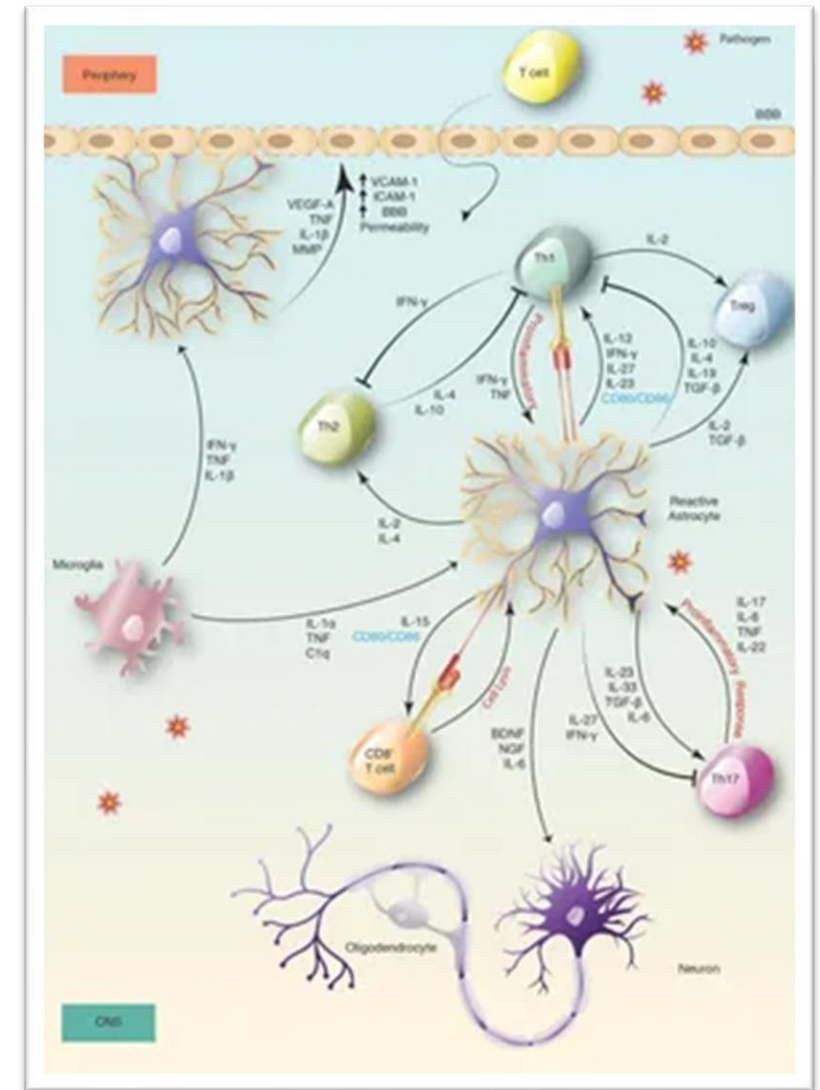


Bacterial infections of  
the central nervous  
system

# Bacterial infections of the CNS

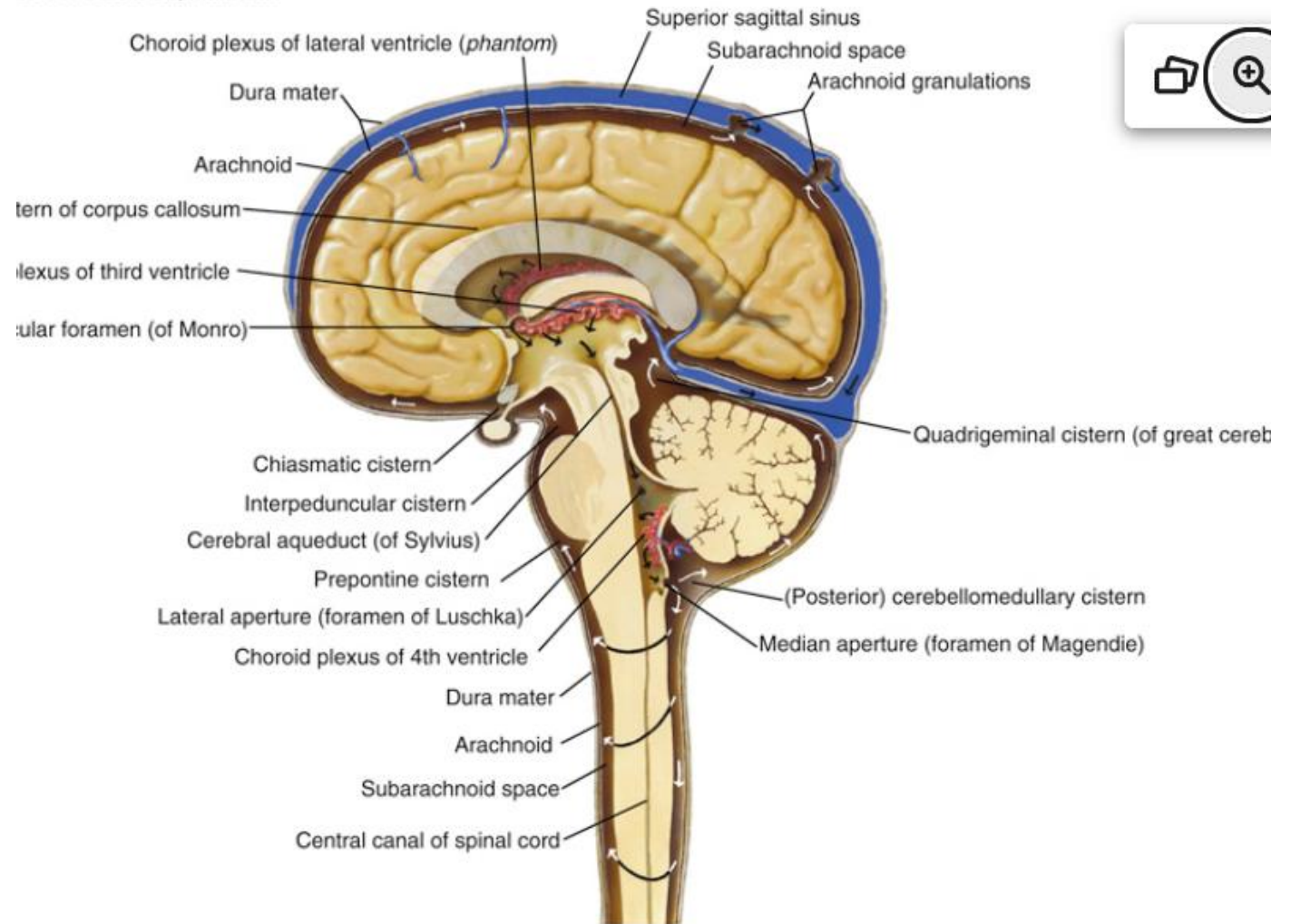
- Clinical syndrome characterized by inflammation of the soft meninges production of pus in the subarachnoid space
- Severe illness high risk of complications and sequelae
- Many presentations of meningitis include altered mentation due to brain inflammation and can be described as meningoencephalitis



# Anatomic and Physiologic Considerations

- CSF is produced by the choroid plexus in the lateral, third, and fourth ventricles
- The choroid plexus consists of projections of vessels and pia mater into the ventricular cavities
- Normally about 500 mL of CSF is produced per day by both filtration and active transport at a rate of about 20 mL/h
- CSF circulates from the lateral ventricles into the third and fourth ventricles and then into the subarachnoid space over the surfaces of the brain and down the spinal cord
- CSF is reabsorbed back into the bloodstream via the arachnoid villi located along the superior sagittal and intracranial venous sinuses and around the spinal nerve roots

Flow of cerebrospinal fluid



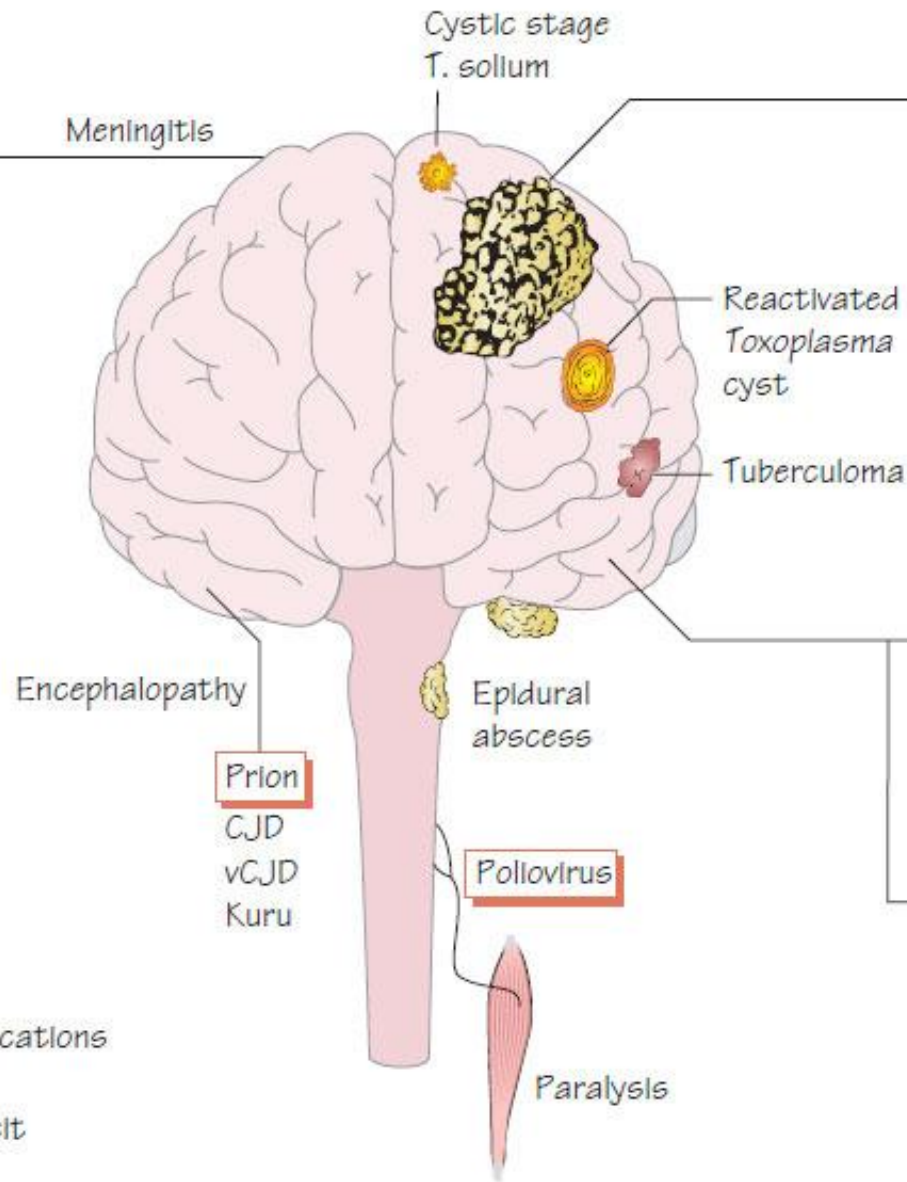


### Bacterial meningitis

- Neonates
- *E. coli*
  - Group B strep
  - *Listeria*
- < 5 yr
- *N. meningitidis*
  - (*H. influenzae*)
- Young adult
- *N. meningitidis*
- Older
- *S. pneumoniae*
  - *Listeria*
- Immunosuppressed
- *M. tuberculosis*
  - *Cryptococcus*
- Shunt
- Staphylococci
- CSF findings
- Glucose low
  - Protein raised
  - Polymorphs raised

