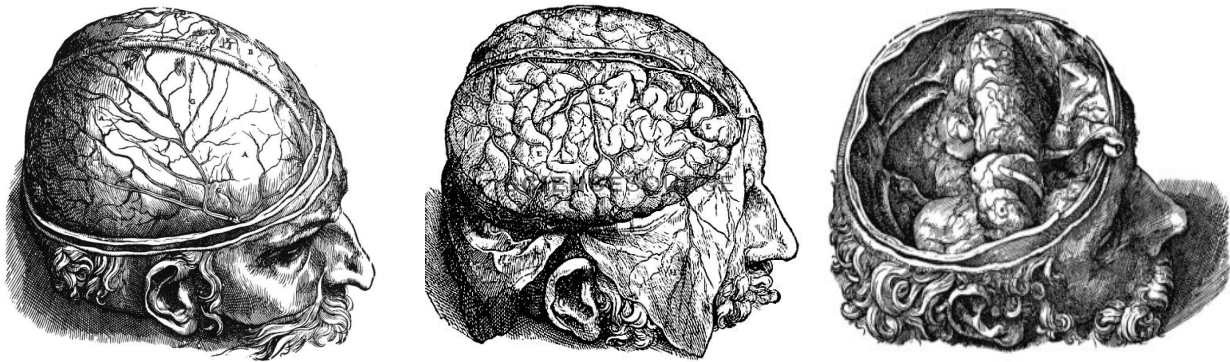


# Microbiology

435's Teamwork  
Neuropsychiatry Block

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- Kindly check our [Editing File](#) before studying the document.
  - Please contact the team leaders for any suggestion, question or correction.
  - Pay attention to the statements highlighted in **red**.
  - Extra explanations are added for your understanding in **grey**.
  - **Footnotes color code:** General | **Females** | **Males**

Revised by

خولة العماري & هشام الغنيلي



# Acute Pyogenic<sup>1</sup> Meningitis

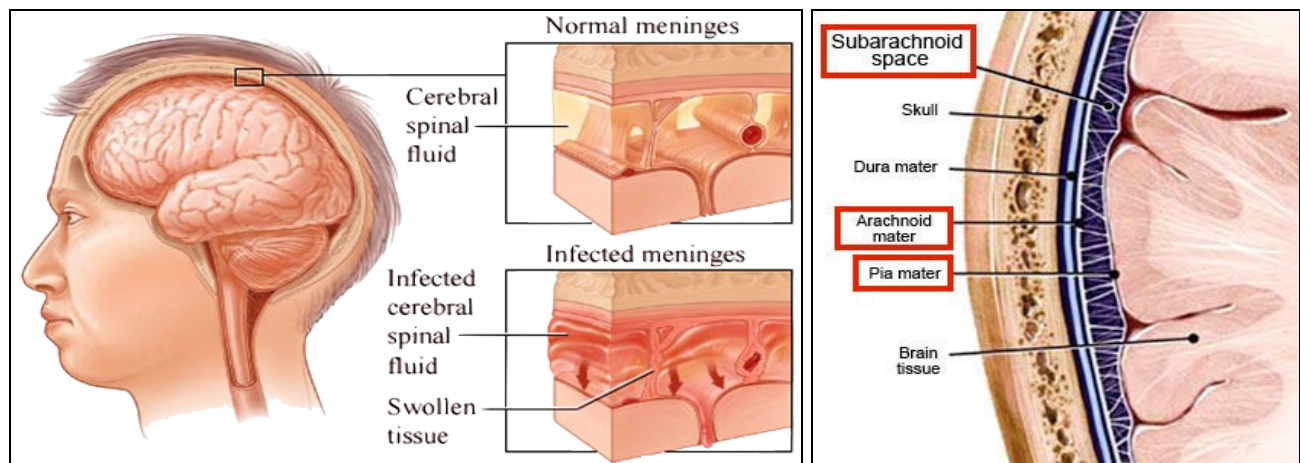
**Resources:** Sherris Medical Microbiology, LIR Microbiology, Robbins Basic Pathology, Prof. Hanan's & Dr. Somily's 2017 lectures.

