Bacterial And Viral Meningitis

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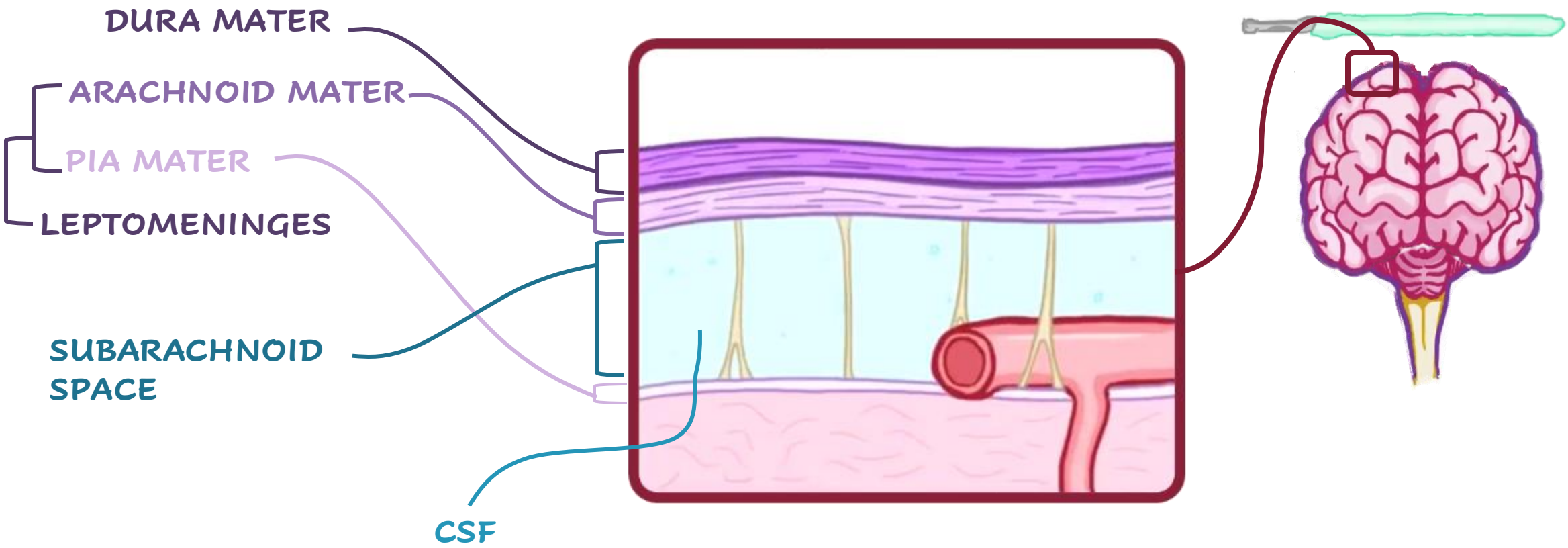
Quick Recap



Meningitis = inflammation of the LEPTOMENINGES

PachyMeningitis = inflammation of the Dura mater

Definitions

- **Meningitis:**
  - Meningitis is a life-threatening infection of the leptomeninges (arachnoid and pia mater) surrounding the brain and spinal cord, with involvement of the subarachnoid space

- **Encephalitis:**
  - Is the inflammation of brain parenchyma

- **Meningoencephalitis**
  - Patients with both meningeal and encephalitic manifestations.

Etiological Classification

- Based on the changes in leukocytes in cerebrospinal fluid (CSF), meningitis can be grouped into:
  - **Pyogenic meningitis:** It is characterized by elevated polymorphonuclear cells in CSF
  - **Aseptic meningitis:** It is characterized by an elevated lymphocyte count in the cerebrospinal fluid (CSF). It is most commonly caused by viruses, but other etiological agents may include tuberculosis, fungi, parasites, certain drugs, and autoimmune conditions

Why the Term "Aseptic"?

- The term "aseptic" means without detectable bacterial pathogens in routine CSF culture.
- It is used to describe cases where the initial CSF studies (e.g., Gram stain and bacterial culture) are negative for common pyogenic bacteria.

Aseptic Meningitis

- **Aseptic technique:** is a method designed to prevent contamination by microorganisms
- **Aseptic meningitis** is the clinical syndrome of meningeal inflammation with **negative culture** for routine bacterial pathogens in a patient who did not receive antibiotics before lumbar puncture

Symptoms of meningeal infection

CSF

No growth

Causes

- The disease can be caused by several pathogens including bacteria, viruses, fungi or parasites, but the highest global burden is seen with bacterial meningitis.

