CNS Infections

Dr. Hana Albulaihe

Consultant Neurologist

Objectives

- Types of meningitis
- Clinical manifestation
- Approach to meningitis
- Diagnosis
- Management
- Prevention

Introductin

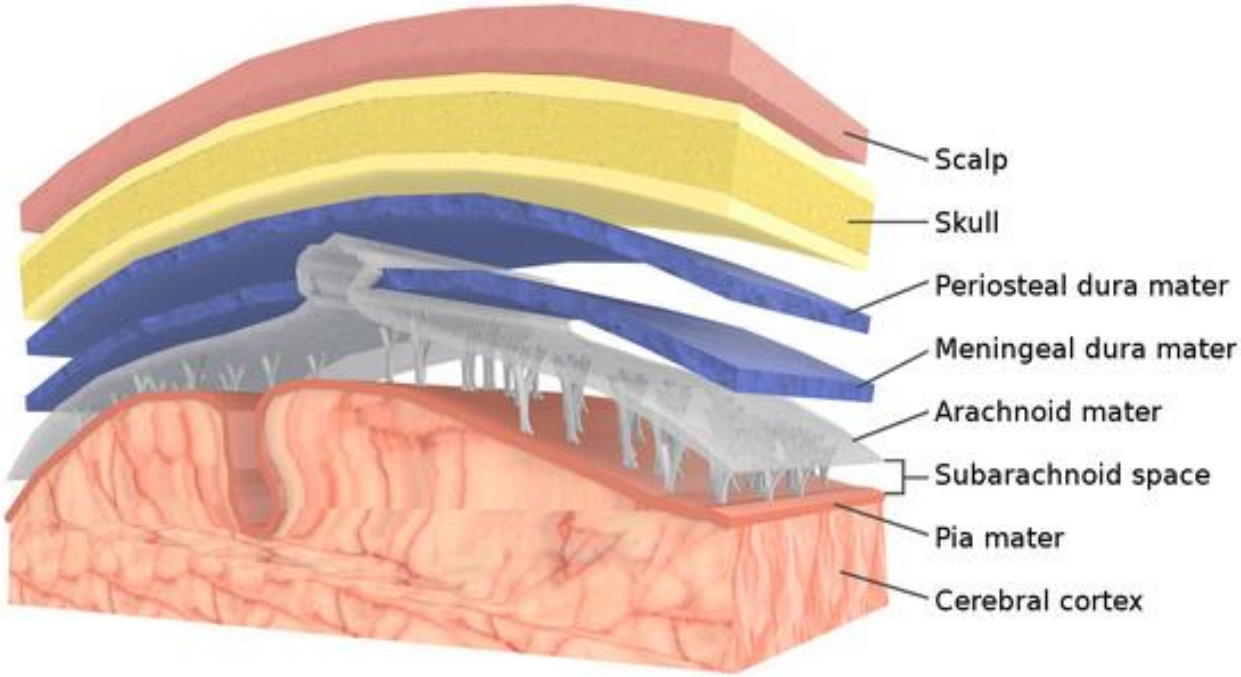
Infections of the central nervous system (CNS) can be divided into 2 broad categories:

- Primarily involving the meninges.
- Primarily confined to the parenchyma.

Introduction

- The meninges consist of three parts: the pia, arachnoid, and dura maters.

- Meningitis reflects infection of the arachnoid mater and the CSF in both the subarachnoid space and the cerebral ventricles.


Scalp
Skull
Periosteal dura mater
Meningeal dura mater
Arachnoid mater
Subarachnoid space
Pia mater
Cerebral cortex

Introduction

Meningitis can also be divided into the following 3 general categories:

- Bacterial (pyogenic)
- Viral
- Granulomatous
- Aseptic

Clinical Manifestations

The classic triad consists of fever, nuchal rigidity, and neck stiffness

Other symptoms include:

- Change in mental status
- Headache
- Photophobia
- Nausea, and/or vomiting

Clinical Manifestations

- Confusion
- Irritability
- Delirium
- Coma

Clinical Manifestations

- Symptoms can develop over several hours or over 1-2 days.
- Chronic symptoms lasting longer than 1 week suggest the presence of meningitis caused by certain viruses or by tuberculosis, syphilis, fungi (especially cryptococci), or carcinomatosis.
- Fever and changes in level of alertness or mental status are less common in partially treated meningitis than in untreated meningitis.