## Learning Objectives:

**By the end of this lecture, you should know the...**

1. Definition
2. Epidemiology
3. Etiology
4. Identification
5. Pathogenesis
6. Complications
7. Clinical presentation
8. Diagnostic approaches
9. Management and Prevention

## Of pyogenic meningitis.



## What is Pyogenic Meningitis?

Pyogenic<sup>2</sup> (**Bacterial**) meningitis is an acute inflammation of the brain's meninges, affecting the pia, arachnoid and subarachnoid spaces.

## How serious is Pyogenic Meningitis?

Untreated Pyogenic Meningitis is often fatal, but with prompt<sup>3</sup> diagnosis and administration of appropriate antibiotics, many patients can be saved.

## What causes Pyogenic Meningitis?

- It is usually caused by bacterial pathogens that vary depending on the age group, which in turn, are associated with remarkable inflammatory exudation.
- It may be preceded by an upper respiratory tract infection.

<sup>1</sup> Pyogenic because there is pus cells.

<sup>2</sup> Involving or relating to the production of pus.

<sup>3</sup> Done without delay; immediate.

## Epidemiology:

- Bacterial meningitis is one of the top 10 infections causing death worldwide.
- Its annual incidence is of approximately 1.2 million cases and 135,000 deaths.
- Half of the survivals suffer neurological damage, and /or permanent side effects.

## General Pathogenesis<sup>45</sup>:

Meningitis results from hematogenous<sup>6</sup> spread of bacteria (Septicemia). The organisms that cause bacterial meningitis colonize the nasopharynx or birth canal and, from there, they get into the bloodstream. They enter the subarachnoid space by passing through endothelial cells, getting across the choroid plexus capillaries. The CSF is an ideal medium for the spread of bacteria because it provides enough nutrients for their multiplication and has few phagocytic cells, and low levels of antibodies and complement. Bacterial products can damage the brain and blood vessels directly. Bacterial toxins cause neuronal apoptosis, and endotoxin released from bacterial cell walls activates clotting, causing intravascular coagulation.

**In short:** Microorganisms colonize the nasopharynx or the birth canal → Septicemia<sup>7</sup> → Organisms cross the BBB → Cause widespread endothelial damage → Bleeding → Skin rash and adrenal hemorrhage → Coagulation activated → Platelets aggregation and thrombosis.

Clinical Presentation		
Most Common	In infants	Advanced Cases
<ul style="list-style-type: none"><li>● Fever</li><li>● Headache</li><li>● Stiff neck<sup>8</sup></li><li>● Nausea and vomiting</li><li>● Sensitivity to light</li><li>● Confusion</li></ul>	<ul style="list-style-type: none"><li>● Inactivity</li><li>● Irritability<sup>9</sup></li><li>● Vomiting</li><li>● Poor feeding</li></ul>	<ul style="list-style-type: none"><li>● Bruises under the skin</li><li>● Rapidly-spread brain damage<sup>10</sup></li><li>● Coma</li><li>● Death</li></ul>

<sup>4</sup> The organism that caused meningitis might come from another organ, blood(septicemia), trauma, surgery (insertion of the shunt) or colonization of the organism without having antibodies for it.

<sup>5</sup> Some of the patients might have congenital anomalies like Spina bifida if the spina bifida opening was close to the anal area then they might be susceptible for gram -ve meningitis.

<sup>6</sup> Through blood.

<sup>7</sup> Blood infection.

<sup>8</sup> In adults and older children but in neonates and children they won't have neck rigidity

<sup>9</sup> Atypical symptoms are usually present in infants and children.

<sup>10</sup> Brain death and Hemiplegia.

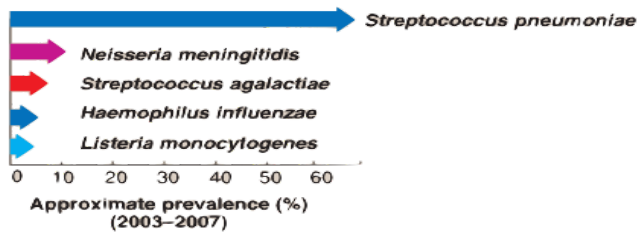
# Etiology

## Three Main Bacterial Species<sup>11</sup>

*Neisseria Meningitidis* | *Streptococcus Pneumoniae* | *Haemophilus influenzae*<sup>12</sup>

