

# Applications of antibiotics

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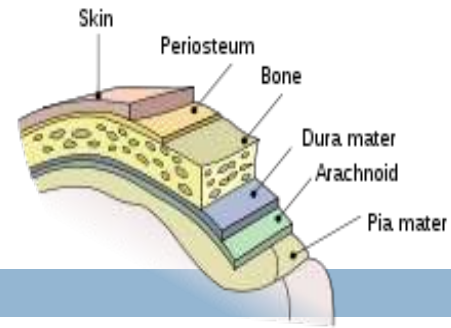
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# 1- CNS infections

## Meningitis





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# meningitis

- . is a serious medical condition in infants. Meningitis is an inflammation of the meninges (the protective membranes of the central nervous system (CNS)) and is more common in the neonatal period (infants less than 44 days old) than any other time in life and is an important cause of morbidity and mortality globally. Mortality is roughly half in developing countries and ranges from 8%-12.5% in developed countries



# DON'T IGNORE

## The signs

Fever? Headache? Vomiting?

Sleepy?  
Confused?

Stiff neck?

Dislike bright lights?

Rash?

Pale, blotchy skin?

Cold hands  
& feet?

Limb pain?

# Meningitis

Dr. Mahmoud H. Taleb / 2020

**Meningitis can kill in hours**



# What is meningitis?.....

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- The brain and spinal cord are covered by connective tissue layers collectively called the meninges which form the blood-brain barrier.

1-the pia mater (closest to the CNS)

2-the arachnoid mater

3-the dura mater (farthest from the CNS).

The meninges contain cerebrospinal fluid (CSF).

Meningitis is an inflammation of the meninges, which, if severe, may become encephalitis, an inflammation of the brain.



# What is Meningitis?

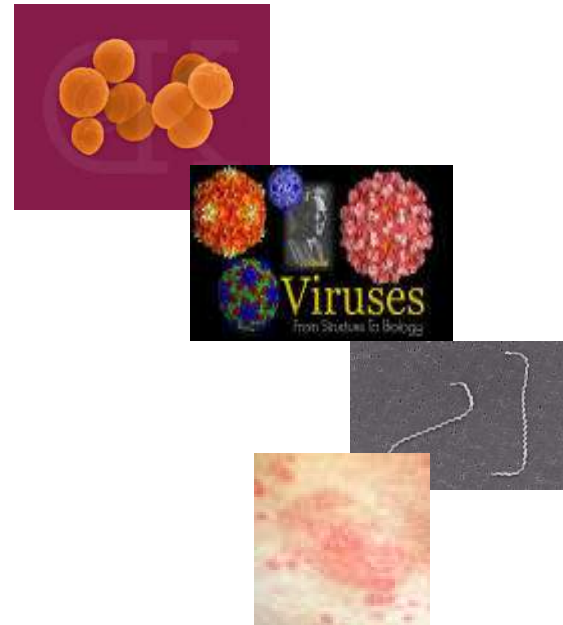
- ❑ Meningitis can be caused by many different organisms including viruses and bacteria.
- ❑ Meningitis, caused by a bacteria, is life threatening and requires urgent medical attention and treatment with antibiotics.
- ❑ Meningitis caused by a virus is very rarely life threatening but can cause the body to become very weak.
- ❑ When bacteria invade the body they can cause meningitis, septicaemia or meningitis and septicaemia together



# Causes of Meningitis

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- Bacterial Infections
- Viral Infections
- Fungal Infections
  - (*Cryptococcus neoformans*  
*Coccidioides immitus*)
- Inflammatory diseases
  - (SLE)
- Cancer
- Trauma to head or spine.