#### Bacterial meningitis complications

- Septicaemia
- Intellectual deficit
- Deafness
- Arthritis
- Skin necrosis



### Brain abscess

#### Route

- Haematogenous
- Local spread
- Foreign body

#### Organisms

- Anaerobic strep.
- *Bacteroides*
- Staphylococci
- Gram negatives

### Viral encephalitis

- Herpes simplex
- Arboviruses
- Mumps
- Measles

### Viral meningitis

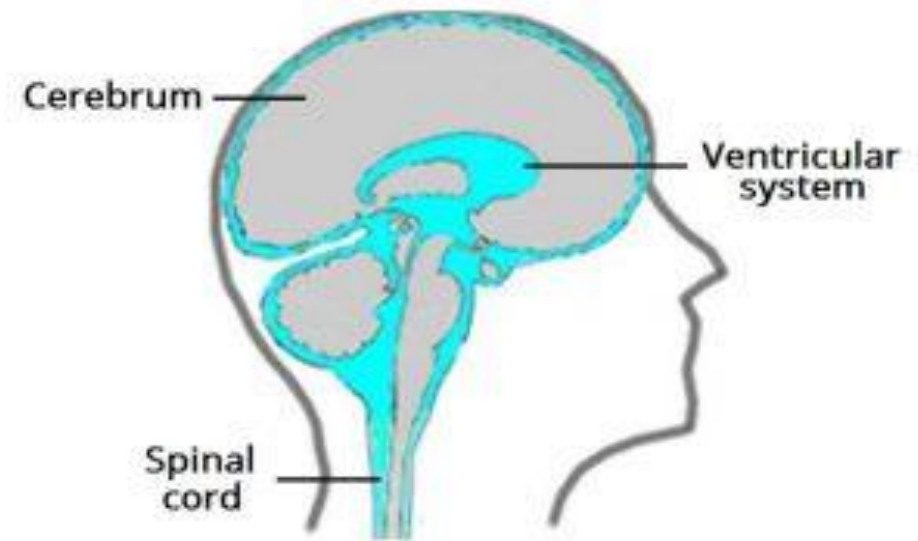
- Enterovirus
- Mumps
- Herpes simplex
- Arboviruses

#### CSF findings

- Glucose normal
- Protein raised
- Lymphocytes raised

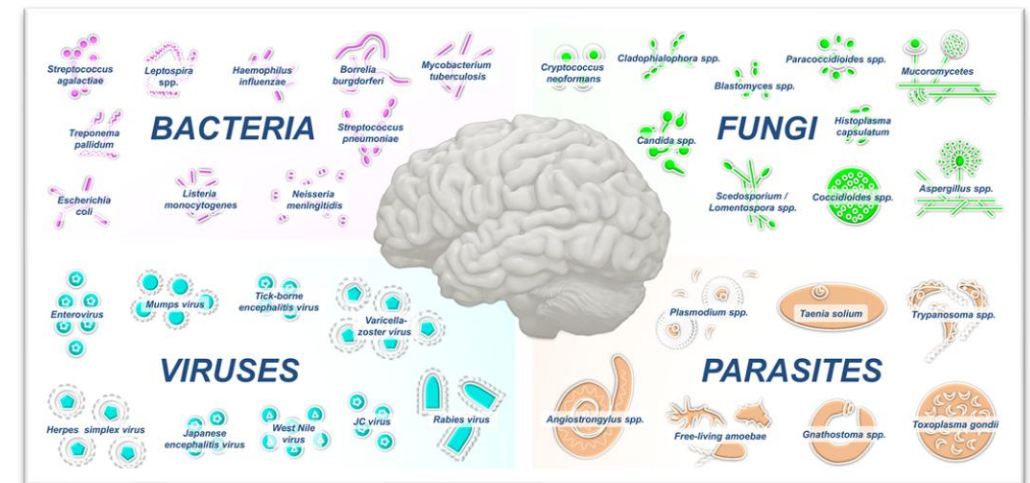
# NORMAL APPEARANCE OF CSF

- Normal pressure
- It may also contain up to **five mononuclear cells** per microliter
- Protein rate less than **0.40 g/L**
- CSF glucose – **1/2 TO – 2/3** OF SERUM GLYCEMIA
- Chlorides depend on the degree of dehydration

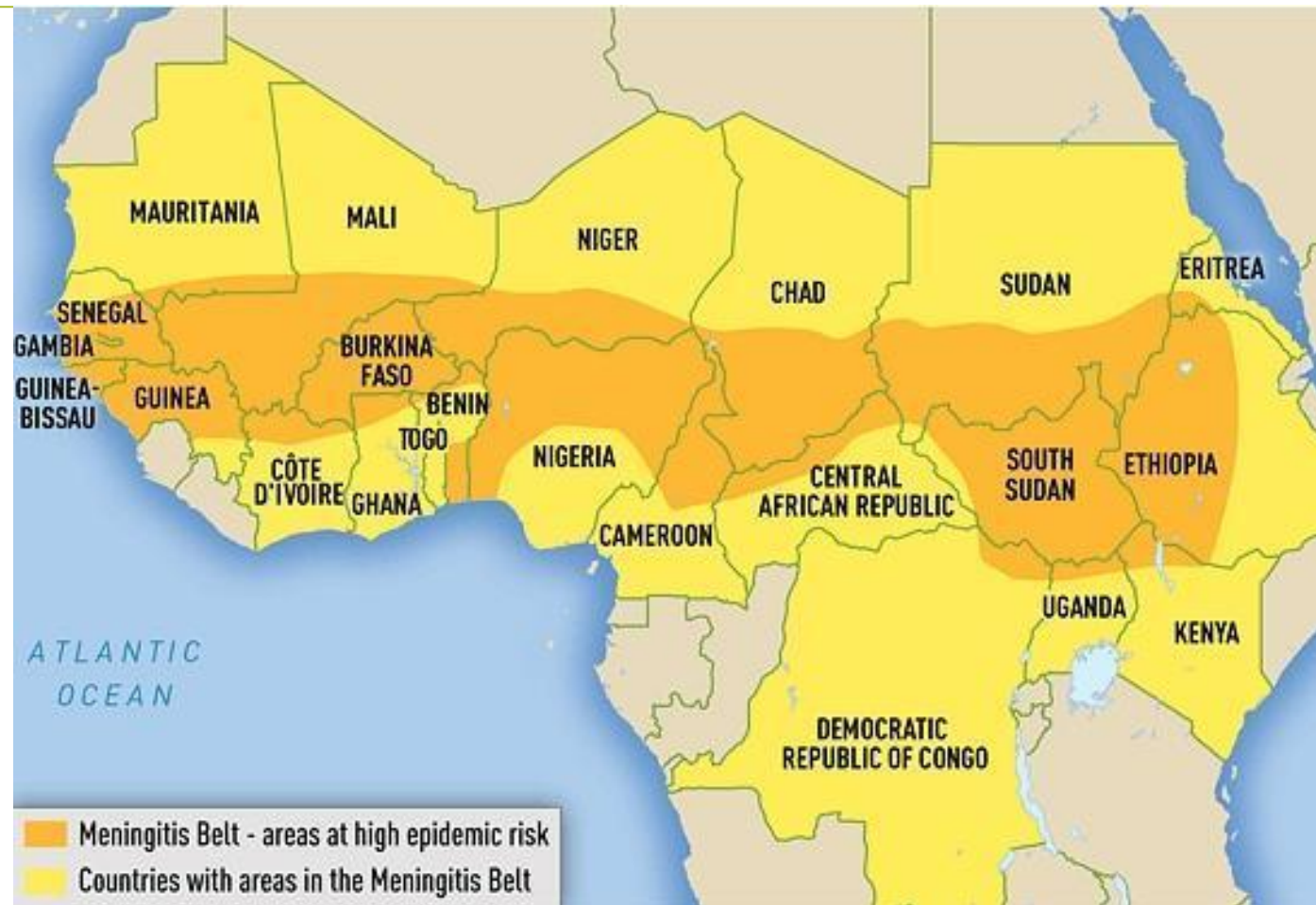


- Globally, the epidemiology of bacterial meningitis has changed dramatically with the introduction of conjugate vaccines
- The Hib conjugate vaccine has essentially eradicated Hib meningitis, and with widespread use of the meningococcal serogroup
- A conjugate vaccine (MACV), the overall burden of suspected meningococcal meningitis cases has been reduced by almost 60% in high-risk countries across northern Africa
- Pneumococcal conjugate vaccines (PCVs) have also resulted in a slight decrease in pneumococcal disease, and in many countries, this pathogen has overtaken H. influenzae
- Despite these advances, there were still over 2.5 million new cases of bacterial meningitis and over 236,000 deaths worldwide in 2019 alone

## Epidemiology



In 2019, there were over 22,000 suspected cases of meningitis, with 1261 deaths reported to the WHO in African countries sharing data. A disproportionately high rate of bacterial meningitis occurs in Africa due to elevated endemic disease, a younger population and regularly occurring epidemics across the “**meningitis belt**”—a span of countries between Ethiopia and Senegal that includes Nigeria, Burkina Faso and Sudan



# Predisposing factors for bacterial meningitis

- Immunodeficiencies
- Traumatic head injuries
- Skull base fractures
- Neurosurgical procedures
- Artificial drainage of the CSF
- Congenital anomalies (meningomyelocele)
- Race (Eskimos, Aborigines, Indians-H. Influenzae)
- Neurological, mental and sensory diseases