Bacterial (pyogenic meningitis) Causes

- **Overall:**
  - Streptococcus pneumoniae (Most common)
  - Neisseria meningitidis (or meningococcus)
  - Streptococcus agalactiae
  - Listeria monocytogenes
  - Haemophilus influenzae
- **Neonates:**
  - GBS → Streptococcus agalactiae
  - Gram-negative bacilli such as Escherichia coli and Klebsiella
  - Listeria monocytogenes
- **Children and teens:**
  - Neisseria meningitidis
  - Streptococcus pneumoniae
- **Adults and Elderly:** Streptococcus pneumoniae (most common), Streptococcus agalactiae and Listeria monocytogenes

Viral Causes (aseptic or lymphocytic)

- Enteroviruses (Coxsackievirus and Echovirus) are the most common (>85% of cases)
- Herpesviruses including herpes simplex virus (HSV), varicella-zoster virus (VZV), Epstein-Barr virus
  - HSV 2 more than HSV1
- Arboviruses (e.g., West Nile virus)
- Mumps virus
- Measles virus
- Influenza virus

Bacterial vs Viral

Bacterial

- Bacterial meningitis is a neurologic emergency
- Fatal if left untreated
- **Altered mental status**
- **Complications:** Abscess, seizures, increased ICP
- Sequelae: Sensorineural hearing loss, intellectual disability