# Bacterial meningitis.....

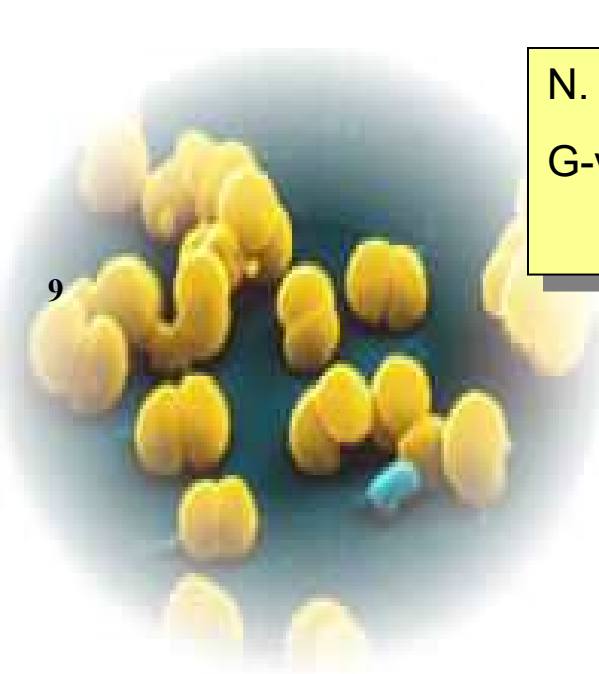
## Etiological Agents:

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- Pneumococcal, *Streptococcus pneumoniae* (38%)
- Meningococcal, *Neisseria meningitidis* (14%)
- *Haemophilus influenzae* (4%).
- *Listeria Monocytogenes*
- Staphylococcal, *Staphylococcus aureus* (5%)
- Tuberculous, *Mycobacterium tuberculosis*
- *Gram negative bacilli*





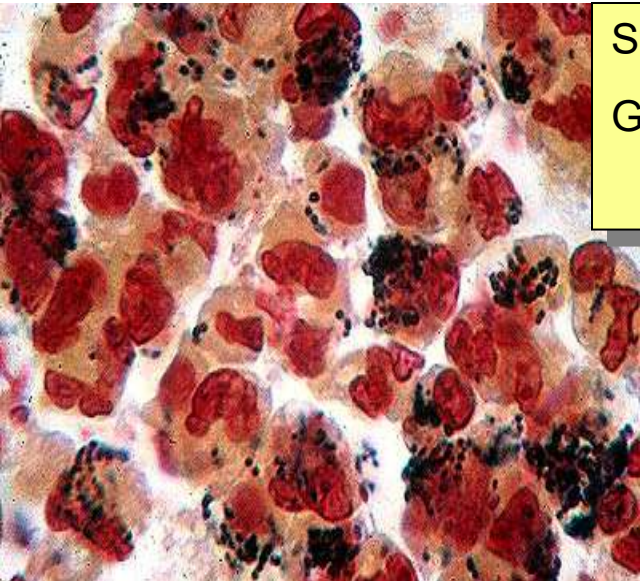


N. meningitidis  
G-ve diplococci

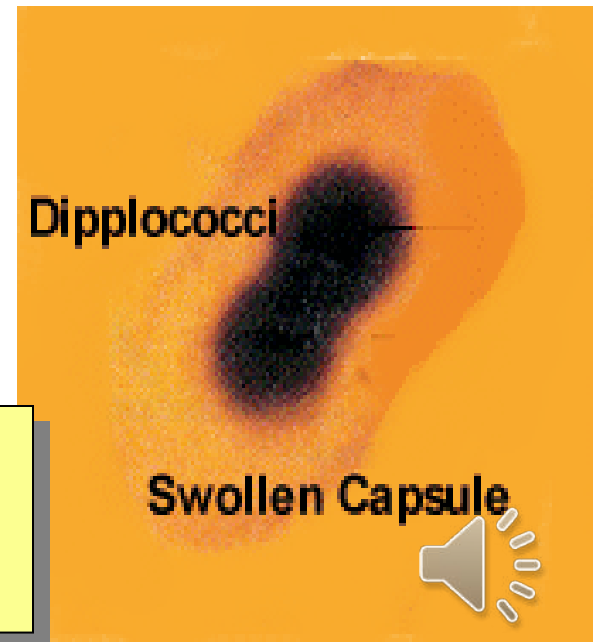


E.Coli  
G-ve bacilli

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New York State Department of Health