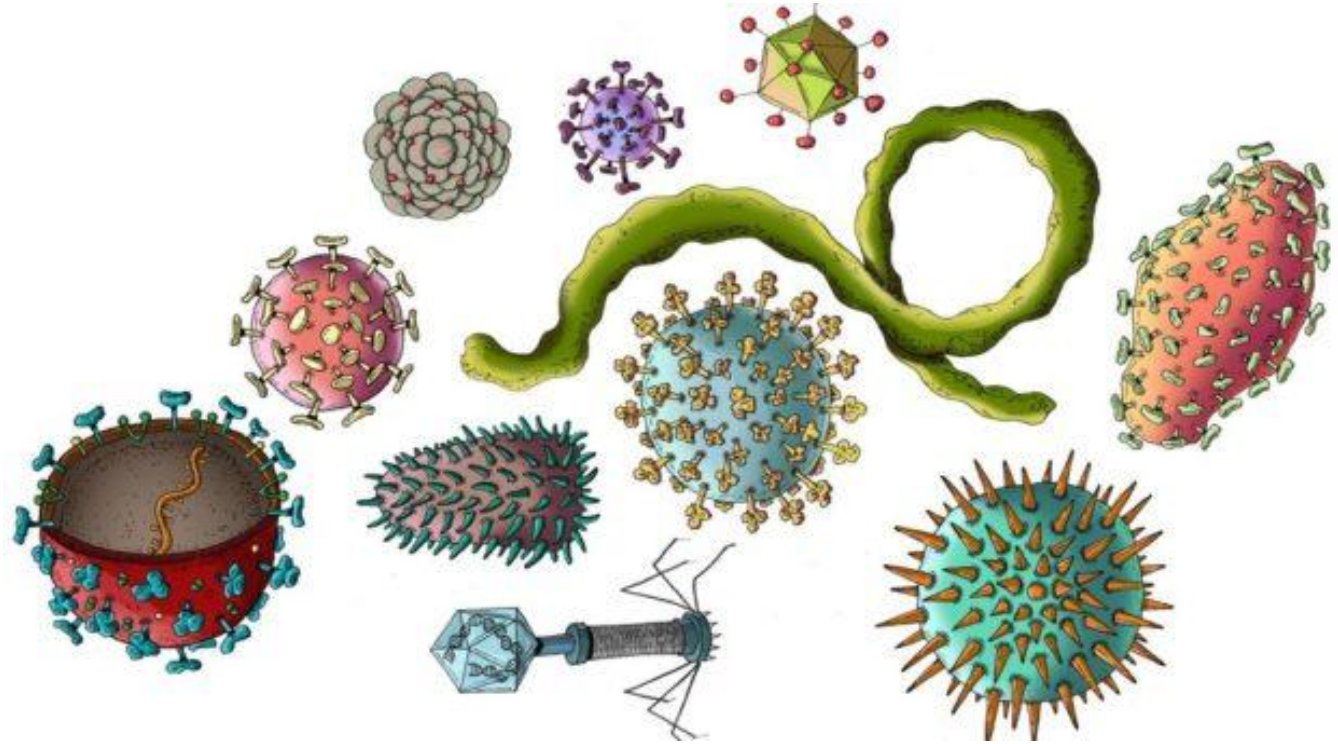


## Predisposing/risk factors

- Asplenia
- Immunosuppressive drugs
- Immunodeficiency (HIV, malignancy)
- Alcoholism
- Intravenous drug addicts
- Septic thrombophlebitis

## Etiology of bacterial meningitis

- *Hemophilus influenzae*
- *Neisseria meningitidis*
- *Streptococcus pneumoniae*
- *Streptococcus grupe B*
- *Listeria monocytogenes*
- *Staphylococcus spp.*
- *Gram negative bacteria*



# Etiology of bacterial meningitis

Risk and/or Predisposing Factor	Bacterial Pathogen
Age < 3 months	<i>S agalactiae</i> (group B streptococci) <i>E coli</i> K1 <i>L monocytogenes</i>
Age 3 months to 18 years	<i>N meningitidis</i> <i>S pneumoniae</i> <i>H influenzae</i>
Age 18-50 years	<i>S pneumoniae</i> <i>N meningitidis</i> <i>H influenzae</i>
Age older than 50 years	<i>S pneumoniae</i> <i>N meningitidis</i> <i>L monocytogenes</i> Aerobic gram-negative bacilli

# Etiology of bacterial meningitis

Risk and/or Predisposing Factor	Bacterial Pathogen
Immunocompromised state	<i>S pneumoniae</i> <i>N meningitidis</i> <i>L monocytogenes</i> Aerobic gram-negative bacilli
Intracranial manipulation, including neurosurgery	<i>Staphylococcus aureus</i> Coagulase-negative staphylococci Aerobic gram-negative bacilli, including <i>Pseudomonas aeruginosa</i>
Basilar skull fracture	<i>S pneumoniae</i> <i>H influenzae</i> Group A streptococci
CSF shunts	Coagulase-negative staphylococci <i>S aureus</i> Aerobic gram-negative bacilli <i>Propionibacterium acnes</i>



# How does the infectious agent reach the meninges?

- Hematogenous
- Direct spread from parameningeal foci (sinusitis, otitis media, trauma, direct inoculation during neurosurgical interventions)



# Direct route of bacterial spread

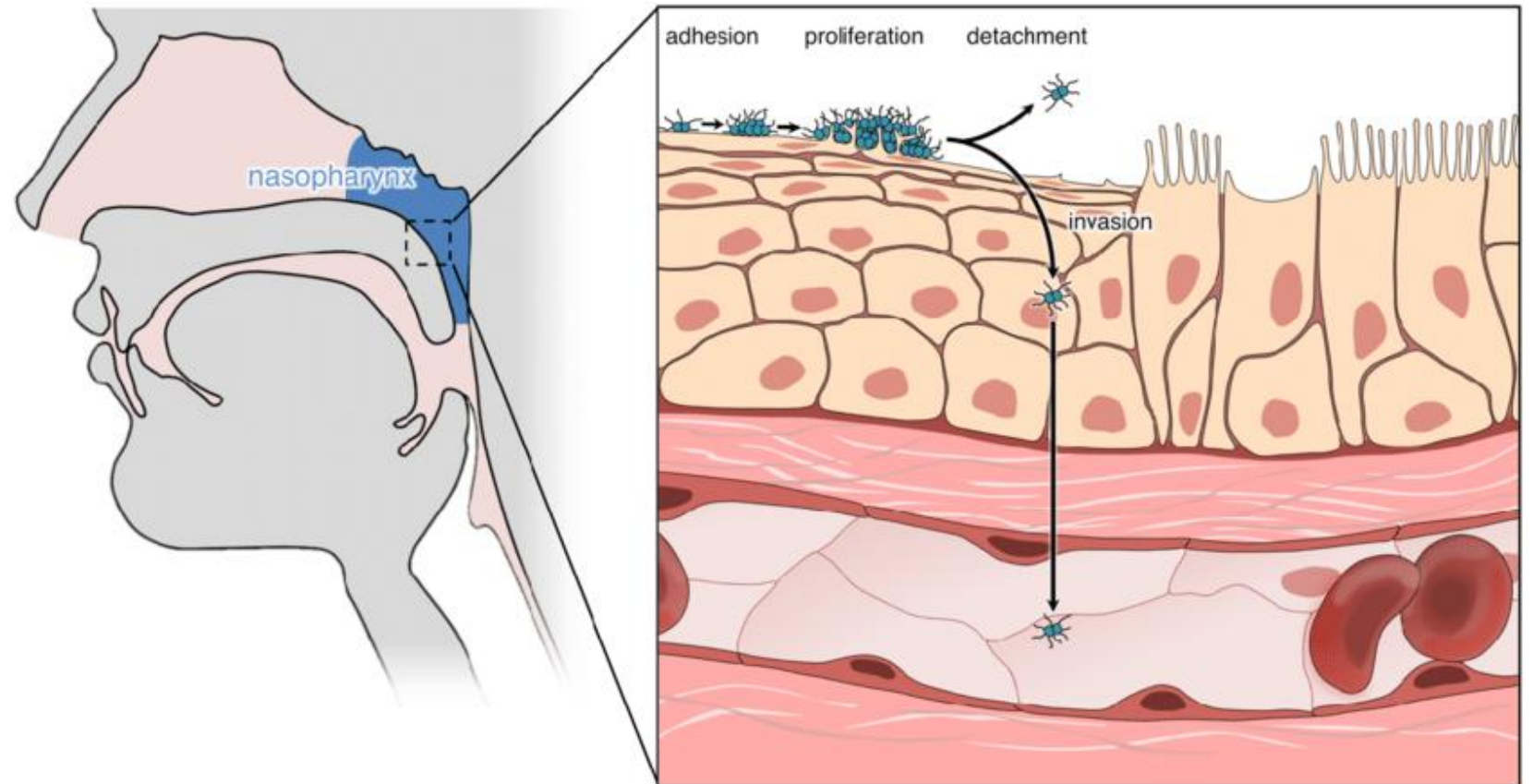
- Dentogenic abscess
- Otitis media
- Mastoiditis
- Sinusitis
- Skull fractures
- Brain and spinal cord surgeries
- Ventriculoperitoneal shunt
- Lumbar puncture

# Pathogenesis of bacterial meningitis

- Nasopharyngeal colonization and passage through mucosal barriers
- Survival in the blood and hematogenous dissemination of bacteria
- Passage of bacteria through the blood-brain barrier
- Development of inflammation in the subarachnoid space

# Nasopharyngeal colonization and passage through mucous membranes

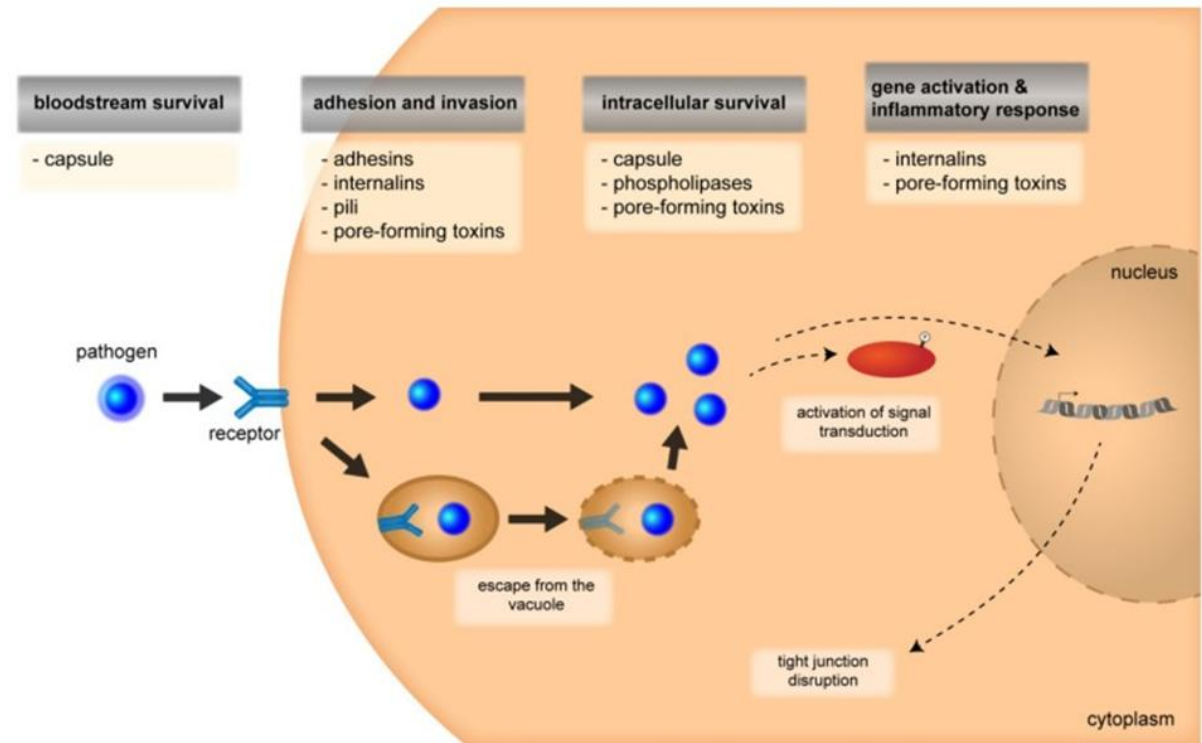
- Adherence of bacteria to receptor sites on the epithelial cells of the nasopharynx
- If the receptor sites are blocked by specific IgA antibodies, infection cannot occur
- Virulence factors of bacteria (meningococcal fimbriae)