- Neutrophilic predominance

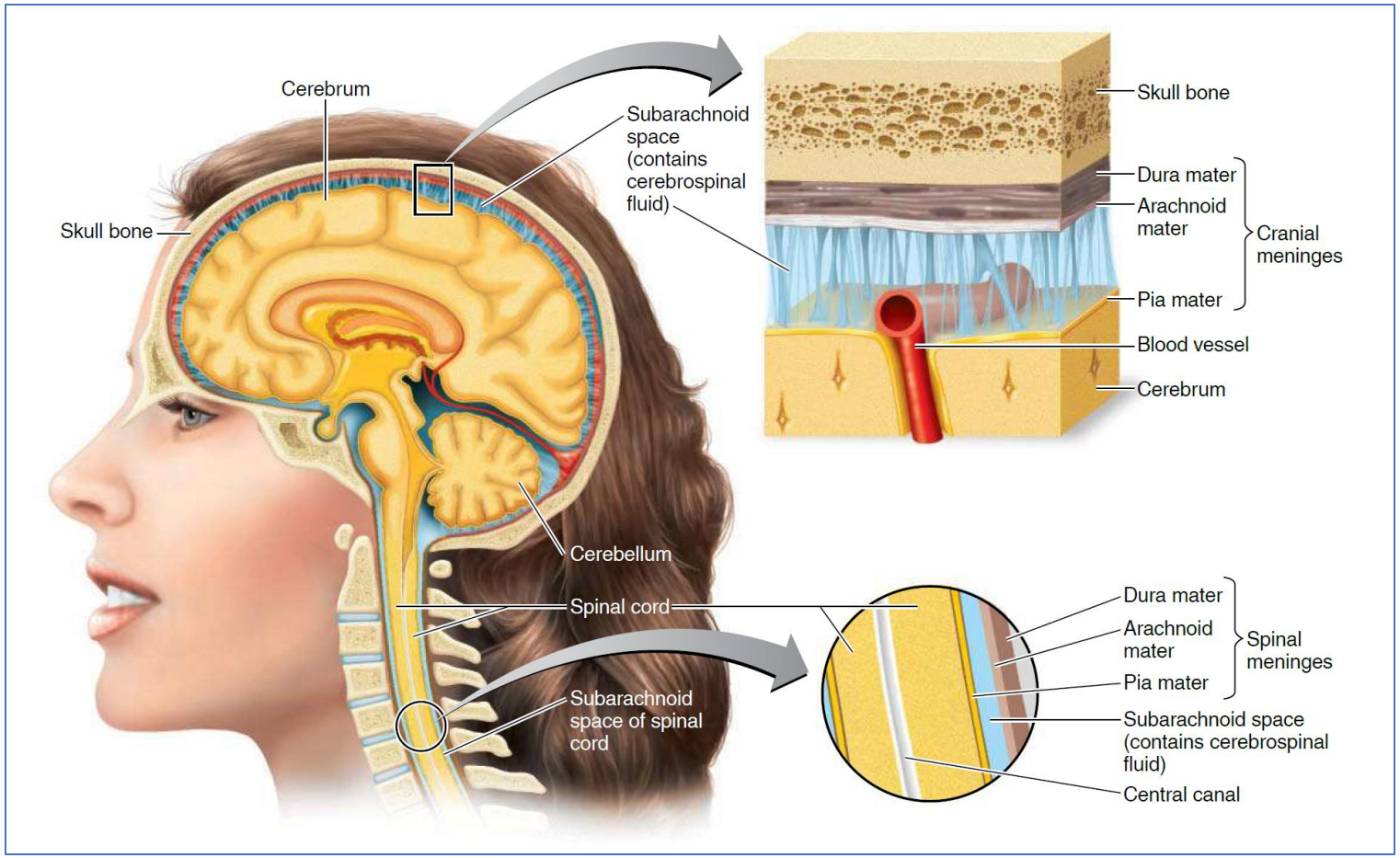
Viral

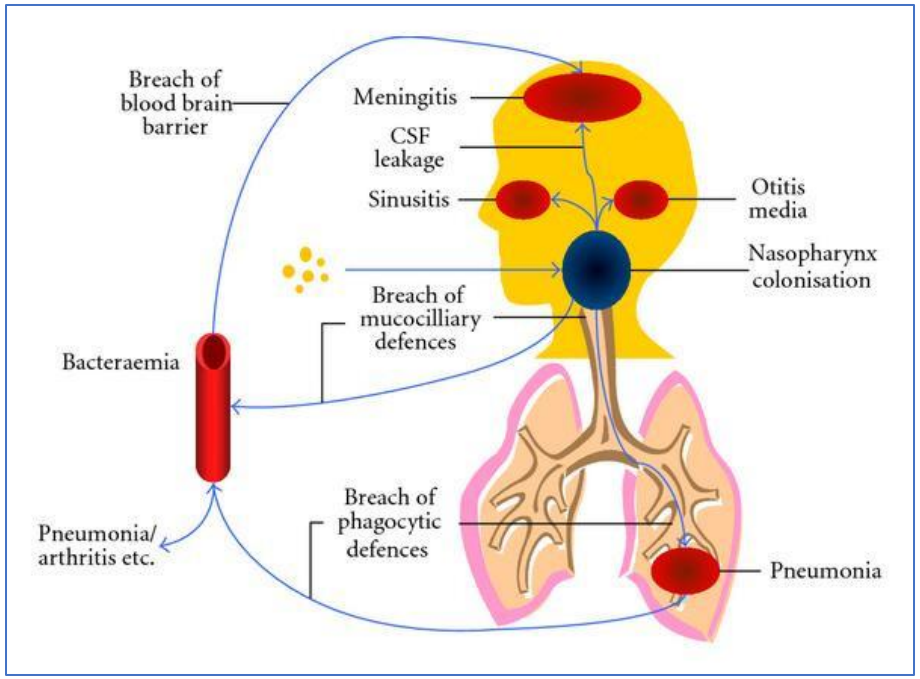
- Less severe than bacterial meningitis
- Resolves spontaneously (not fatal, nor an emergency)
- There should be **no altered mental status** (If so, diagnosis may be bacterial meningitis or encephalitis)
- **Supportive care** (with exceptions → see treatment)
- Lymphocytes predominance

Pathophysiology

- **Pathways of infection**
  - Most pathogens that cause meningitis colonize the nasopharynx or the upper airways before entering the CNS via:
    - Hematogenous dissemination → most common route
    - Contiguous spread of infections in nose, eyes, and ears (otitis media, mastoiditis, sinusitis)
    - Retrograde transport along or within peripheral or cranial nerves
- Direct infection (e.g., due to trauma or head surgery)

How viruses gain access to the CNS?





Clinical features

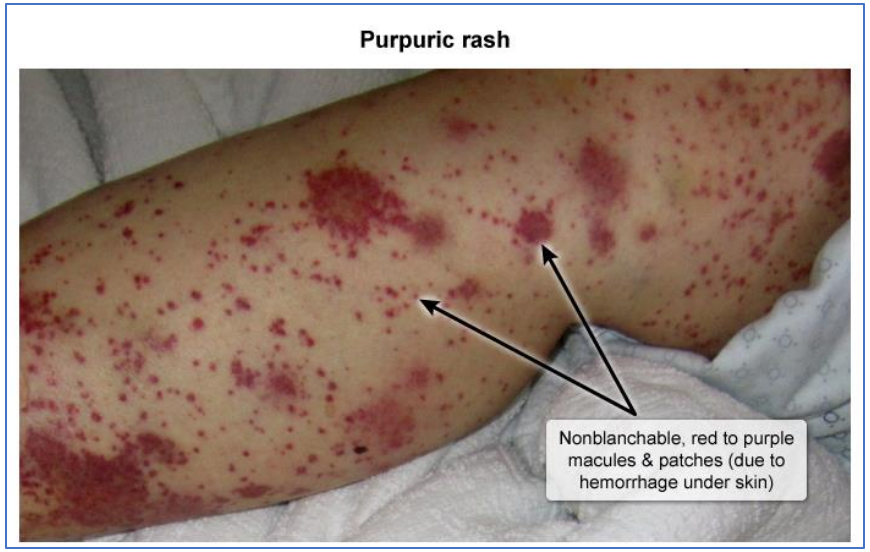
- Clinical features of bacterial and viral meningitis are similar, although viral meningitis is less acute and usually self-limiting within 5–14 days.
- **Symptoms of meningitis**

1. Classic triad of meningitis
   - Fever
   - Meningismus
     - Headache
     - Neck stiffness
     - Photophobia
   - Altered mental state (typically in bacterial)
2. Nausea, vomiting
3. Malaise
4. Seizures
5. Neonates and young children often present with nonspecific symptoms

Clinical features (cont.)