Streptococci-GBS  
G+ve cocci



Strep. pneumoniae  
G+ve diplococci



# Bacterial Meningitis - Organisms

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- Birth - 4 wks:, E.coli
- 4 - 12 wks:, E.coli, Pneumococcus  
Salmonella, Listeria, H. Influenza
- 3 mths - 3 yrs: Pneumococcus, Meningococcus  
H. Influenza
- 3 yrs+ adult: Pneumococcus, Meningococcus



# Bacterial Meningitis - Pathogenesis

- Infection of upper respiratory tract
- Invasion of blood stream (bacteraemia)
- Seeding & inflammation of meninges



# Signs and Symptoms

Usually occur one week after exposure

- ❖ Fever
- ❖ Headache
- ❖ Stiff neck
- ❖ Tiredness
- ❖ Rash
- ❖ Sore Throat
- ❖ Vomiting



# Signs and Symptoms

- The following is a list of common signs and symptoms found with neonatal meningitis

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- Fever

- poor appetite

anterior fontanelle bulging

seizure

dyspnea

irritability

anorexia

vomiting

diarrhea

abdominal distention (increase in abdominal size)

neck rigidity

cyanosis

jaundice

and sunset eyes (downward gaze of the eyes)



# CHILDREN/ADULTS



Stiff neck



Headache



Fever



Vomiting



Light Sensitivity



Drowsiness or confusion



Joint pain



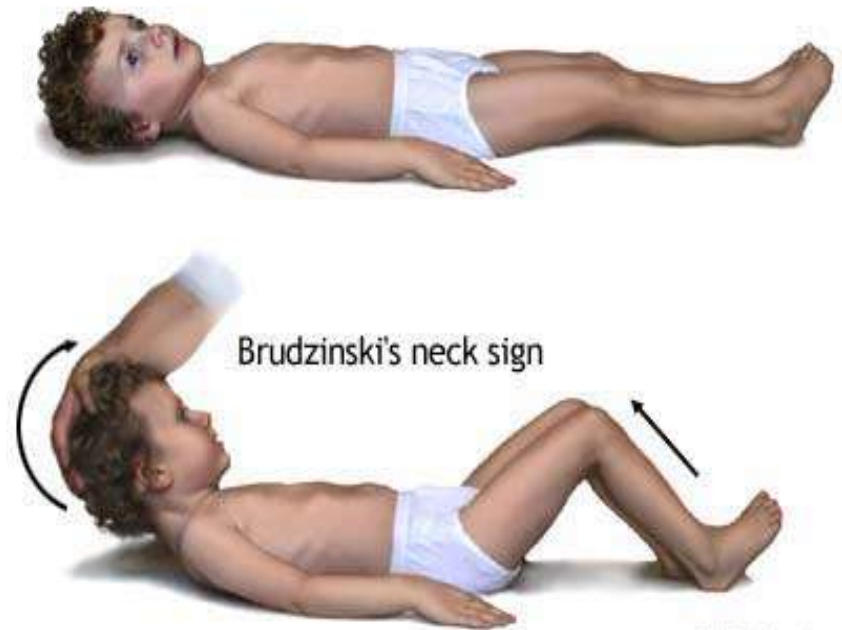
Fitting



One of the physically demonstrable symptoms of meningitis is Kernig's sign. Severe stiffness of the hamstrings causes an inability to straighten the leg when the hip is flexed to 90 degrees.



Another physically demonstrable symptoms of meningitis is Brudzinksi's sign. Severe neck stiffness causes a patient's hips and knees to flex when the neck is flexed.



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## Under Age 2

Fever

Headache

Stiff neck

Inactivity

Vomiting

Poor feeding

Seizures

❖ May be hard to  
detect in infants

## Over age 2

High fever

Headache

Stiff neck

Nausea and vomiting

Sensitivity to light

Confusion

Sleepiness

Petechiae that spreads rapidly  
seizures



# DIAGNOSIS

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## Investigations

- \*\* Physical Examinations:
- \*\* Microscopic Examinations
- \*\* Lumbar puncture
  - Blood gas
  - Glucose & Protein content



# Bacterial Meningitis Management

## *Pharmacotherapy of Meningitis*

### Desired outcome

The goal of treatment include eradication of infection with amelioration of signs and symptoms and prevention of neurologic consequences, such as seizures, deafness, coma, and death.