Newborns <sup>13</sup>	Infants & Children	Adults <sup>14</sup>	Special Circumstances <sup>15</sup>
<p><i>Group B Streptococcus</i><sup>16</sup></p> <p><i>Escherichia Coli</i></p> <p><i>Listeria Monocytogenes</i></p> <p>Other gram -ve Bacteria</p>	<p><i>Streptococcus Pneumoniae</i></p> <p><i>Neisseria Meningitidis</i></p> <p><i>Haemophilus Influenzae</i></p>	<p><i>Streptococcus Pneumoniae</i></p> <p><i>Neisseria Meningitidis</i></p>	<p><i>Staphylococcus Aureus</i></p> <p><i>Staphylococcus Epidermidis</i></p> <p><i>Streptococcus Pneumoniae</i><sup>17</sup></p> <p><i>Pseudomonas Aeruginosa</i></p> <p>Anaerobes</p>

### A Overview of common causes of bacterial meningitis in adults<sup>1</sup>



### B Classification of pathogens

#### Gram (+) cocci

*Streptococcus agalactiae*  
*Streptococcus pneumoniae*

#### Gram (+) rods

*Listeria monocytogenes*

#### Gram (-) cocci

*Neisseria meningitidis*

#### Gram (-) rods

*Haemophilus influenzae*

#### *Haemophilus influenzae*

- *H. influenzae* is a normal resident of the human upper respiratory tract. Transmission is by respiratory droplets.
- After attaching to and colonizing the respiratory mucosa, the infection can become systemic, with bacteria spreading via the blood to the CNS. *H. influenzae* was a leading cause of bacterial meningitis, especially in infants and young children. A conjugated vaccine against *H. influenzae* capsular polysaccharide type b is now administered to infants and has dramatically lowered the number of meningitis cases attributable to this organism.

#### *Streptococcus pneumoniae*

- *S. pneumoniae* is an important cause of meningitis and pneumonia. It is carried in the nasopharynx of many healthy individuals. Infection can be either endogenous (in a carrier who develops impaired resistance to the organism) or exogenous (by droplets from the airway of a carrier).
- *S. pneumoniae* infections can result in a bacteremia leading to infection of several sites in the human body, including the central nervous system (CNS). This meningitis has a high mortality rate, even when treated appropriately. *S. pneumoniae* is the most common cause of bacterial meningitis in adults.

#### *Streptococcus agalactiae*

- *S. agalactiae* causes meningitis and septicemia in neonates. It is found normally in the genital tract of female carriers and the urethral mucous membranes of male carriers, as well as in the gastrointestinal (GI) tract (especially the rectum). Transmission occurs during birth and is sexually transmitted among adults.
- Infection of an infant occurs as it traverses the birth canal. *S. agalactiae* infection is a leading cause of neonatal meningitis, and it has a high mortality rate.

#### *Neisseria meningitidis*

- *N. meningitidis* is a common cause of meningitis. Transmission is via respiratory droplets. Pili allow the attachment of *N. meningitidis* to the nasopharyngeal mucosa.
- If meningococci penetrate the epithelial lining of the nasopharynx and enter the bloodstream, they rapidly multiply, causing meningococemia. If *N. meningitidis* crosses the blood-brain barrier, it can infect the meninges, causing an acute inflammatory response that results in a purulent meningitis. The initial fever and malaise can rapidly evolve into severe headache, rigid neck, vomiting, and sensitivity to bright light. Coma can occur within a few hours. *N. meningitidis* is the most common cause of bacterial meningitis between the ages of 2 and 18 years.

#### *Listeria monocytogenes*

- *L. monocytogenes* infections are most common among older adults, pregnant women, fetuses or newborns, and immunocompromised individuals. Meningitis is a common presentation. Listeria infections, which may occur as sporadic cases or in small epidemics, are usually foodborne, with the organism entering the body via the GI tract.

<sup>11</sup> We cannot ask what is the most common cause for meningitis because it differs based on the age group.

<sup>12</sup> Used to be a common cause but now it isn't because of vaccination and it is normal flora in the oral cavity.

<sup>13</sup> They are mainly in the genital tract of the mother and move to the baby.