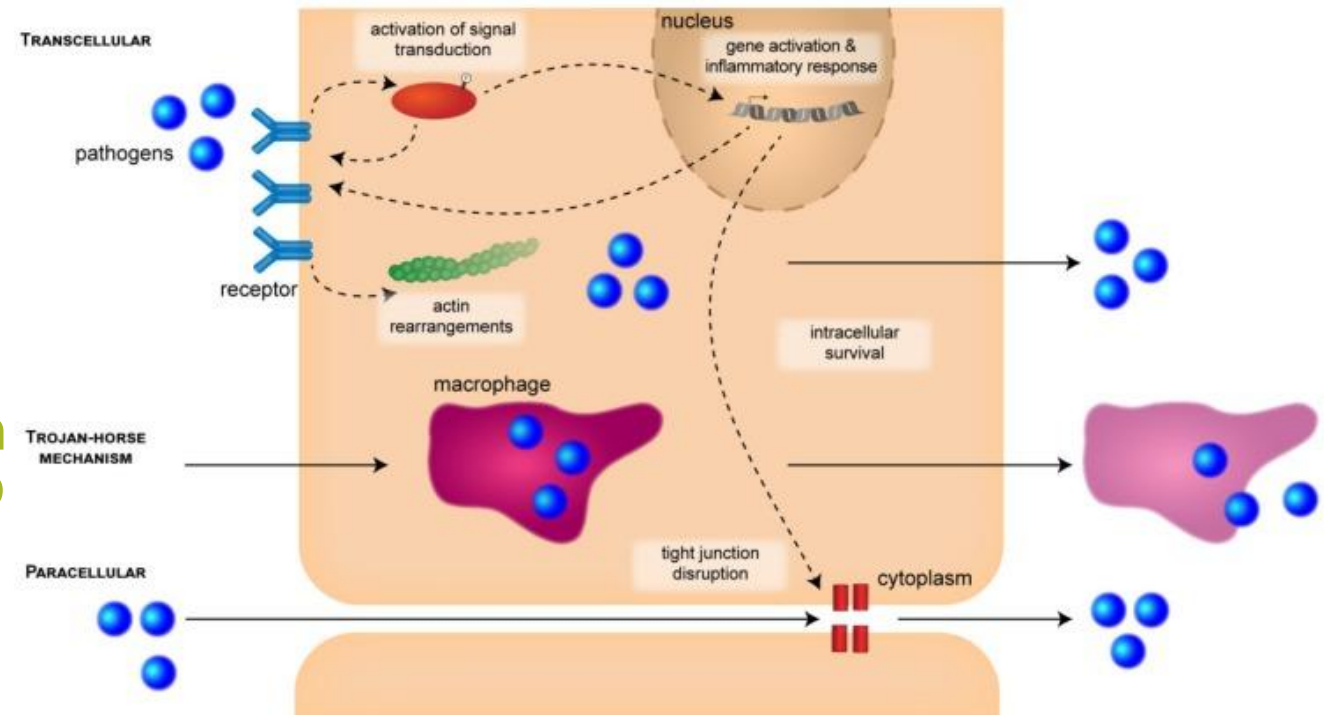
# Survival in the blood and hematogenous dissemination

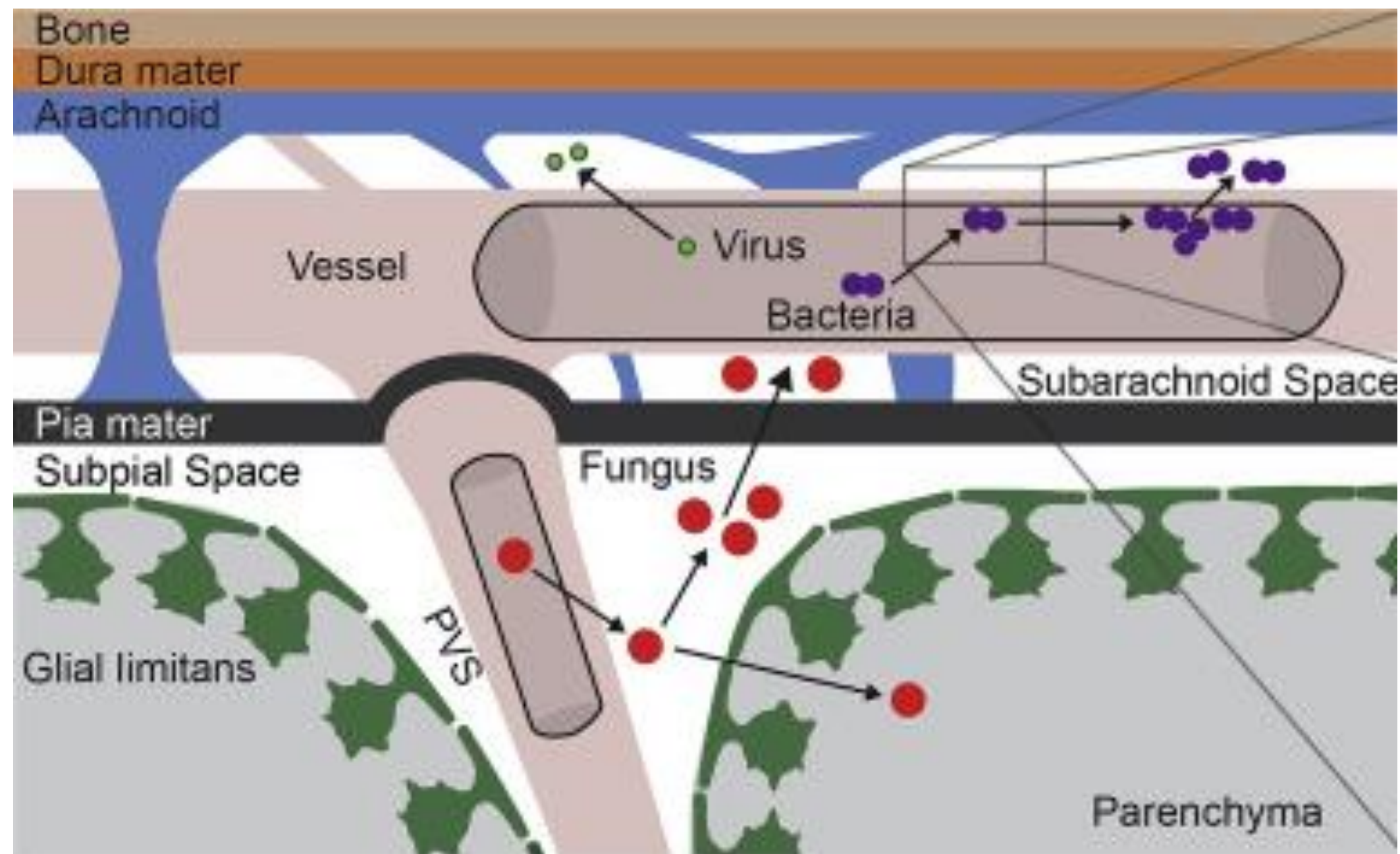
- The ability of bacteria to resist the body's defenses
- Inadequate opsonization and phagocytosis
- Deficiency of IgM and IgG antibodies in non-immune, young individuals
- Immunodeficiency states (deficiency of various components of the complement system)



# Bacterial passage through the blood-brain barrier

- It takes place through the choroid plexus of the lateral ventricles
- Binding of bacteria to specific receptor sites on the blood-brain barrier
- Increased capillary permeability due to endothelial cell relaxation
- Passage of bacteria, leukocytes, albumin and other substances from the blood into the subarachnoid space
- Production of proinflammatory cytokines (IL-1, IL-6, TNF)





# Clinical picture of bacterial meningitis

- **Infectious syndrome** - fever, malaise, adynamia
- **Meningeal symptoms** (headache, vomiting, painful neck stiffness, hypersensitivity to stimuli, constipation)
- **Consciousness disturbance** (somnolence, stupor, coma, confusional-delirious state)
- Presence of meningeal signs



- The clinical picture bacterial meningitis includes:

Infective sy

Meningeal sy

Neurological sy

## Symptoms of Meningitis



**Fever.**



**Headache.**



**Stiff neck.**



**Sensitivity to light  
(photophobia).**



**Nausea,  
vomiting.**



**Confusion/altered  
mental state.**

## Complications of bacterial meningitis

- Cranial nerve damage (III, IV, VI, VII, VIII)
- Seizures
- Localized inflammation of the brain parenchyma
- Central motor neuron damage
- CNS circulatory disorders (hydrocephalus)
- Cardiovascular disorders
- Acute respiratory failure

# Diagnosis of bacterial meningitis

- CSF is cloudy or turbid
- Large number of cellular elements (several hundred per mm<sup>3</sup> and 90% are polymorphonuclear)
- Elevated proteinuria - usually greater than 2.2 g/l
- Reduced glycouria - sometimes unmeasurable
- Elevated CRP, lactate, LDH
- Cerebrospinal fluid culture