Pathogen-specific symptoms

- Patients with *N. meningitidis*: signs of meningococcemia
  - Myalgia: more common in children
  - Possibly petechial or purpuric rash: more common in children
- Patients with viral meningitis
  - Prodrome with flu-like symptoms (Low-grade fever, Malaise and fatigue, and Myalgia)
  - Upper respiratory symptoms (e.g., sore throat)
  - Pharyngitis, and/or rash



Physical examination

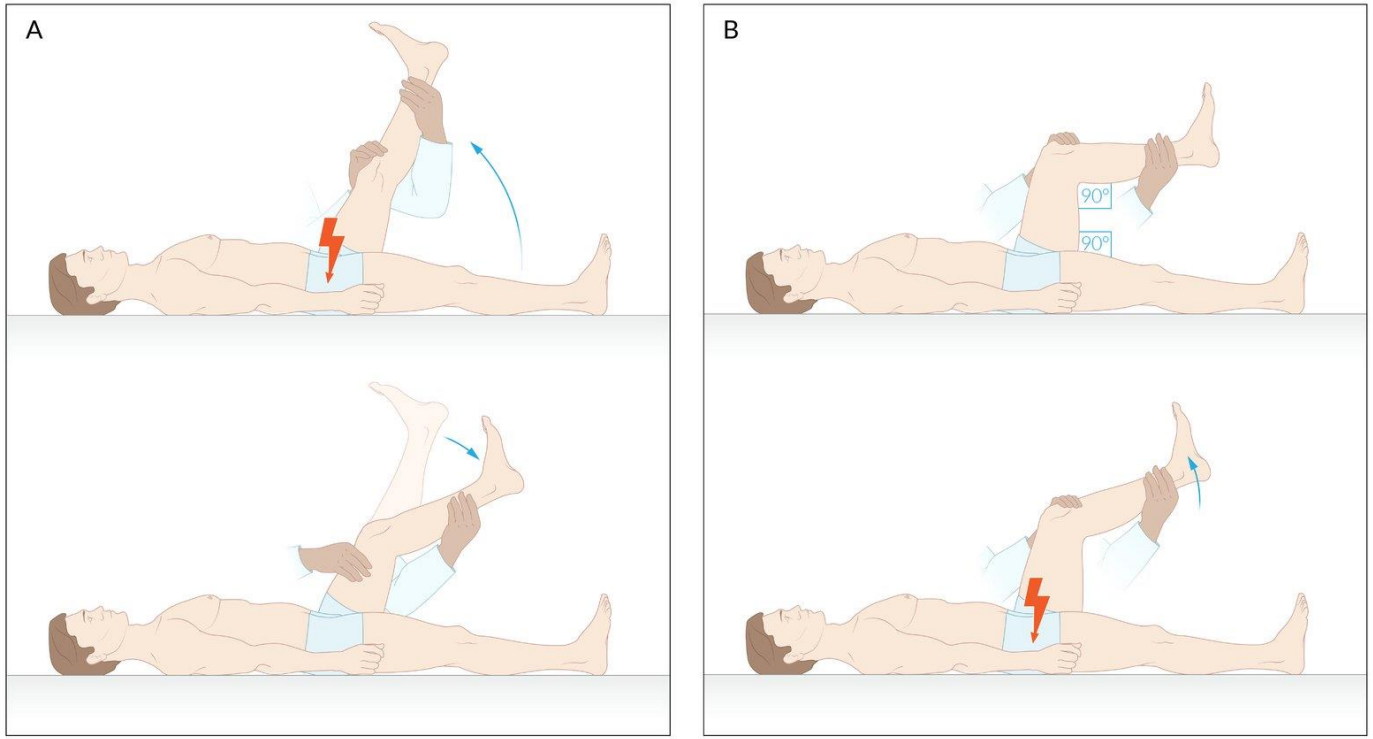
- Most important signs of meningeal irritation
  - Neck stiffness (the patient can not touch his chest with his chin)
  - Kernig sign
  - Brudzinski sign

- Signs of increased intracranial pressure (< 5% of cases), e.g., cranial nerve palsies, papilledema
- Signs of underlying infections:
  - Redness of tympanic membrane → acute otitis media
  - Nonblanching rash → meningococcal meningitis

Physical examination- Kernig sign

The Kernig sign can be assessed using two methods.