<sup>14</sup> When we grow older Listeria might also be a common cause for meningitis.

<sup>15</sup> The doctor usually won't ask about the special circumstances.

<sup>16</sup> GI flora in the genital tract in the mother therefore they might be transmitted to the infant that's why they're common in the pediatric patients.

<sup>17</sup> If the patient had fracture of the base of skull then the strep. Pneumonia might go to the meninges and cause meningitis.

<i>Neisseria Meningitidis</i> <sup>18 19</sup>	
Definition	Gram negative diplococci <sup>20</sup>   Oxidase +ve   Present in the nasopharynx of 10% of people <sup>21</sup>
Transmission	By inhalation of aerosolized droplets through close contact
Prevalence	Common in children < 6 years
Risk factors	Susceptible individuals <sup>22</sup>
Serotypes <sup>23</sup>	B, C, Y, and W135
	A
Pathogenesis	<p>Cause isolated, sporadic, small epidemics in closed populations</p> <p><b>Has an epidemic potential in the Sub-Saharan African Meningitis Belt<sup>24</sup></b></p> <p><b>Bacterial pili attach to the microvilli of nasopharynx → Invasion → Bacteremia → Endotoxin Lipopolysaccharide produced → Spreads to the meninges<sup>25</sup>.</b></p> <ul style="list-style-type: none"> <li>• In carriers, it stimulates antibody production.</li> <li>• Its capsule resists phagocytosis.</li> </ul>
Prognosis	<ul style="list-style-type: none"> <li>• 11-20% of recovered patients suffer permanent hearing loss and mental retardation.</li> <li>• 10-14% of cases are fatal.</li> </ul>

<i>Streptococcus Pneumoniae</i> <sup>26</sup>	
Definition	Gram positive diplococci   Catalase -ve <sup>27</sup>
Prevalence	Infection rate decreases due to vaccination
Risk Factors	May develop after trauma to the skull
Pathogenesis	<ul style="list-style-type: none"> <li>• May follow a Pneumococcal pneumonia, or any other site infected with the organism.</li> <li>• Pneumolysin decreases inflammatory immune response and leads to severe infection.</li> </ul>
Prognosis	<ul style="list-style-type: none"> <li>• <b>High mortality rate &gt;30%</b> due to invasive disease<sup>28</sup>.</li> <li>• Recovered cases develop sustained learning disabilities.</li> </ul>

<sup>18</sup> *Neisseria Meningitidis* ferment glucose and maltose.

<sup>19</sup> One of the famous organisms causing meningitis and is still causing it because there's still different serotypes that aren't covered in the vaccine transmitted by inhalation and close contact.

<sup>20</sup> Pus cells are also seen in the chocolate agar, can be differentiated from *Neisseria gonorrhoeae* by sugar fermentation, it ferments glucose and maltose and its latex agglutination is positive.

<sup>21</sup> People who carry it normally are partially immune but they are carriers and they maybe the source of infection to others who do not have it normally in their nasopharynx.

<sup>22</sup> People who do not carry the antibodies because they do not have it normally in their nasopharynx.

<sup>23</sup> A serotype is a subdivision of a species that is distinguishable from other strains depending on the basis of antigenicity (antigen-antibody reaction).

<sup>24</sup> Picture.

<sup>25</sup> In some patients it also causes adrenal hemorrhage and bloody skin rash.

<sup>26</sup> Alpha hemolytic thus there is only one test to differentiate it from the other alpha hemolytic organisms which is Viridans group (optochin disk).

<sup>27</sup> Sensitive to optochin disk

<sup>28</sup> Because it is covered with a capsule thus avoiding phagocytosis and they penetrate and suppress the immune system.