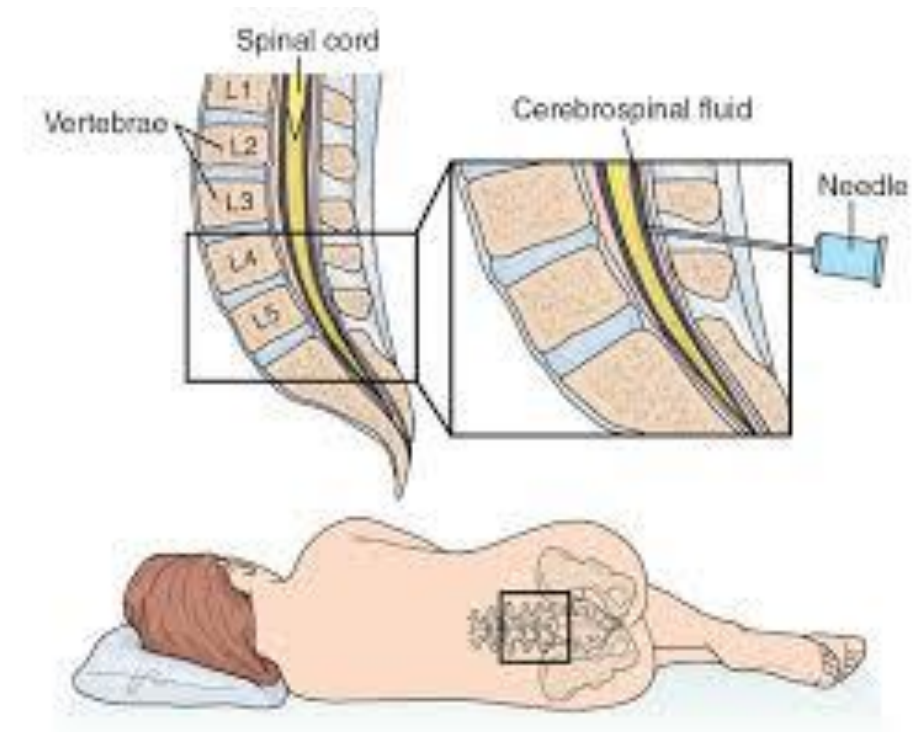
## Lumbar puncture

- An imaginary line connecting the iliac crests of the pelvic bones
- L 3 and 4 intervertebral space - the first space below/above that line



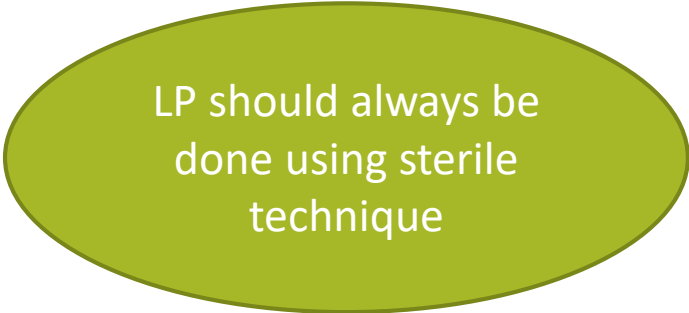
# CSF Sampling

- Tube 1 - Cellular Elements
- Tube 2 - CSF Biochemistry (Protein CSF and Glucosae in CSF)
- Tube 3 - CSF Culture
- Tube 4 - CSF PCR



## Complications of lumbar puncture

- Hematoma
  - **post-LP headache**
  - Intracranial hypertension
  - Brain herniation
  - Infection
- 
- **Contraindication**
    - Skin or deep tissue infection
    - Significant coagulation problem



LP should always be  
done using sterile  
technique

# Diagnosis based on CSF findings

	Color CSF	Cells	Glucose	Proteins
Normal	transparent, clear	<5 (lymphocytes)	1/2-2/3 serum glycemia	0.15 to 0.4 g/L
Bacterial meningitis	cloudy, purulent	>100 neutrophils	low	elevated >2 g/L
Viral meningitis	transparent, clear	Increased lymphocyte count	normal	mildly elevated
TB meningitis	transparent, clear, opalescent	Increased lymphocyte count	low	elevated (>1g/L)

# Treatment of bacterial meningitis

- Antimicrobial therapy
- Anti-inflammatory
- Antiedemaous therapy
- Symptomatic therapy
- Vital function monitoring



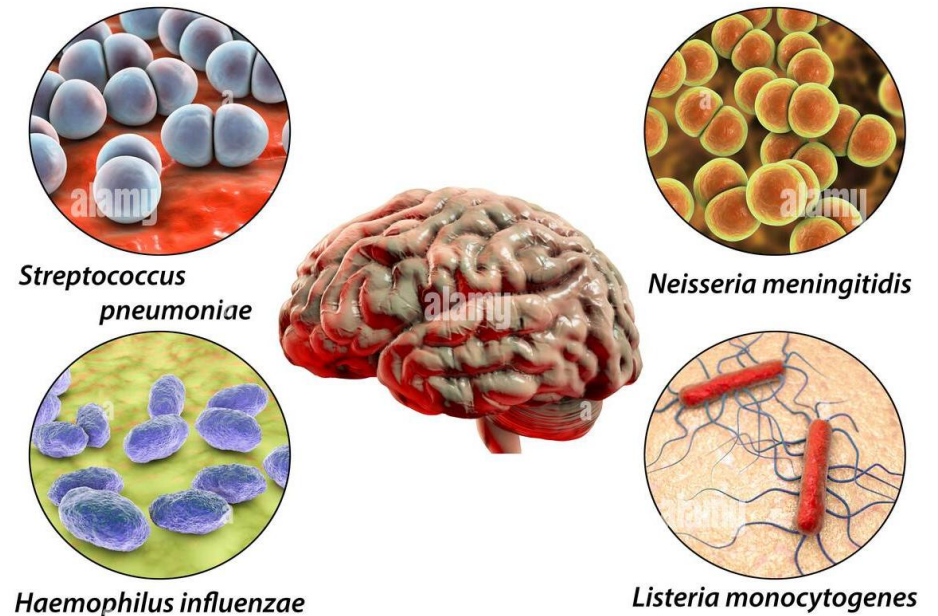
## Treatment of bacterial meningitis

- Use of corticosteroids, dexamethasone, significantly reduces the inflammatory response (improves the outcome of meningitis and reduces neurological sequelae)
- Especially in patients with *H. influenzae*, *S. pneumoniae* and *M. tuberculosis*
- Administered half an hour before the first dose of antibiotics and given for 4 days, as it can reduce the penetration of antibiotics into the cerebrospinal fluid



# Treatment of bacterial meningitis

- Anti-inflammatory - dexazone 0.6-0.8 mg/kg every 6 hours, ibuprofen, pentoxifylline
- Anti-edematous - mannitol, furosemide, dexazone
- Symptomatic - treatment of convulsions (lorazepam or diazepam, midazolam, phenobarbitone), antipyretics
- Control of vital functions (in severe patients with convulsions and impending respiratory failure)



# Treatment of bacterial meningitis

**Table 3. Recommendations for antimicrobial therapy in adult patients with presumptive pathogen identification by positive Gram stain.**

Microorganism	Recommended therapy	Alternative therapies
<i>Streptococcus pneumoniae</i>	Vancomycin plus a third-generation cephalosporin <sup>a,b</sup>	Meropenem (C-III), fluoroquinolone <sup>c</sup> (B-II)
<i>Neisseria meningitidis</i>	Third-generation cephalosporin <sup>a</sup>	Penicillin G, ampicillin, chloramphenicol, fluoroquinolone, aztreonam
<i>Listeria monocytogenes</i>	Ampicillin <sup>d</sup> or penicillin G <sup>d</sup>	Trimethoprim-sulfamethoxazole, meropenem (B-III)
<i>Streptococcus agalactiae</i>	Ampicillin <sup>d</sup> or penicillin G <sup>d</sup>	Third-generation cephalosporin <sup>a</sup> (B-III)
<i>Haemophilus influenzae</i>	Third-generation cephalosporin <sup>a</sup> (A-I)	Chloramphenicol, cefepime (A-I), meropenem (A-I), fluoroquinolone
<i>Escherichia coli</i>	Third-generation cephalosporin <sup>a</sup> (A-II)	Cefepime, meropenem, aztreonam, fluoroquinolone, trimethoprim-sulfamethoxazole

**Table 4. Recommendations for empirical antimicrobial therapy for purulent meningitis based on patient age and specific predisposing condition (A-III).**

Predisposing factor	Common bacterial pathogens	Antimicrobial therapy
<b>Age</b>		
<1 month	<i>Streptococcus agalactiae</i> , <i>Escherichia coli</i> , <i>Listeria monocytogenes</i> , <i>Klebsiella</i> species	Ampicillin plus cefotaxime or ampicillin plus an aminoglycoside
1–23 months	<i>Streptococcus pneumoniae</i> , <i>Neisseria meningitidis</i> , <i>S. agalactiae</i> , <i>Haemophilus influenzae</i> , <i>E. coli</i>	Vancomycin plus a third-generation cephalosporin <sup>a,b</sup>
2–50 years	<i>N. meningitidis</i> , <i>S. pneumoniae</i>	Vancomycin plus a third-generation cephalosporin <sup>a,b</sup>
>50 years	<i>S. pneumoniae</i> , <i>N. meningitidis</i> , <i>L. monocytogenes</i> , aerobic gram-negative bacilli	Vancomycin plus ampicillin plus a third-generation cephalosporin <sup>a,b</sup>
<b>Head trauma</b>		
Basilar skull fracture	<i>S. pneumoniae</i> , <i>H. influenzae</i> , group A $\beta$ -hemolytic streptococci	Vancomycin plus a third-generation cephalosporin <sup>a</sup>
Penetrating trauma	<i>Staphylococcus aureus</i> , coagulase-negative staphylococci (especially <i>Staphylococcus epidermidis</i> ), aerobic gram-negative bacilli (including <i>Pseudomonas aeruginosa</i> )	Vancomycin plus cefepime, vancomycin plus ceftazidime, or vancomycin plus meropenem
Postneurosurgery	Aerobic gram-negative bacilli (including <i>P. aeruginosa</i> ), <i>S. aureus</i> , coagulase-negative staphylococci (especially <i>S. epidermidis</i> )	Vancomycin plus cefepime, vancomycin plus ceftazidime, or vancomycin plus meropenem
CSF shunt	Coagulase-negative staphylococci (especially <i>S. epidermidis</i> ), <i>S. aureus</i> , aerobic gram-negative bacilli (including <i>P. aeruginosa</i> ), <i>Propionibacterium acnes</i>	Vancomycin plus cefepime, <sup>c</sup> vancomycin plus ceftazidime, <sup>c</sup> or vancomycin plus meropenem <sup>c</sup>