- In the first method (A), the extended leg is passively elevated at the hip joint. If there is pain, there is reflex flexion of the knee.
- Alternatively (B), the Kernig sign can be assessed by flexing the hip and knee at a 90° angle. Subsequent extension of the leg causes stretching of the nerve roots or meninges, which can result in pain and muscle guarding against extension.



YouTube

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https://www.youtube.com/watch?v=euNPB3OjrdM
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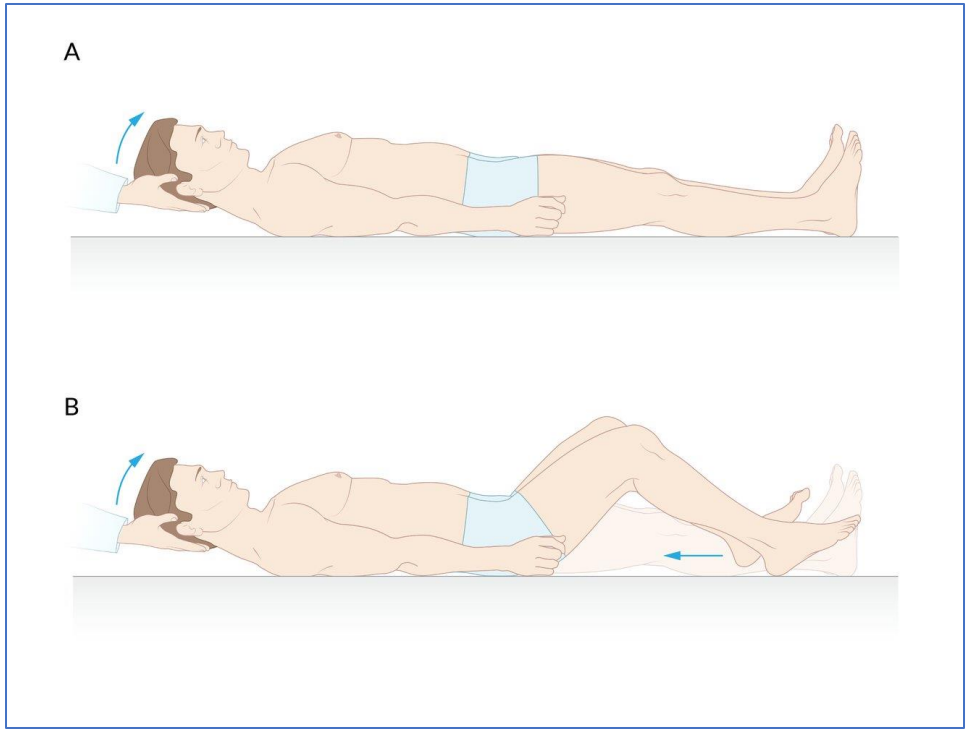
Physical examination - Brudzinski sign

- Passive flexion of the neck (A) leads to spontaneous flexion of the hips (B) as a reflex, which provides relief of painful strain on the meninges.



YouTube

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Initial management

- Bacterial meningitis is a medical emergency and requires immediate treatment.
- Diagnostic and treatment steps should be initiated simultaneously and empiric treatment should not be delayed for diagnostic steps.
  - If the patient is stable and has no LP contraindications: Perform LP as soon as possible before starting empiric antibiotics.
  - If the patient is unstable, requires neuroimaging, or has relative contraindications to LP (e.g., coagulopathy): Defer LP and start empiric antibiotic treatment
- Empiric antibiotic treatment must be initiated as soon as possible (i.e., often prior to diagnosis).