Clinical Manifestations

- 25% of patients have concomitant sinusitis or otitis that could predispose to *S pneumoniae* meningitis.

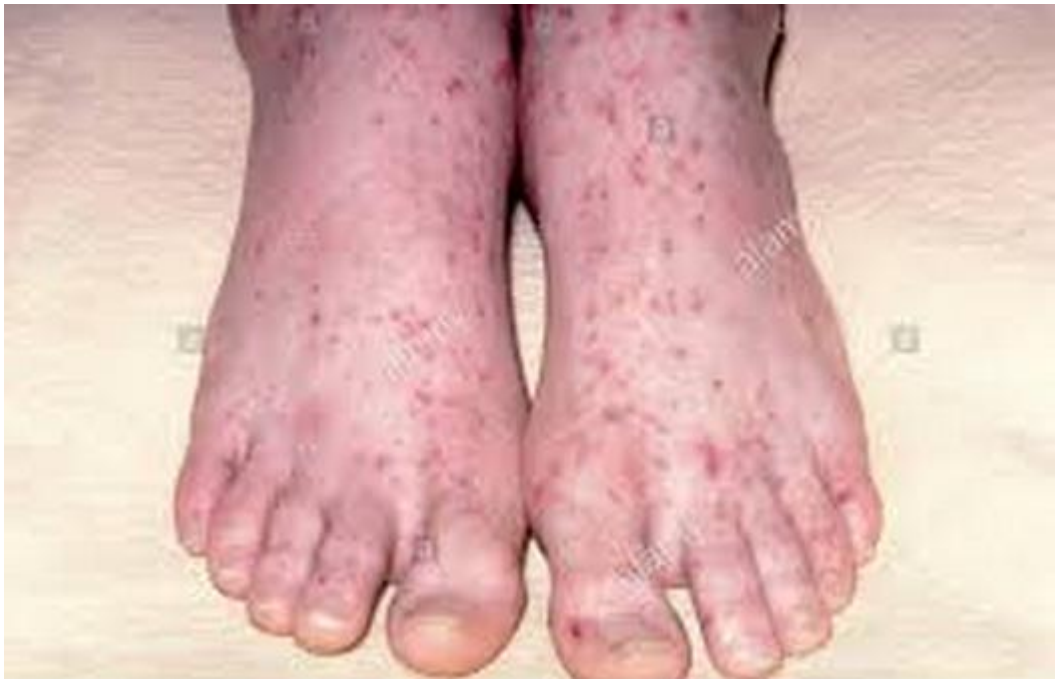
- Atypical presentation may be observed in certain groups like Elderly individuals with underlying comorbidities (lethargy, an absence of meningeal symptoms).

Clinical Manifestations

- A history of exposure to a patient with a similar illness is an important diagnostic clue. It may point to the presence of epidemic disease, such as viral or meningococcal meningitis.

Clinical Manifestations

- Certain bacteria, particularly *N. meningitidis*, can cause characteristic skin manifestations, such as petechiae and palpable purpura. Arthritis occurs in some patients with bacterial meningitis



Clinical manifestation

- History of sexual contact or high-risk behavior >>>>Herpes simplex virus (HSV) meningitis and HIV infection.

- Animal contacts >>>> Brucellosis may be transmitted through contact with infected farm animals The intake of unpasteurized milk and cheese also predisposes to brucellosis, as well as to *L monocytogenes* infection

Clinical Manifestations (examination)

- No focal neurologic deficits in the majority of cases.

Clinical Manifestations (examination)