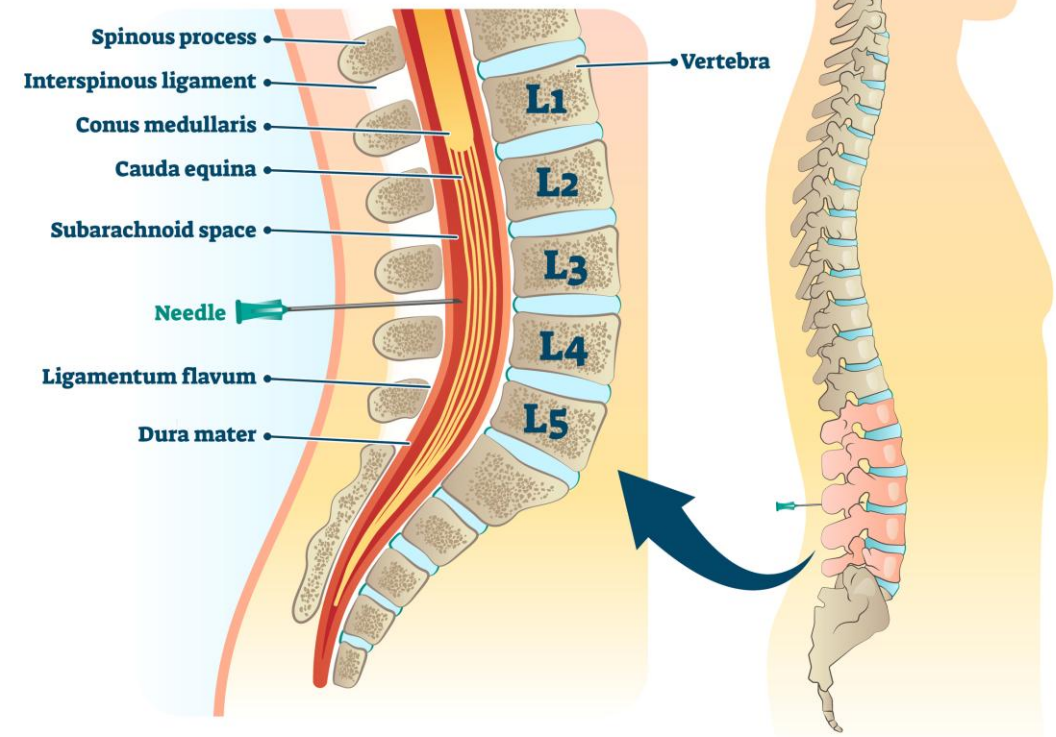
# Treatment of bacterial meningitis

**Table 8. Duration of antimicrobial therapy for bacterial meningitis based on isolated pathogen (A-III).**

Microorganism	Duration of therapy, days
<i>Neisseria meningitidis</i>	7
<i>Haemophilus influenzae</i>	7
<i>Streptococcus pneumoniae</i>	10–14
<i>Streptococcus agalactiae</i>	14–21
Aerobic gram-negative bacilli <sup>a</sup>	21
<i>Listeria monocytogenes</i>	≥21

<sup>a</sup> Duration in the neonate is 2 weeks beyond the first sterile CSF culture or ≥3 weeks, whichever is longer.

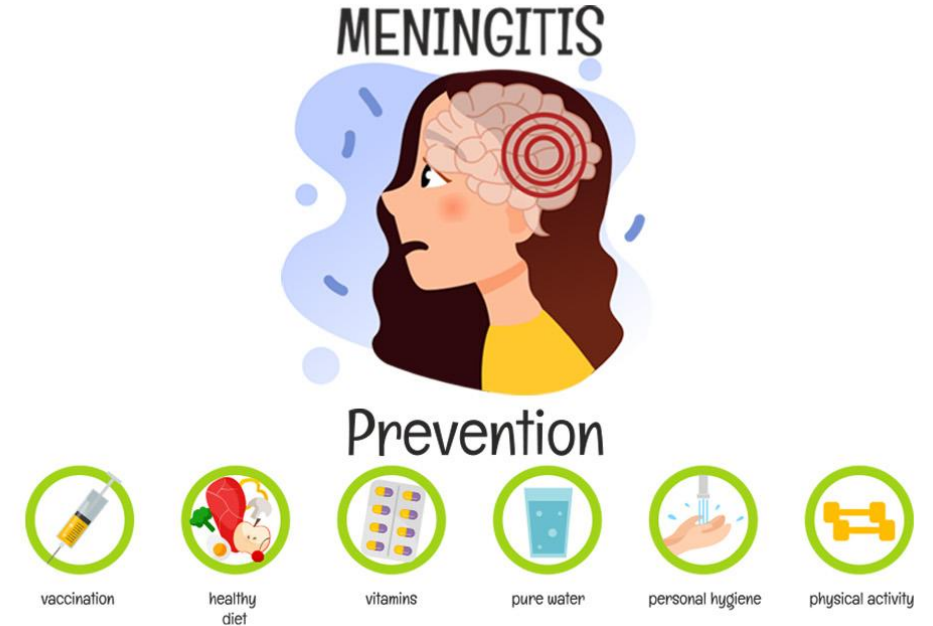
## LUMBAR PUNCTURE





# Prevention of bacterial meningitis

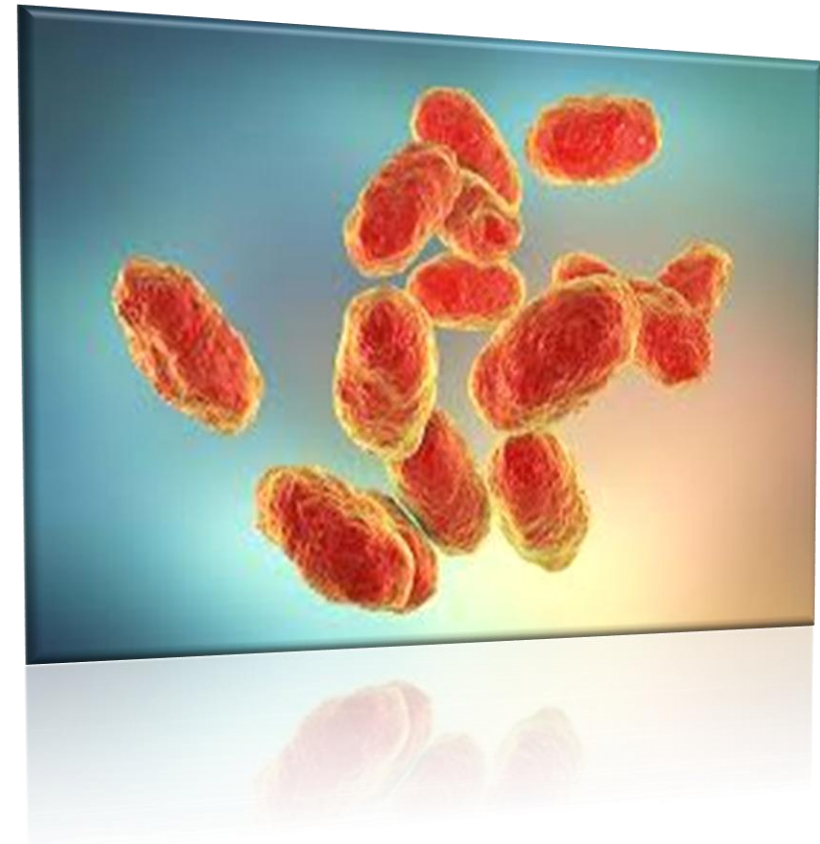
- Chemoprophylaxis *H. influenzae* b
- Rifampicin (20 mg/kg 4 days)
- Immunoprophylaxis *H. influenzae* b
- Chemoprophylaxis of meningococcal disease:
  - Rifampicin 600mg every 12 hours, and for children 10 mg/kg 2 days or
  - Ceftriaxone 250 mg and for children 125 mg in a single dose
- Immunoprophylaxis - vaccination





# Haemophilus meningitis

- Often part of the normal flora of the upper respiratory tract
- Transmitted by respiratory droplets or direct contact with secretions
- Meningitis is caused by capsular type b
- Primarily causes illness in children under 3 years of age
- If isolated in adults, it suggests the presence of sinusitis, otitis media, alcoholism, skull fracture with cerebrospinal fluid leak, decreased spleen function, and hypogammaglobulinemia



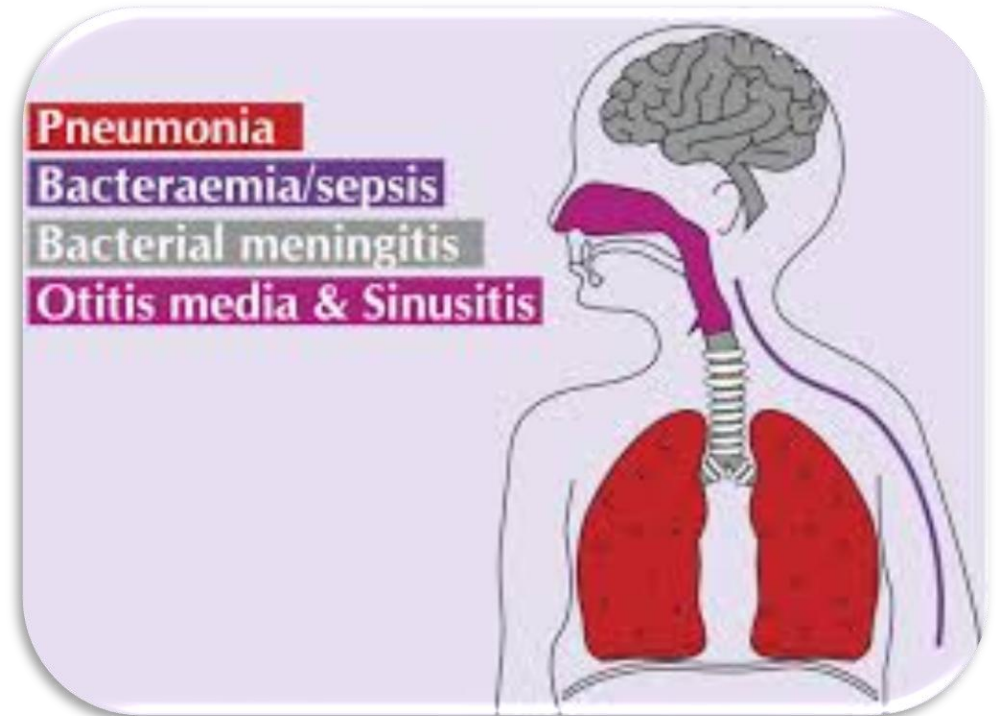
# Haemophilus meningitis

- The disease develops gradually with signs of respiratory disease
- Convulsions are common, cranial nerve VIII is often involved
- Subdural effusions and syndrome of inappropriate ADH secretion
- Cefotaxime or ceftriaxone 10-14 days



# Pneumococcal meningitis

- Caused by *S. pneumoniae*, a gram-positive cocci, colonizes the nasopharynx
- The most common cause of meningitis, incidence is 47%, with a mortality rate of 19-26%
- **Caused by:**
  - hematogenous
  - direct spread from the sinuses or inner ear (otogenic)



# Predisposing factors

- Skull base fracture with CSF protrusion
- Patients with hyposplenism or splenectomy
- Hypogammaglobulinemia, multiple myeloma
- Long-term corticosteroid therapy
- Diabetes mellitus, renal failure, alcoholism, malnutrition, and chronic liver disease



# Pneumococcal meningitis

- Predisposition to the onset of the disease
- Onset is abrupt with stiff neck, headache, convulsions and impaired consciousness
- 3rd generation cephalosporins, Vancomycin
- More common sequelae