Diagnosis

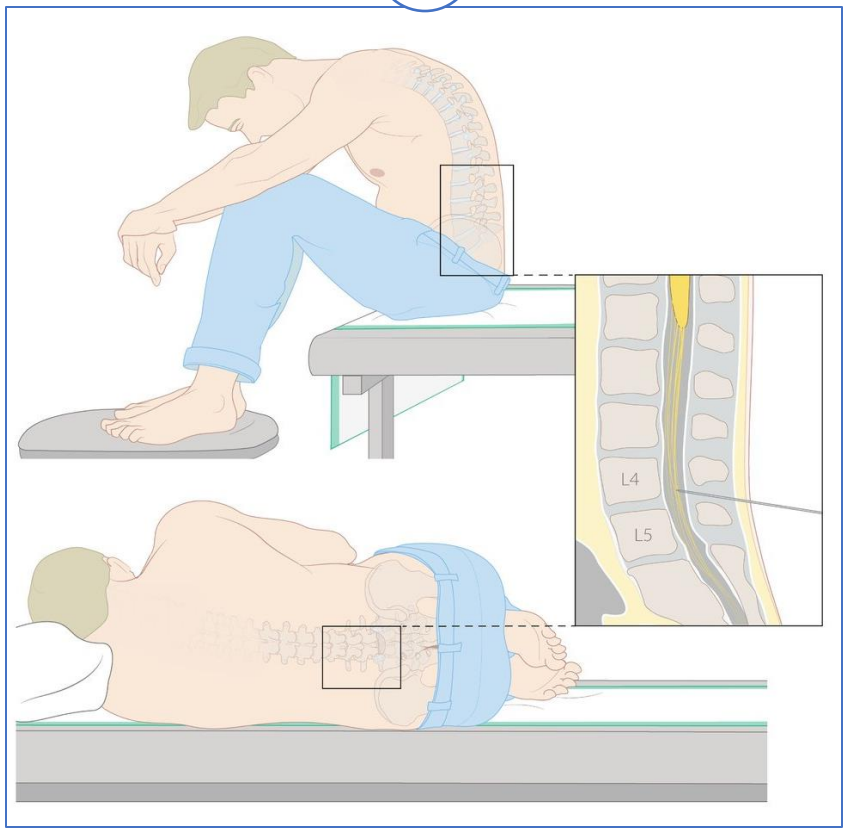
1. History and examination
2. Radiology:
   - Chest X rays.
   - Computed tomography scan (CT scan):
     - Masses and abscess result in increased intracranial pressure (ICP) → Risk of herniation
     - The primary goal of obtaining neuroimaging before LP is to mitigate the risk of brain herniation, which can be precipitated by the transient decrease in ICP caused by LP. The actual risk of brain herniation after LP is extremely low.

Diagnosis (cont.)

3. Laboratory studies
   - Blood cultures (two sets): obtain before starting antibiotic therapy
   - Basic metabolic panel: Blood glucose is needed to analyze CSF glucose.
   - Coagulation panel: especially if there is suspicion for disseminated intravascular coagulation (e.g., petechiae, purpura)
4. Lumbar puncture (LP) → for CSF analysis
5. PCR for viral meningitis and specific bacterial subtype

Lumbar puncture

1



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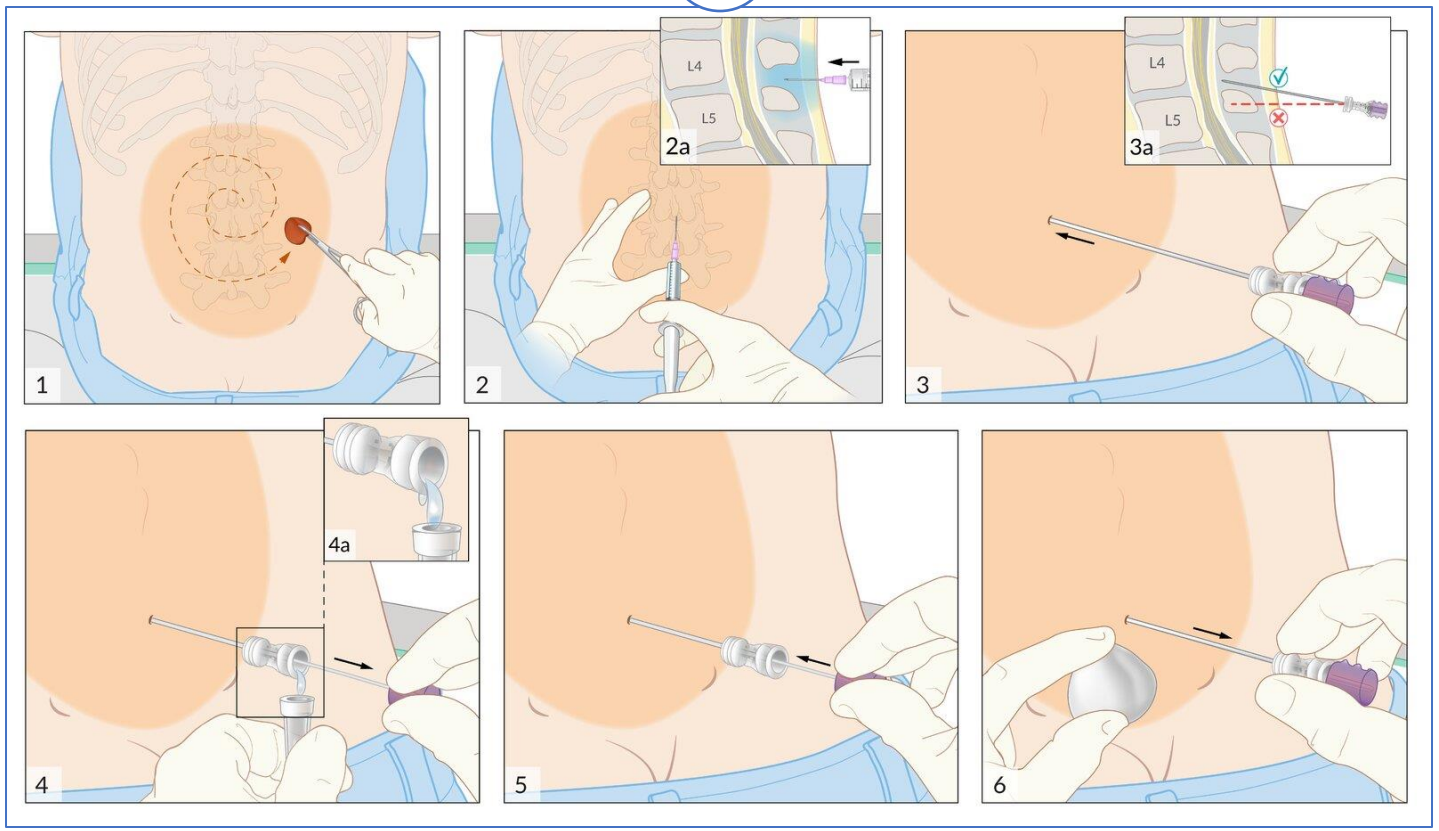