### Group B Streptococcus (*Streptococcus Agalactiae*)<sup>29</sup>

<b>Definition</b>	<b>Gram positive cocci in chains</b>   Catalase -ve   Resident Bacteria in GIT and vagina (10-30%)
<b>Risk Factors</b>	1) Premature rupture of membrane 2) Prematurity 3) Low infant innate immunity
<b>Pathogenesis</b>	<b>Gain access to the amniotic fluid during delivery → Colonize the newborn as it passes the birth canal → Cause sepsis<sup>30</sup> and meningitis in the first few days of life or after 4 weeks.</b>

### *Haemophilus Influenzae*

<b>Definition</b>	<b>Small gram negative coccobacilli</b>   Found in the nasopharynx normal flora
<b>Prevalence</b>	Infection rate decreases since the routine use of HIB <sup>31</sup> vaccine
<b>Characteristics</b>	<ul style="list-style-type: none"> <li>● Has a polysaccharide capsule, other species have no capsule.</li> <li>● Need blood for optimal growth, Hematin (factor X) and NAD ( factor V).</li> <li>● Major cause of LRTI.</li> <li>● Occasionally invade deeper tissues and cause bacteremia.</li> </ul>
<b>Serotypes</b>	<ul style="list-style-type: none"> <li>● Has many serotypes (from A to F).</li> <li>● <b>HIB</b> has a capsule made of a polymer of Polyribosylribitol Phosphate (PRP) that cause acute life threatening invasive infections.</li> </ul>
<b>Prognosis</b>	<ul style="list-style-type: none"> <li>● 3-6% mortality rate<sup>32</sup>.</li> <li>● 1/3 of survivals have significant neurological sequelae.</li> </ul>

<sup>29</sup> If we discovered Group B in pregnant ladies usually between the age of 35 to 37 after swapping the vagina we give the baby prophylaxis because if the baby was born while the mother had Group B streptococcus or UTI this will cause an early or late infection to the baby. Early infection( from the mother) usually have sepsis or pneumonia while the late infection (from the people surrounding the baby) might develop meningitis.

<sup>30</sup> The difference between septicemia and bacteremia is that in septicemia symptoms are present.

<sup>31</sup> Haemophilus influenzae type B (HIB).

<sup>32</sup> Has the least mortality rate when compared to streptococcus pneumoniae and neisseria meningitidis.

<i>Escherichia Coli</i> <sup>33</sup>	
<b>Definition</b>	<b>Gram negative bacilli</b>   Catalase +ve   Oxidase +ve   Lactose Fermenter
<b>Prevalence</b>	Most common cause of neonatal meningitis
<b>Characteristics</b>	Similar to Group B Streptococcus
<b>Pathogenesis</b>	<ul style="list-style-type: none"> <li>● Vaginal <i>Escherichia Coli</i> colonize the infant via a rupture of the amniotic membrane or during birth.</li> <li>● Failure of preterm maternal IgM to cross the placenta, leading to a special susceptibility of the newborn to infections.</li> <li>● <b>K1 sialic acid capsule</b> of some strains invade the brain microvascular endothelial cells.</li> </ul>

<i>Listeria Monocytogenes</i> <sup>34</sup>	
<b>Definition</b>	<b>Gram positive rods</b>   Catalase +ve   Human intestinal colonization (2-12%)
<b>Pathogenesis</b>	<ul style="list-style-type: none"> <li>● Widespread among animals in nature including those associated with food supply.</li> <li>● Spread to fetus following hematogenous spread in the mother, or from the birth canal<sup>35</sup>.</li> <li>● Has tropism<sup>36</sup> to the CNS.</li> </ul>

<sup>33</sup> E.coli has the same same mechanism as Group B and is also coming for the GI

<sup>34</sup> Serious but not common. The source is food thus the pregnant lady should not eat leftover food or dairy products specially Feta cheese in order to not increase the susceptibility for getting Listeria Monocytogenes but is very rare.

<sup>35</sup> Only causes meningitis in newborns,elderly and immunocompromised patients.

<sup>36</sup> Favoring.

## Diagnosis:

1. **Clinical signs symptoms**<sup>37</sup>.
2. **Specimen:** CSF<sup>38</sup> acquired through lumbar puncture + blood specimen.
3. **CSF Analysis:** Cells, proteins, and glucose.
4. **Culture.**
5. **Antimicrobial susceptibility testing:** CSF + blood.