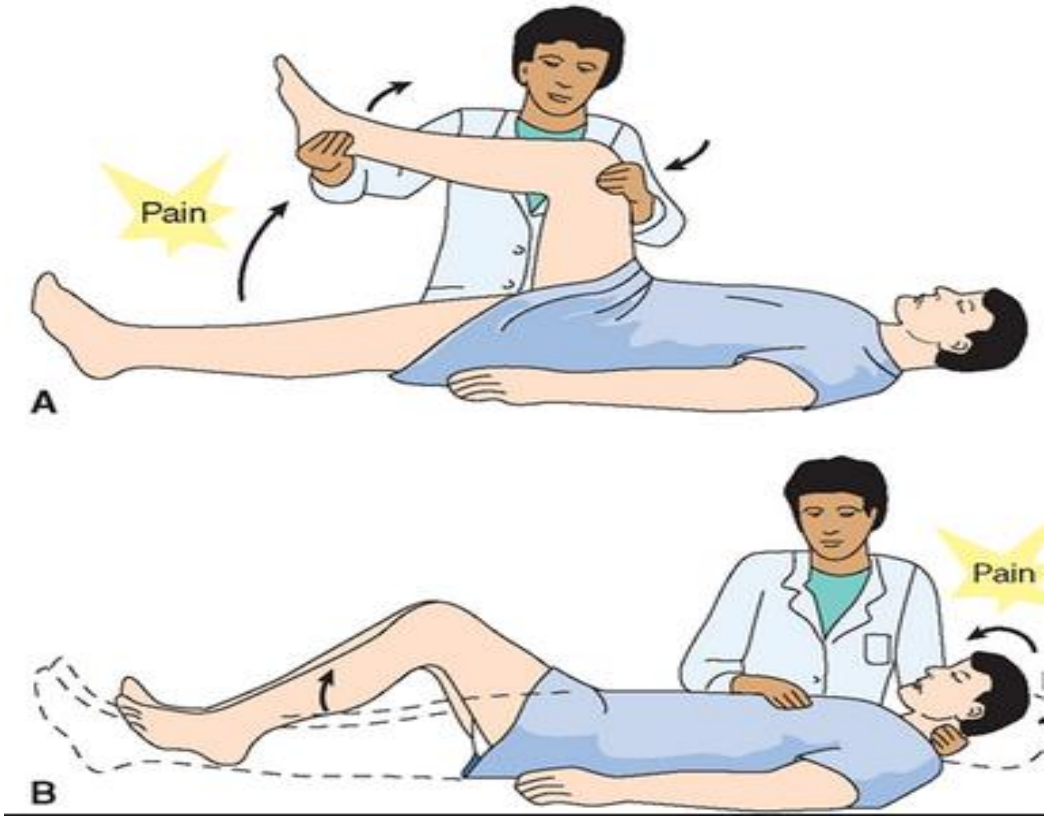
Focal neurologic signs

- Isolated cranial nerve abnormalities (principally of cranial nerves III, IV, VI, and VII).
- Focal cerebral signs as a result of ischemia from vascular inflammation and thrombosis.
- Papilledema

Clinical Manifestations (examination)

Examination for nuchal rigidity

- Brudzinski sign
- The Kernig sign


Pain
A
Pain
B

Clinical Manifestations (examination)

Systemic and extracranial findings

- Rash with pharyngitis and adenopathy may suggest a viral etiology (EBV, CMV, adenovirus, HIV). Macules and petechiae that rapidly evolve into purpura suggest meningococcal meningitis.
- Vesicular lesions in a dermatomal distribution suggest VZV meningitis.

Clinical Manifestations (examination)

Systemic and extracranial findings:

- Sinusitis or otitis suggests direct extension into the meninges, usually with *S pneumoniae* or, less often, *H influenzae.*
- Rhinorrhea or otorrhea suggests a cerebrospinal fluid (CSF) leak from a basilar skull fracture, with meningitis most commonly caused by *S pneumoniae.*

Clinical Manifestations (examination)

Systemic and extracranial findings:

- Endotoxic shock with vascular collapse is characteristic of severe *N meningitidis* (meningococcal) infection
- Nonblanching petechiae and cutaneous hemorrhages may be present in meningitis caused by *N meningitidis* (50%), *H influenzae, S pneumoniae*, or *S aureus*.
- Arthritis is seen with meningococcal infection.

Clinical manifestations chronic meningitis

Tuberculous meningitis

- The classic presentation is subacute over weeks.
- Patients generally have a prodrome consisting of fever of varying degrees, malaise, and intermittent headaches.
- Cranial nerve palsies (III, IV, V, VI, and VII) often develop, suggesting basilar meningeal involvement.
- Other symptoms include Lymphadenopathy, Papilledema and tuberculomas during funduscopy
- Meningismus

Syphilitic meningitis

- The median incubation period is 21 days
- Meningitis usually occurs during the primary or secondary stage of syphilis.
- Its presentation including headache, nausea, vomiting, and meningismus.
- Meningovascular syphilis occurs later in the course of untreated syphilis

Complications

Immediate complications of meningitis include the following:

- Septic shock and (DIC)
- Focal neurologic deficits (eg, cranial nerve palsy, hemiparesis)
- Coma
- Seizures
- Cerebral edema
- Septic arthritis
- Pericardial effusion
- Hemolytic anemia (*H influenzae*)

Complications

Delayed complications include the following:

- Decreased hearing or deafness
- Other cranial nerve dysfunctions
- Focal paralysis
- Subdural effusions
- Hydrocephalus
- Ataxia

Approach to meningitis

- Acute bacterial meningitis is a medical emergency, and delays in starting effective antimicrobial therapy result in increased morbidity and mortality.
- If the diagnosis of meningitis is strongly considered, a lumbar puncture should be performed.
- CSF analysis is the cornerstone of the diagnosis.