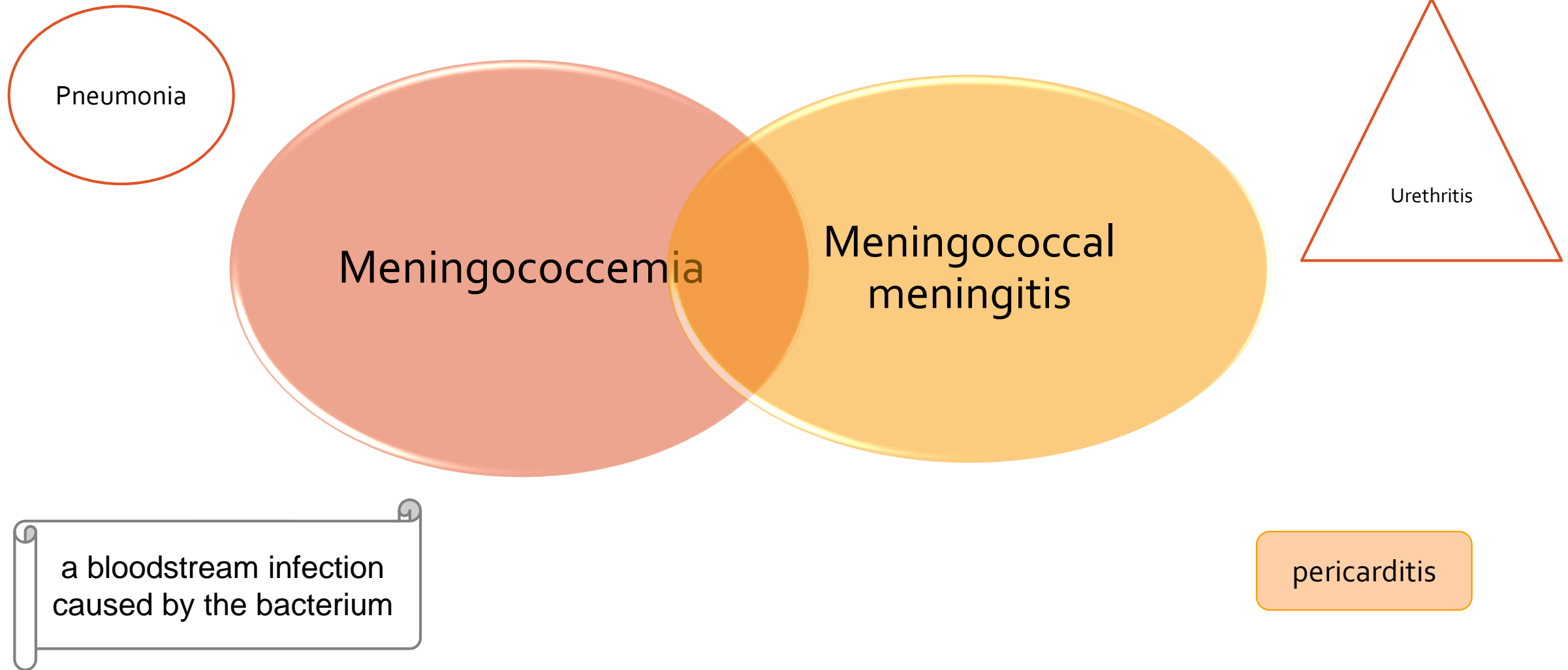


# Meningococcal infection

- Meningitis and bloodstream infections are the two most common types of meningococcal infections
- Both are serious and can be deadly in a matter of hours
- Symptoms of meningococcal disease can first appear as a flu-like illness and rapidly worsen
- Seek medical attention immediately for symptoms of meningococcal disease



# Meningococcal infection



# Etiology

- Most patients with meningococcal meningitis, caused by the gram-negative diplococcus **Neisseria meningitidis**, recover completely if appropriate antibiotic therapy is introduced promptly
- There are at least 12 serotypes based on unique capsular polysaccharides of N meningitidis, with serotypes A, B, C, W, X, and Y responsible for the majority of meningococcal infections
- Serotypes A and C are the main serotypes responsible for meningococcal disease in **Africa**
- Serotypes B, C, and Y are the main serotypes causing disease in **Europe**, the **United States**, and **Canada**



# Meningococcal sepsis

- 20-100% mortality
- petechiae, bruising, disseminated intravascular coagulation (DIC), septic shock
- bacterial endotoxin causes increased capillary permeability,
- decreased blood flow,
- i.v. thrombosis leads to decreased coagulation factors,
- hemorrhage (Waterhouse Friderichsen syndrome),
- metabolic acidosis, hypoxia, necrosis.











- Recent reports indicate a concerning uptick in cases involving non-vaccine serogroup X within Ghana's meningitis belt
- This shift underscores the importance of ongoing surveillance efforts to monitor changes in serogroup distribution and inform vaccination strategies to address emerging serogroups

Areas with frequent epidemics of meningococcal disease. This is known as the meningitis belt of Africa; visitors to these locales may benefit from meningitis vaccine. *Image courtesy of CDC.*

# Meningococcal meningitis

- The CSF is cloudy or turbid
- A large number of cellular elements (>hundreds per mm, 90% polymorphonuclear)
- Proteinorrhagia elevated (usually over 2.2g/L)
- Glycorrhagia decreased

## Therapy

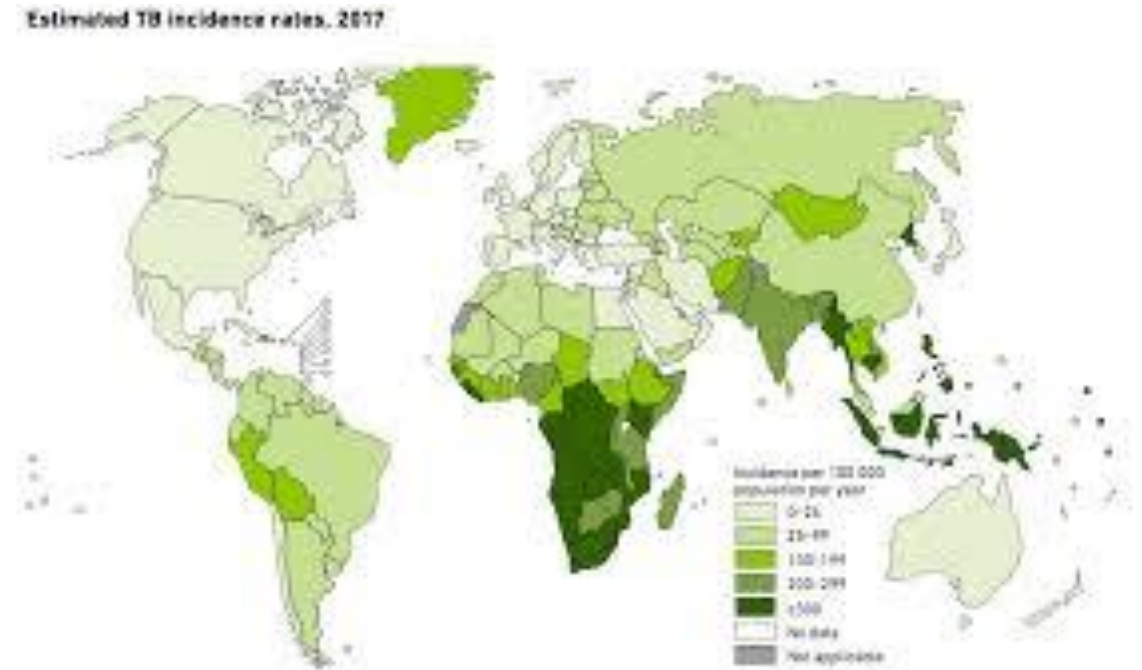
- Penicillin G (250,000 IU/kg) every 4 hours and for adults 24 million IU/day, 7-10 days
- Ceftriaxone, cefotaxime in case of penicillin allergy
- Chloramphenicol
- Treatment of coagulopathy - fresh frozen plasma 20 mL/kg over 20 minutes, cryoprecipitates, Tr
- Replacement of antithrombin III or recombinant activated protein C

# Tuberculous meningitis


- It is a chronic inflammation of the soft meninges most often caused by the human strain of the tubercle bacillus
- *M. tuberculosis* is an aerobic, acid-fast rod. It grows slowly on nutrient media, and multiplication takes 15-20 hours. It is cultivated on liquid or solid Lowenstein medium, where colonies become visible after 4-6 weeks

# Epidemiology

- In recent years, the incidence of extrapulmonary tuberculosis has increased due to the HIV pandemic, increased use of cytostatics and corticosteroids, which increases the risk of reactivation of latent tuberculosis.
- Risk factors for the development of TB meningitis include poor socioeconomic conditions, malnutrition, age and genetic factors



# Pathogenesis of TBC meningitis



Hematogenous  
dissemination

Tuberculosis foci



## Pathogenesis of TB meningitis

- It occurs by hematogenous dissemination of microorganisms from some extraneural tuberculous foci, which may be active but are often clinically inapparent (occurring by previous hematogenous dissemination, during the pre-allergic phase of pulmonary primary infection).
- Activation of tuberculous foci in the nervous tissue and on the meninges when the body's defenses are reduced.
- Inflammatory exudate is most pronounced at the base of the brain, vasculitis with thrombosis and ischemic cerebral infarction, obstructive or communicating hydrocephalus

First, prodromal stage – gradual onset, nonspecific symptoms, lasts 2-3 weeks

Second stage – symptoms and signs of meningitis, damage to cranial nerves III, IV, VI and VII – ptosis, strabismus, anisocoria, facial paralysis (basilar signs)

Third stage – impaired consciousness, signs of brainstem dysfunction, decerebrate rigidity, convulsions, multiple cranial nerve lesions occur

# Complication

- In untreated patients, death most often occurs between the 4th and 6th week of the disease
- Hydrocephalus – occurs in 30-80% of patients
- Visual and hearing impairment
- Hemiparesis
- Thromboses of the veins of the extremities
- Cardiocirculatory and respiratory failure