Findings of CSF analysis				
Normal				Pyogenic Meningitis
Adults	Neonates			
	Term	Preterm		
<b>WBC</b>	0-5 / $cm^3$	0-32 / $cm^3$	0-29 / $cm^3$	5-5000 / $cm^3$
<b>PMN</b> <sup>39</sup>	0%	> 60%	> 60%	> 60%
<b>Protein</b>	< 30 mg/dl	20-170 mg/dl	60-150 mg/dl	> 60 mg/dl
<b>Glucose</b>	> 60%	> 60%	> 60%	< 45%
<b>Chloride</b>	115-130 mmol/L	-	-	110 mmol/L

## Management:

URGENT, A MEDICAL EMERGENCY.

## Treatment:

Prescribe antibiotics after taking specimens for lab diagnosis.

- **Parenterally:** Ceftriaxone (or Cefotaxime) + Vancomycin<sup>40</sup>.
- **For neonates**<sup>41</sup>: Ampicillin + Gentamicin (or Cefotaxime).<sup>42</sup>

**Duration:** 10-14 days (or more) according to the medical condition.

## Prevention:

Vaccination, prophylaxis of contacts (*HIB* and *Neisseria Meningitidis*).

<sup>37</sup> Having a negative result doesn't rule out meningitis, the clinical tests are Brudzinski's sign (when the patient is lying in a supine position and the doctor flexes his/her neck the patient's knees suddenly flex and it's very painful). Kernig's sign (when the doctor flexes the hip joint at a 90 degree the subsequent extension of the knee is painful).

<sup>38</sup> Cerebrospinal Fluid.

<sup>39</sup> Polymorphonuclear cells (Neutrophils)

<sup>40</sup> Empirical treatment should cover *Neisseria meningitidis*, *H.influenzae*, *Streptococcus pneumoniae*.

<sup>41</sup> Might come as a one month old baby or a 22 days old baby and the most common cause is *Listeria* and it is resistant for ampicillin that's why we add Gentamicin.

<sup>42</sup> To cover Group B streptococci, *E.coli* and *Listeria Monocytogenes*.



Etiology according to age

Newborns	Group B Streptococcus - E.coli - Listeria monocytogenes
Infants / Children	S.pneumoniae - N.meningitidis - H.influenzae
Adults	S.pneumoniae - N.meningitidis
Special circumstances "trauma"	S.aureus - S.epidermidis - S.pneumoniae – anaerobes - P.aeruginosa

Etiologic agents

Neisseria meningitidis	Streptococcus pneumoniae
<ul style="list-style-type: none"> <li>Gram -ve diplococci "bean/kidney-shaped"</li> <li>Glucose &amp; maltose fermenter</li> <li>Transmitted by inhalation &amp; close contact</li> <li>Serotypes "B, C, Y, W135" → sporadic in close population</li> <li>Serotype A → epidemic in sub-Saharan Africa "meningitis belt"</li> <li>Pili attach to microvilli of nasopharynx → invasion → bacteremia</li> </ul> <p>Its capsule:</p> <ul style="list-style-type: none"> <li>❖ Produce endotoxin (LPS).</li> <li>❖ Resists phagocytosis.</li> </ul>	<ul style="list-style-type: none"> <li>Gram +ve diplococci</li> <li>Optochin sensitive</li> <li>The <b>most invasive</b> pathogen</li> <li>Its capsule: produce <u>pnemolysin</u> → immune response</li> </ul>
Group B Streptococcus "agalactiae"	Haemophilus influenzae
<ul style="list-style-type: none"> <li>Gram +ve cocci in chains / Beta-hemolytic</li> <li>Colonize infant via rupture of amniotic membrane or during birth.</li> <li><u>Risk factors</u>: premature rupture of membrane, prematurity, low infant innate immunity</li> <li>Cause sepsis in the first few days of life &amp; meningitis after 4 weeks</li> </ul>	<ul style="list-style-type: none"> <li>Gram -ve coccobacilli / pleomorphic</li> <li>Need blood for optimal growth, Hematin (factor X) &amp; NAD (factor V)</li> <li><u>H.influenzae type b</u> has a capsule made of a polymer of <u>PRP (Polyribosyl Ribitol Phosphate)</u> cause acute life threatening invasive infection</li> <li>Major cause of lower RTI, occasionally invade deeper tissues and cause bacteremia</li> </ul>
Escherichia coli	Listeria monocytogenes
<ul style="list-style-type: none"> <li>Gram -ve bacilli / Lactose fermenter</li> <li>Most common cause of neonatal meningitis Colonize infant via rupture of amniotic membrane or during birth.</li> <li>K1 sialic acid capsule → invasion of brain microvascular endothelial cells</li> </ul>	<ul style="list-style-type: none"> <li>Gram +ve rods / Beta-hemolytic</li> <li>Animal "cheese &amp; meat"</li> <li>Spread to fetus following hematogenous dissemination in mother or from birth canal</li> <li>Has tropism to the CNS</li> <li>In extremities (neonates/elderly) &amp; pregnant women</li> </ul>