Approach to meningitis

- The decision to obtain a brain CT scan before LP should not delay the institution of antibiotic therapy
- Herniation can occur in patients with bacterial meningitis who have a normal brain CT scan.
- The most reliable clinical signs that indicate the risk of herniation include deteriorating level of consciousness, brainstem signs, and a very recent seizure.

Investigations

Blood Studies

- complete blood count (CBC) with differential
- Serum electrolytes
- Serum glucose
- Blood urea nitrogen (BUN) or creatinine and liver profile, to assess organ function and adjust antibiotic dosing
- A coagulation profile and platelet count

Investigations

- Cultures and Bacterial Antigen Testing:
- Blood -50% positive in meningitis caused by *H influenzae, S pneumoniae,*or *N meningitidis*
- Latex agglutination of blood, urine, and CSF for specific bacterial antigens
- PCR testing for diagnosis of HSV meningitis.
- Serum Procalcitonin Testing

Investigations

Lumbar puncture:

- Lowering of CSF pressure from withdrawal of CSF could precipitate herniation of the brain.
- It can occur as the consequence of severe cerebral edema or acute hydrocephalus. Clinically, this is manifested by an altered state of consciousness, abnormalities in pupil reflexes, and decerebrate or decorticate posturing.
- A screening CT scan of the head may be performed before LP to determine the risk of herniation.

Investigations

Indications for imaging before LP:

- Age ≥60 years
- Immunocompromise (ie, HIV infection/AIDS, immunosuppressive therapy, or transplantation)
- A history of CNS disease
- A history of seizure within 1 week before presentation
- Any abnormality on neurologic examination

Investigations

- **If LP is delayed** : blood cultures should be obtained and antimicrobial therapy should be administered empirically before the imaging study, followed as soon as possible by the LP.

- Prior administration of antimicrobials tends to have minimal effects on the chemistry and cytology findings but can reduce the yield of Gram stain and culture

Investigations
CSF analysis

Opening pressure:

- Typically elevated in patients with bacterial meningitis.

Gram stain:

- It should be obtained whenever there is suspicion of bacterial meningitis.
- The following findings may be seen:

●Gram-positive diplococci suggest pneumococcal infection

●Gram-negative diplococci suggest meningococcal infection

●Small pleomorphic gram-negative coccobacilli suggest *Haemophilus influenzae* infection

●Gram-positive rods and coccobacilli suggest listerial infection

Agent	Opening Pressure (mm H_2O)	WBC count (cells/µL)	Glucose (mg/dL)	Protein (mg/dL)
Bacterial meningitis	200-300	100-5000; >80% PMNs	< 40	>100
Viral meningitis	90-200	10-300; lymphocytes	Normal, reduced in LCM and mumps	Normal but may be slightly elevated
Tuberculous meningitis	180-300	100-500; lymphocytes	Reduced, < 40	Elevated, >100
Cryptococcal meningitis	180-300	10-200; lymphocytes	Reduced	50-200
Aseptic meningitis	90-200	10-300; lymphocytes	Normal	Normal but may be slightly elevated

Investigations
CSF analysis

CSF characteristics of acute bacterial meningitis

- neutrophilic pleocytosis (cell count usually ranging from hundreds to a few thousand, with >80% PMNs).
- In some (25-30%) cases of *Lmonocytogenes* meningitis, a lymphocytic predominance may occur.
- CSF glucose−to−blood glucose ratio of 0.4 or lower
- CSF WBC count of 500/µL or higher
- CSF lactate level of 31.53 mg/dL or higher

Investigations
CSF analysis

CSF characteristics of viral meningitis

- WBC count is 10-300/µL.
- Glucose is typically normal
- Protein concentration slightly elevated