- Medical emergency
- Early diagnosis essential
- Immediate optimum treatment
- Intensive supportive therapy
- Rehabilitation
- Prophylaxis to family



# Bacterial Meningitis/Meningococcaemia

## Management

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- ABC
- Fluid management: aggressive resuscitation
- Dexamethasone: only in Pneumococcal and HiB, given before antibiotics
- Inotropes: increasing aortic diastolic pressure and improving myocardial contractility



# Treatment and Management

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Treatment for meningitis is antibiotics. The particular drugs used are based off the infecting bacteria, but a mix of ampicillin, gentamicin, and cefotaxime is used for early-onset meningitis before identification of infection. A regimen of antistaphylococcal antibiotic, such as nafcillin or vancomycin, plus cefotaxime or ceftazidime with or without an aminoglycoside is recommended for late-onset neonatal meningitis. The aim for these treatments is to sterilize the CSF of any meningitis-causing pathogens. A repeated LP 24–48 hours after initial treatment should be used to declare sterilization



# Antibiotics

## ➤ Definition :-

- Antibacterial substances produced by various species of microorganisms (bacteria, fungi, and actinomycetes) that suppress the growth of other microorganisms (MO).

## ➤ Ideal Antibiotic :-

- Have the appropriate spectrum of activity for the clinical setting.
- Have no toxicity to the host, be well tolerated.
- Low development of resistance.
- Not induce hypersensitivity reaction in the host.
- Have rapid and extensive tissue distribution
- Have a relatively long half-life.
- Be free of interactions with other drugs.
- Be convenient for administration.
- Be relatively inexpensive.



Age commonly affected	Most likely organisms	Empirical therapy
<b>Newborn–1 month</b>	Gram-negative enterics <sup>a</sup> Group B Streptococcus Listeria monocytogenes	<b>Ampicillin + cefotaxime or ceftriaxone</b>
<b>1 month–4 years</b>	H. influenzae N. meningitidis S. pneumoniae	<b>Vancomycin<sup>b</sup> and cefotaxime or ceftriaxone</b>
<b>5–29 years</b>	N. meningitidis S. pneumoniae H. influenzae	<b>Vancomycin<sup>b</sup> and cefotaxime or ceftriaxone</b>
<b>30–60 years</b>	S. pneumoniae N. meningitidis	<b>Vancomycin<sup>b</sup> and cefotaxime or ceftriaxone</b>
<b>&gt;60 years</b>	<b>S. pneumoniae</b> <b>Gram-negative enterics</b> <b>L. monocytogenes</b>	<b>Ampicillin + vancomycin<sup>b</sup> + cefotaxime or ceftriaxone</b>



## ***Treatment of meningitis by specific antibiotic according to culture***

### ***1- Neisseria meningitidis (Meningococcus)***

Aggressive, early intervention with high-dose intravenous crystalline penicillin G, 50,000 units/kg every 4 hours, is usually recommended for the treatment of *N. meningitidis*

- Several third-generation cephalosporins (**e.g., cefotaxime, ceftazidime, ceftizoxime, ceftriaxone, and cefuroxime**) have indications for the treatment of meningitis and are acceptable alternatives to penicillin G.
  - **Chloramphenicol** is bactericidal for *N. meningitidis* and may be used in place of penicillin G. However, chloramphenicol has unpredictable metabolism in young infants and several drug- drug interactions and is used rarely in developed countries. Chloramphenicol frequently is used as initial empirical therapy for meningitis in developing countries owing to the low cost.
  - Prophylaxis of close contacts should be started without delay. In general, rifampin is give as prophylaxis for 2 days.
- Intramuscular ceftriaxone and oral ciprofloxacin are alternatives to rifampin.