Management

<p><u>Treatment (10-14 days):</u></p> <ul style="list-style-type: none"> <li><u>Children &amp; Adults:</u> <b>Ceftriaxone + Vancomycin</b></li> <li><u>Neonates:</u> <b>Ampicillin + Cefotaxime</b></li> </ul>	<p><u>Prevention</u></p> <ul style="list-style-type: none"> <li>Vaccination</li> <li>Prophylaxis antimicrobial agent for contacts "3 days"</li> </ul>
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## Multiple Choice and Short Answer Integrated Questions

-To open an answered sheet, please click [here](#)-

### CASE-1

**A pregnant woman was diagnosed with meningitis and treated empirically. After delivery, her newborn showed signs and symptoms of Meningitis too.**

Which one of the following is the most likely causative organism?

- A. *Group B Streptococcus*
- B. *E.coli*
- C. *Listeria*
- D. *Streptococcus Pneumoniae*

What would you see under microscope?

Explain the mechanism of transmission from the mother to her body?

### CASE-2

**31-year-old male was presented to the ER. He reported having headache and fever. He was wearing sunglasses, and refused to take them off claiming that the room is too bright. On history taking, he told the doctor that he came back from South Sudan a week ago. Lumbar puncture confirmed that he had meningitis with a gram negative microorganism.**

What is the most likely causative organism?

- A. *H. influenzae*
- B. *Streptococcus pneumoniae*
- C. *Neisseria meningitidis*
- D. *Listeria*

What is the most appropriate antibiotics?

What does him coming back from “South Sudan” have to do with your diagnosis?

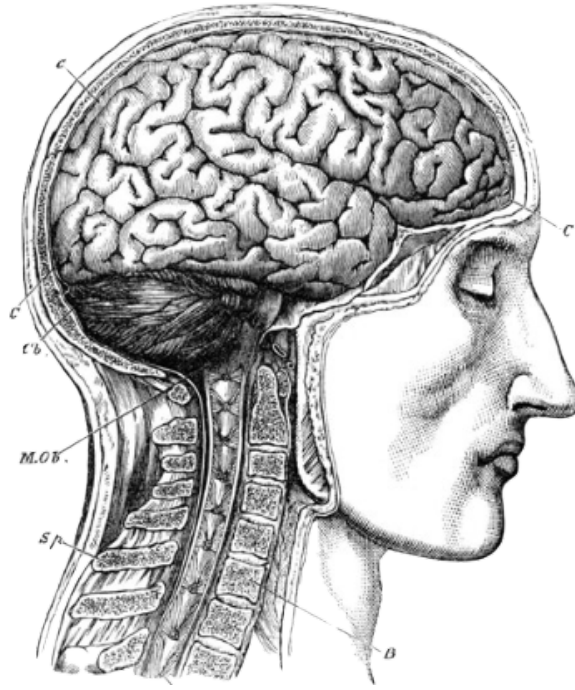
### CASE-3

**A 34 years old woman from an underdeveloped country went through surgery after a penetrating trauma with a knife above her umbilicus. Three days later, she was presented to the ER by her sister suffering from fever, confusion and severe headache. Doctor confirmed that he has meningitis.**

Which one of the following is the most likely causative organism?

- A. *H. influenzae*
- B. *Streptococcus pneumoniae*
- C. *Neisseria meningitidis*
- D. *Listeria*

How does organism enter his meninges?



كَذَلِكَ يُبَيِّنُ اللَّهُ لَكُمْ آيَاتِهِ لَعَلَّكُمْ تَعْقِلُونَ ﴿٢٤٢﴾

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### **Heartful thanks to our phenomenal team members**

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