Investigations
CSF analysis

CSF characteristics of tuberculous meningitis

- Lymphocytic pleocytosis
- Elevated protein level
- Low glucose level (< 40 mg/dL).
- PCR testing can provide a rapid diagnosis

Treatment of meningitis

Antibiotic regimen

- There are general requirements of antimicrobial therapy for bacterial meningitis

●Use of bactericidal drugs effective against the infecting organism

●Use of drugs that enter the CSF, since the blood-brain barrier prevents macromolecule entry into the CSF

Treatment of meningitis

Community-acquired meningitis

- Most common organisms: *S. pneumoniae*, *N. meningitidis*, and, less often, *H. influenzae* and group B *Streptococcus*

- Ceftriaxone – 2 g intravenously (IV) every 12 hours

  or

- Cefotaxime – 2 g IV every 4 to 6 hours

  plus

- Vancomycin – 15 to 20 mg/kg IV every 8 to 12 hours (not to exceed 2 g per dose or a total daily dose of 60 mg/kg; adjust dose to achieve vancomycin serum trough concentrations of 15 to 20 mcg/mL)

  plus

  In adults >50 years of age, ampicillin – 2 g IV every 4 hours

Treatment of meninigitis

Healthcare-associated meningitis

- following head trauma or neurosurgery, and in patients with internal or external ventricular drains
- Most common causative organisms gram-negative bacilli a, *S. aureus*, and coagulase-negative staphylococci

- Vancomycin – 15 to 20 mg/kg IV every 8 to 12 hours (not to exceed 2 g per dose or a total daily dose of 60 mg/kg; adjust dose to achieve vancomycin serum trough concentrations of 15 to 20 mcg/mL)

  plus

  One of the following:

  •Ceftazidime – 2 g IV every 8 hours

  or

  •Cefepime – 2 g IV every 8 hours

  or

  •Meropenem – 2 g IV every 8 hours

Management

- Most cases of viral meningitis are benign and self-limited.
- Usually patients need only supportive care and require no specific therapy.
- Herpes simplex meningitis should be treated with Acyclovir (10 mg/kg IV every 8 hours) for HSV-1 and HSV-2 meningitis.

Management

SUPPORTIVE CARE

- **Fluid management**

  Intravenous maintenance fluids

- **Reduction of intracranial pressure**

  Elevating the head of the bed to 30º

  Hyperventilation

  Oral administration of the hyperosmolar agent

Management

REPEAT CSF ANALYSIS

- When there is no evidence of improvement by 48 hours after the initiation of appropriate therapy

- Persistent fever for more than eight days without another explanation

Prevention

- Vaccination
- Chemoprophylaxis

Prevention

- Vaccination against *H influenzae* type B (Hib) is strongly recommended in susceptible individuals.

- Vaccination against *S pneumoniae* is also strongly encouraged for susceptible individuals, including people older than 65 years and individuals with chronic cardiopulmonary illnesses.

- Vaccination with quadrivalent meningococcal polysaccharide vaccine should be offered to all high-risk populations, including those who have underlying immune deficiencies, those who travel to hyperendemic areas and epidemic areas, and those who do laboratory work that involves routine exposure to *N meningitidis.*

Prevention

- In October 2014, the FDA approved the first meningococcal vaccine for serogroup B (Trumenba)

Prevention

Chemoprophylaxis

- After exposure to cases involving *H influenzae, N meningitidis,* or *S pneumoniae*, temporary nasopharyngeal carriage of the organism can occur.
- To eliminate nasopharyngeal carriage of Hib and to decrease invasion of colonized susceptible individuals, rifampin (20 mg/kg/day for 4 days) is given.

Prevention

- Prophylaxis is suggested for contacts of persons with meningococcal meningitis (eg, household contacts, daycare center members, close contacts in schools, and medical personnel performing mouth-to-mouth resuscitation).
- Rifampin (600 mg PO every 12 hours for 2 days) can rapidly eradicate the carrier stage, and the prophylaxis persists for as long as 10 weeks after treatment.
- Alternative agents for adults include ceftriaxone (250 mg IM in a single dose); this agent is also the safest choice in pregnant patients.

Prognosis

Mortality

- The mortality rate of bacterial meningitis increases with increasing age.
- The mortality rate was higher with healthcare-associated compared with community-acquired infection
- Higher with infection due to *S.pneumoniae* and *L. monocytogenes* compared with *N. meningitidis*

Thank you