## ***2- Streptococcus pneumoniae (Pneumococcus or Diplococcus)***

- Ceftriaxone and vancomycin are the agents of choice to treat presumed pneumococcal meningitis empirically until the susceptibility is known.
- Penicillin may be used for drug-susceptible, but for intermediate isolates, ceftriaxone or cefotaxime is used, and for highly drug resistant isolates, a combination of ceftriaxone and vancomycin should be used. Vancomycin should not be used as monotherapy.
- Alternative therapy includes meropenem, linezolid, and flouoroquinolone.



### ***3- Listeria monocytogenes***

- Treatment of *L. monocytogenes* meningitis with penicillin G or ampicillin may result in only a bacteriostatic effect and possible persistence of infection.
- Usually the combination of penicillin G or ampicillin with an aminoglycoside results in a bactericidal effect. Patients should be treated for 2 to 3 weeks after defervescence to prevent relapse. Combination therapy usually is employed for at least 10 days, with the remaining course of therapy completed with penicillin G or ampicillin alone.
- Trimethoprim-sulfamethoxazole may be an effective alternative because adequate CSF



## ***4-Haemophilus influenzae***

- In the past, ampicillin and chloramphenicol were the drugs of choice to treat pediatric meningitis. However, since approximately 30% to 40% of *H. influenzae* are now ampicillin-resistant, many clinicians use a third-generation cephalosporin (cefotaxime or ceftriaxone) or the combination of chloramphenicol and ampicillin for initial antimicrobial therapy. If the organism is sensitive to ampicillin, the patient then can be switched from the third-generation cephalosporin to ampicillin, and chloramphenicol, if used initially, can be discontinued. Cefepime and fluoroquinolones are suitable alternatives regardless of  $\beta$ -lactamase activity.



## 5- Gram negative Bacteria

Currently, gram-negative bacteria are the fourth leading cause of meningitis.

- Optimal antimicrobial therapies for gram-negative bacillary meningitis have not been fully defined. - The therapy of gram-negative meningitis is complex owing to the variety of organisms that can infect the CNS.

- The treatment of meningitis due to *P. aeruginosa* remains a unique problem because antibiotics showing good antibacterial activity against *P. aeruginosa*, such as antipseudomonal penicillins and aminoglycosides, penetrate the CSF poorly. Cases of *P. aeruginosa* meningitis should be treated with an extended-spectrum  $\beta$ -lactam such as ceftazidime, cefepime, piperacillin plus tazobactam, or meropenem plus an aminoglycoside, usually tobramycin. Since aminoglycosides penetrate the CSF poorly, their inclusion is predominantly to aid in the treatment of extracerebral infections.



If multidrug-resistant *Pseudomonas* is suspected initially, intraventricular administration of aminoglycoside should be considered along with intravenous administration.

- Other gram-negative organisms causing meningitis, excluding *P. aeruginosa*, most likely can be treated with a third or fourth generation cephalosporin, such as cefotaxime, ceftriaxone, or ceftazidime or cefepime



# Antibiotics

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## Less than 2 months of age:

- Ampicillin + Cefotaxime+ / Gentamycin-
- Treat for 3 weeks

## Over 2 months:

- Cefotaxime
- Treat for 7-10 days



# Prophylaxis

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- Rifampicin:

Children 5mg/kg bd x 2/7

Adults: 600 mg bd x 2/7

Pregnant contact:

Cefuroxime IM x 1 dose

OR

Just do T/S and await result



## Duration of treatment

- Although the length of treatment for bacterial meningitis generally is based on the causative organism, there is no universally accepted standard.

- meningitis caused by *S. pneumoniae* and *H. influenzae* has been treated successfully with

10 to 14 days of antibiotic therapy. Meningitis caused by *N. meningitidis* usually can be treated with a 7-day course of antibiotics. In contrast, a longer duration of 14 to 21 days has been recommended for patients infected with *L. monocytogenes* or group B streptococci because of a high probability of relapse. Likewise, a minimum of 3 weeks of treatment is recommended for meningitis caused by gram-negative bacilli.

- Therapy should be individualized, and some patients may require longer courses.





THANK YOU