YouTube

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CSF analysis

Differences between bacterial & viral meningitis		
	Viral	**Bacterial**
Common microbes	• Enteroviruses (most common) • Arboviruses • Herpes simplex virus type 2	• Adults: *Streptococcus pneumoniae* & *Neisseria meningitidis* • Neonates: Group B *Streptococcus* & gram-negative bacilli
CSF cell differential	• WBC count often 10-500/mm^3 • Lymphocytic predominance	• WBC count often >1,000/mm^3 • Neutrophilic predominance
CSF glucose & protein	• Glucose levels are normal or slightly reduced • Protein generally <150 mg/dL	• Glucose levels <40 mg/dL • Protein is often >250 mg/dL
CSF Gram stain & culture	• No organisms identified	• Often positive for a specific organism

CSF = cerebrospinal fluid; **WBC** = white blood cell.

CSF analysis

Cerebrospinal fluid analysis			
Diagnosis	**WBC count (mm^3)**	**Glucose (mg/dL)**	**Protein (mg/dL)**
Normal	0-5	40-70	<40
Bacterial meningitis	>1,000	<40	>250
Viral meningitis	10-500	40-70	<150
WBC = white blood cell.			

Treatment – Viral meningitis

- Viral meningitis is usually **self-limiting** and requires only **supportive management**. Antiviral therapy is indicated only in selected and/or severe cases.
- Indications of antiviral therapy:
  - Patients with HIV
  - Herpes simplex meningitis: acyclovir
  - Cytomegalovirus meningitis: ganciclovir, foscarnet
  - Cases associated with encephalitis

Treatment – Bacterial meningitis

- Antibiotics should not be delayed while awaiting results of CT scan or lumbar puncture.
- Initially, broad-spectrum antibiotics are given.
- Later, antibiotics are adjusted based on culture and sensitivity:
  - S. pneumoniae: vancomycin + ceftriaxone
  - N. meningitidis: 3rd-generation cephalosporin; penicillin G or ampicillin if susceptible
  - H. influenzae: 3rd-generation cephalosporin; penicillin G or ampicillin if susceptible
  - L. monocytogenes: ampicillin or penicillin G + gentamicin
  - Gram-negative bacilli: 3rd-generation cephalosporin

Treatment – Bacterial meningitis (cont.)

- IV administration is used for maximum efficacy.
- Penetration of blood–brain barrier is facilitated by active meningeal inflammation.
- Intrathecal administration of antibiotics is considered in patients who are unresponsive to IV antibiotics or in nosocomial meningitis.
- Steroid administration:
  - Corticosteroids, especially dexamethasone, are used as an adjunctive treatment for bacterial meningitis
  - Decreases mortality
  - Decreases rate of neurologic complications (e.g., hearing loss)

Prognosis

- Bacterial meningitis
  - Fatal if left untreated
  - Prognosis in treated patients depends on age, overall condition, immune status and the pathogen(s) involved.
- Viral meningitis
  - Resolves spontaneously in the majority of cases
  - Residual symptoms such as sensorineural hearing loss, epilepsy, and cognitive deficits are rare.

- Mortality increases with age:
  - 18–34 years old: Case fatality is 8.9%.
  - > 65 years old: Case fatality is 22.7%.

- Neurologic complications (hearing loss, intellectual impairment, focal deficits) affect up to 28% of patients.