# Diagnosis of TB meningitis

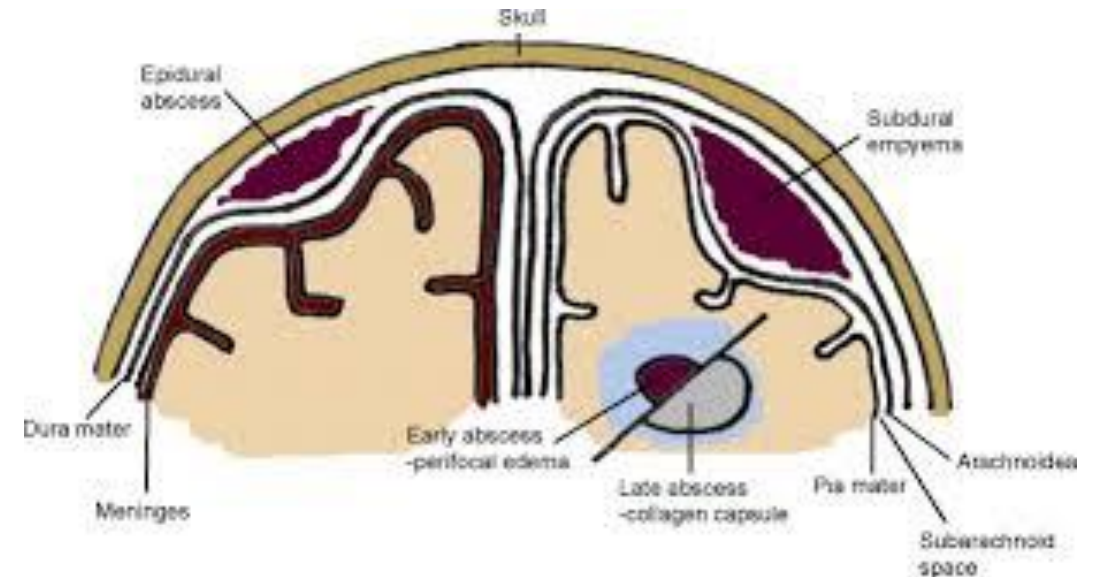
- Clinical picture
- Isolation of Koch's bacillus by culture of CSF on Lowenstein's medium (positive in less than 50%)-6 weeks! (repeated LP!)
- CSF is clear or opalescent, 100-500 cells per mm, proteinuria of 1-5g/L, glycorrhagia is reduced, lymphocytes dominate
- PCR in CSF (method of choice)!!!!
- Neuroradiological examinations

## Treatment

- Simultaneous administration of multiple ATLs due to:
  - naturally resistant strains,
  - prevention of secondary resistance
  - achieving a synergistic effect.
- Intermittent regimen consisting of an initial, intensive phase when ATL therapy is administered daily for 2 months and an intermittent, pulse phase when the drugs are administered twice a week for 7 months

# Focal bacterial infections in the CNS

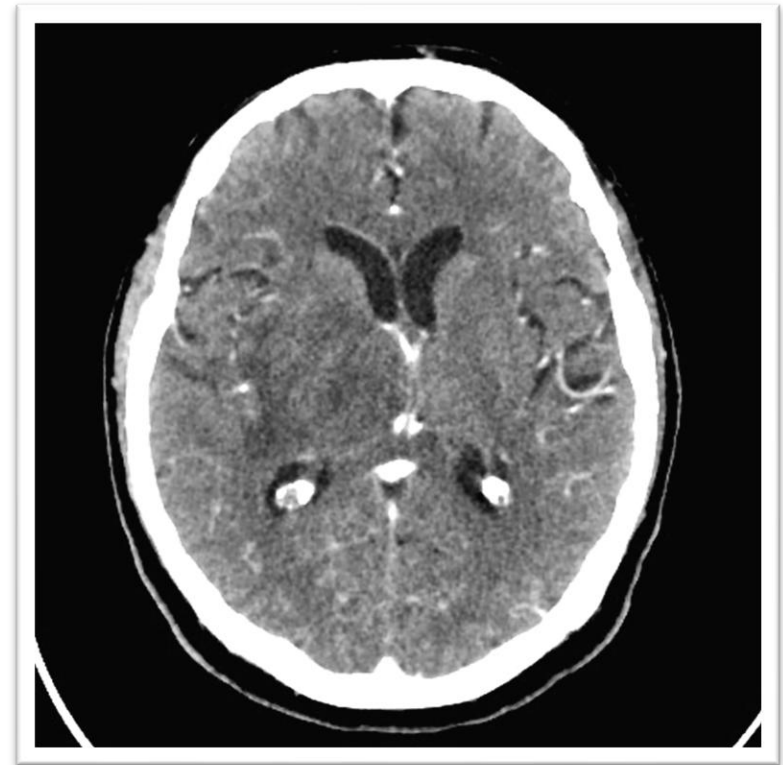
- Focal infections are limited areas of inflammation or suppuration.
- **They can be localized in the brain parenchyma and spinal cord.**
- They arise as secondary diseases due to **hematogenous dissemination** of pathogens from an existing focus of infection, during bacteremia or sepsis.
- **The pathogens can be introduced into the CNS directly, through injuries or surgical interventions**

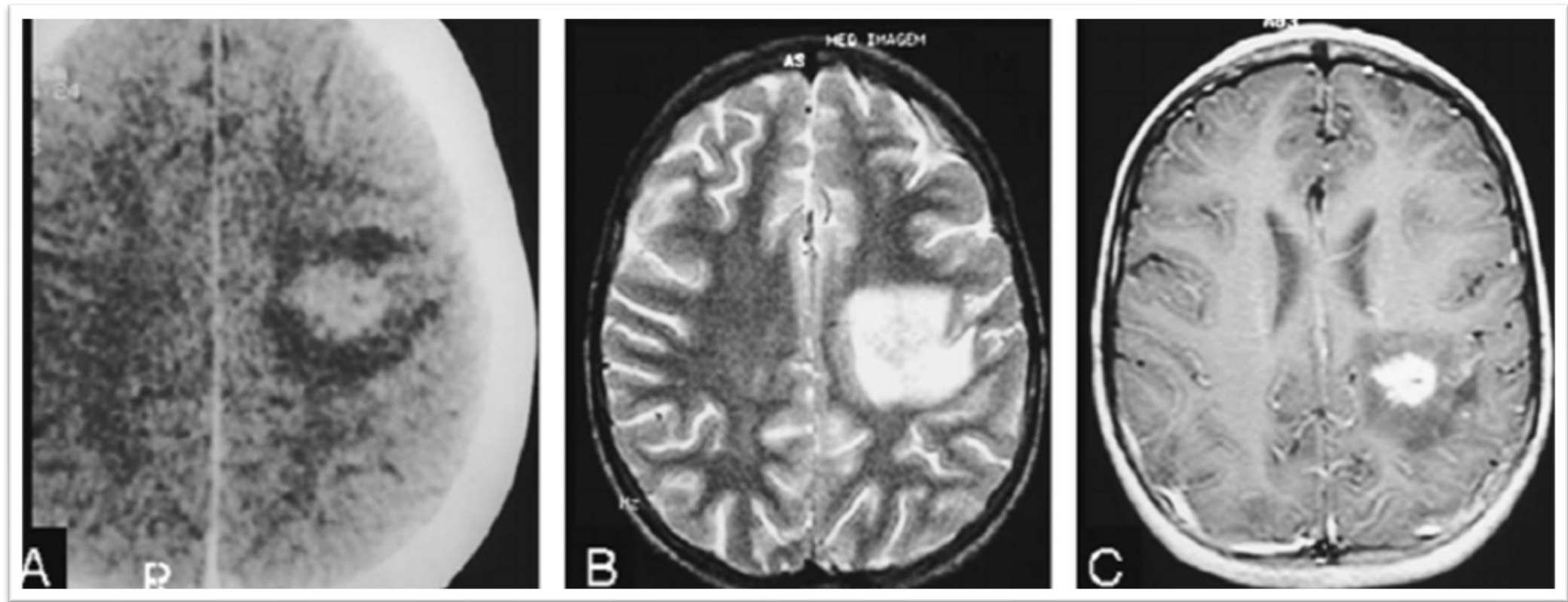




# Cerebritis and brain abscess

- Cerebritis is an early stage in the development of a focal infection in the CNS, which can end with the formation of a brain abscess.
- The clinical significance of cerebritis lies in the fact that timely DG and adequate therapy can lead to complete recovery, otherwise a brain abscess may form, requiring surgical treatment.

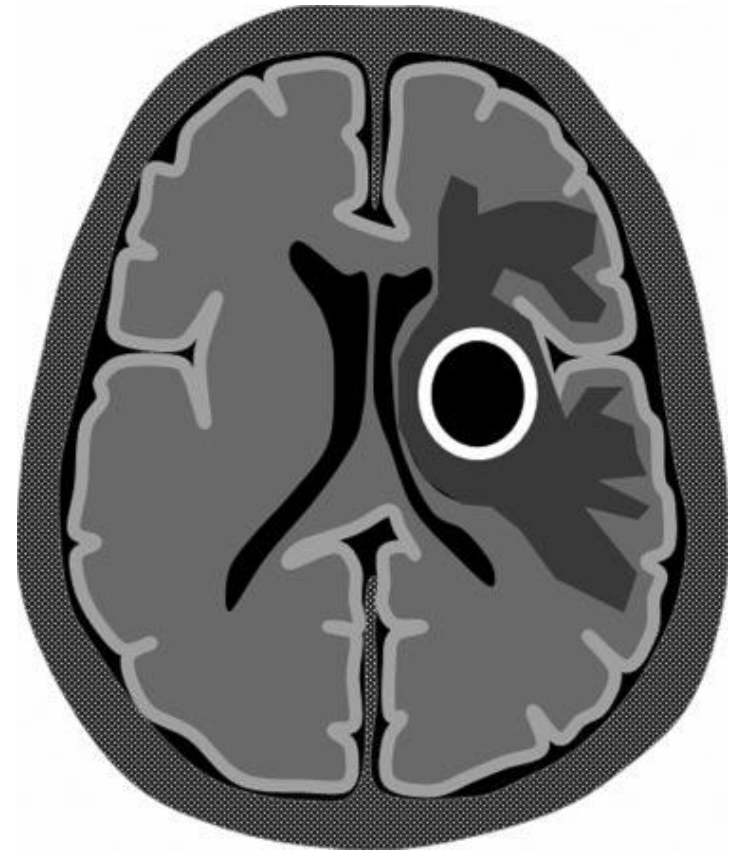




Early cerebritis phase in post-contrast CT (A), T2WI (B), and post-contrast T1WI (C).  
Source publication

# Cerebritis and brain abscess

- Bacterial invasion and colonization of the endocranium and spinal space
- **Early phase** lasts **1-3 days**, dominated by bacterial activity and neutrophil migration with destruction of brain cells
- **Late cerebritis phase** occurs from **4-9 days**, when edema, destruction of brain tissue and necrosis predominate
- **Capsule** formation around the focus in a period of **10-13 days**
- Brain abscess after **14 days**



# Localization of cerebritis and abscesses

- Frontal
- Temporal
- Parietal region of the brain
- In 5% of cases, localization is in the brainstem
- Multifocal arrangement in sepsis and endocarditis

# Diagnosis

- Clinical picture
- Laboratory indicators of inflammation
- Hemocultures
- Biochemical examination and culture of CSF
- CT
- Magnetic resonance imaging (MRI)
- X-ray of the paranasal cavities

## Treatment of cerebritis

- Ceftriaxone, **metronidazole** and vancomycin
- Ampicillin and chloramphenicol
- Meropenem
- Duration of therapy is 4-6 weeks
- If abscess formation occurs, neurosurgical treatment is performed
- Antiedema therapy
- Anticonvulsant



- Thank you