Prevention

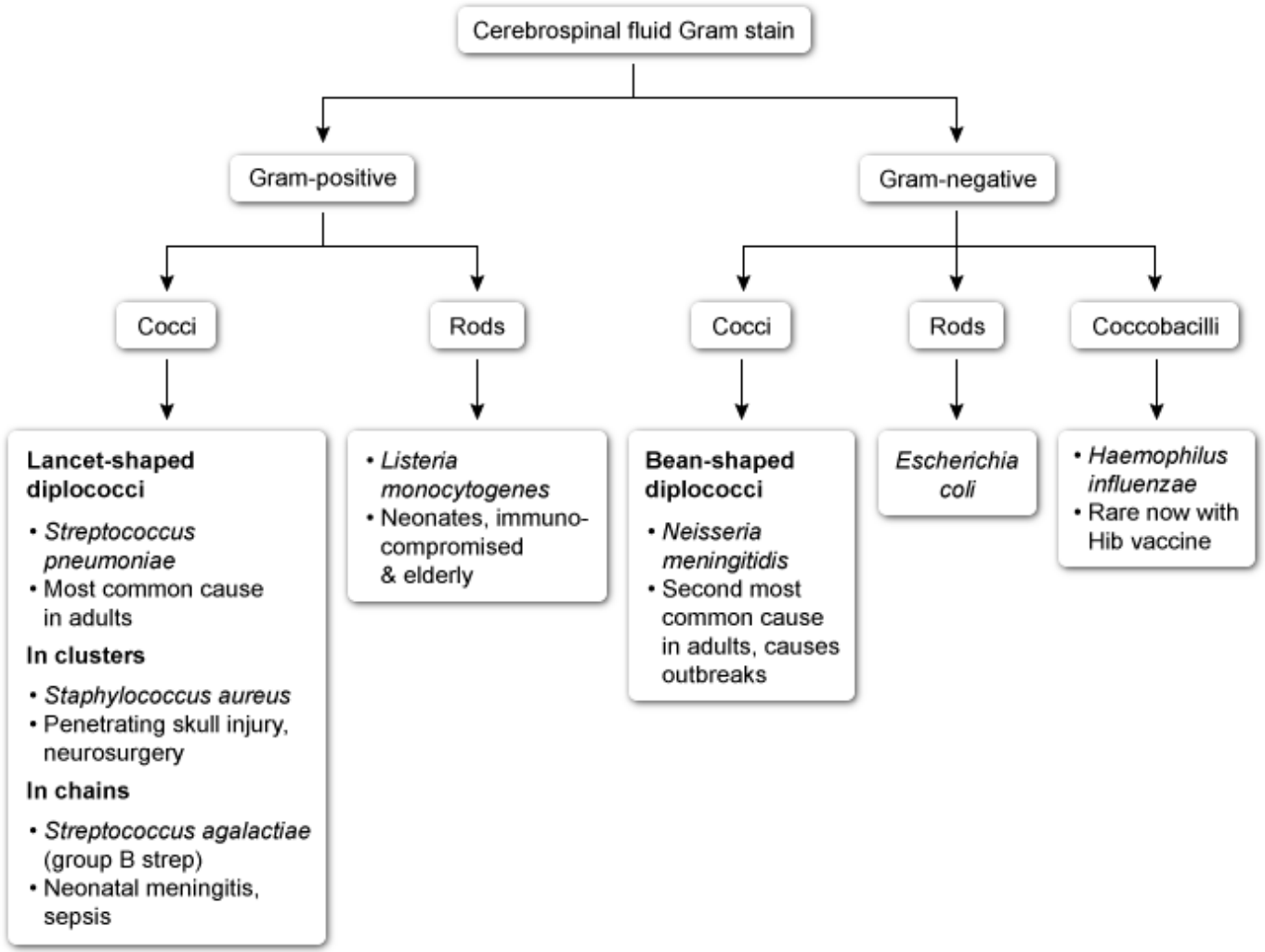
- Vaccinations can protect against certain types of meningitis:
  - Haemophilus influenzae type B (Hib) vaccine
  - Pneumococcal conjugate vaccine
  - Meningococcal vaccine

- Meningococcal vaccine
  - There are three types of meningococcal vaccine.
    - Meningococcal ACWY vaccines (protein-conjugate)
    - Meningococcal B vaccines (protein-based)
    - Pentavalent meningococcal vaccine (MenABCWY)

Prevention of onward transmission

- Provide postexposure chemoprophylaxis for close contacts.
- N. meningitidis
  - Rifampin → 1st line in children < 1 month in age
  - OR ceftriaxone
  - OR ciprofloxacin (be cautious to the contraindications)
- H. influenzae
  - Rifampin

Common causes of bacterial meningitis



Osmosis