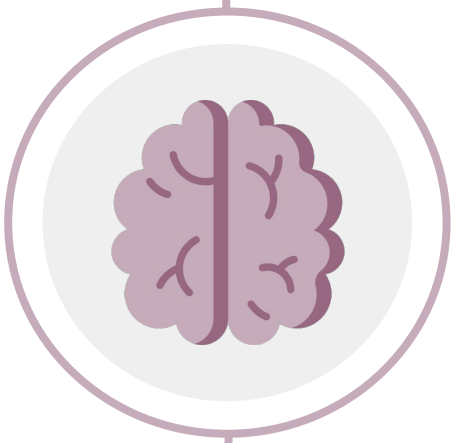
CNS infections



Objectives :

- ★ To be familiar with the most common CNS infections world-wide and in Saudi Arabia.
- ★ To understand the approach for meningitis treatment.
- ★ To be familiar with the different investigations for CNS infections.
- ★ To understand the prognosis and outcomes of the most common CNS infections.
- ★ Most important things to know about bacterial meningitis : complications + most common organism based on each group.

Editing file

Color index

Original text
Females slides
Males slides
Doctor's notes [438]
Doctor's notes [439]
Text book
Important
Golden notes
Extra

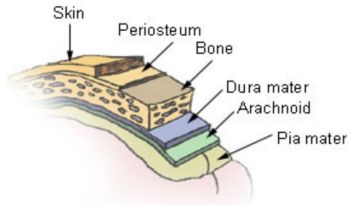
Introduction

◀ CNS infections :

- **By anatomy:**
  - Meningitis
  - Encephalitis
  - Abscess and empyema
- **By microbe:**
  - Viral
  - Bacterial
  - Fungal
  - Parasitic

◀ Definitions :

- **Meningitis:**
  - Inflammation of the leptomeninges (the covering of the brain)
  - **Leptomeninges:** the arachnoid and the pia mater (inner two layers)
  - Usually caused by bacteria
- **Encephalitis:**
  - Inflammation of the brain tissue itself
  - Caused by many types of organisms but mainly viruses
- **Meningoencephalitis** :
  - Inflammation of brain + meninges
- **Aseptic meningitis :**
  - Inflammation of meninges with sterile CSF
- **Acute vs chronic:**
  - Acute lasting < 4 weeks
  - Chronic lasting > 4 weeks



Meninges of the CNS

CSF is under the arachnoid mater (Subarachnoid space)

◀ Causes of meningitis :

Infectious	Non-infectious
Microorganisms reach the meninges either by **direct extension** from the ears, nasopharynx, cranial injury or congenital meningeal defect, or by **bloodstream spread.**	Non-infectious are inflammatory most of them, and the most important autoimmune.
Bacterial (**most important**); because it's a life threatening condition and more severe than viral	Aseptic meningitis Aseptic can be infectious (caused by viral) or noninfectious (caused by drugs), So you need to differentiate between bacterial and Aseptic: other causes.
Viral	Malignancy : breast and bronchial cancer, leukemia and lymphoma
Mycobacterial	Sarcoidosis
Brucella	Behcet disease , SLE
Fungal (especially cryptococcosis)	Mollaret's syndrome [1]

1- In which the recurrent meningitis is associated with epithelioid cells in the spinal fluid ('Mollaret' cells). Recent evidence suggests that this condition may be due to herpes simplex virus type 2 and is therefore infective after all.

Bacterial Meningitis

Definition

- **Meningitis:**[1] inflammation of the (leptomeninges meninges) pia mater and the arachnoid mater **(dura mater is usually spared)**, with suppuration of the CSF . Because CSF is located between the two inflamed layers of the meninges.
- Usually the organism (infection) comes from the CSF.
- Considered an infectious disease emergency that can cause significant patient morbidity and mortality.
- Morbidity and mortality depend on pathogen, patient's age and condition, and severity of acute illness.

◀ Risk factors for bacterial meningitis in adults :

- Living in groups or retirement homes
- Pulmonary disease
  - Concurrent pneumonia
  - COPD, Asthma
  - Smoking
- Chronic sinus or middle ear disease
- Immunodeficiency
  - HIV infection
  - Organ transplants
  - Severe anemia, asplenia
  - Alcoholism
  - Complement C3 deficiency
- Indwelling catheters or central venous lines, especially into CSF spaces
- Malignancy
  - Melanoma
  - Chronic lymphocytic leukemia
  - Chemotherapy
  - Metastatic cancers
- DM
- Autoimmune disease
  - RA , SLE
- Chronic renal disease dialysis, UT catheter, kidney infection or infected renal stones
- Chronic liver disease, cirrhosis
- Positive blood cultures
- Shock or hypotension
- Recurrent cranial neurosurgery

◀ S&S of Acute Bacterial Meningitis (ABM) :

Clinical symptoms [2]

- **Classic triad: fever, neck /nuchal stiffness and confusion.**
- **The usual presenting features are:**
  - **Severe Headache**
  - **High grade sudden fever**
  - **Vomiting**
  - Seizures, rash (Rash mostly with N.meningitidis)
  - Bulging fontanel in infants, sometimes with hydrocephalus.
  - Altered level consciousness and irritability
  - **Photophobia** (intolerance to light) and **Phonophobia** (intolerance to loud noises) can be specific to bacterial meningitis.
  - Progressive **drowsiness**, lateralizing signs and cranial nerve lesions indicates the existence of a complication, e.g. venous sinus thrombosis, severe cerebral oedema or cerebral abscess.

- **Adults > 65 :**
  - Usually have atypical presentation
  - Nonspecific confusion is common

Note: When accompanied by sepsis, presenting signs may evolve rapidly, with abrupt onset of obtundation due to cerebral oedema.

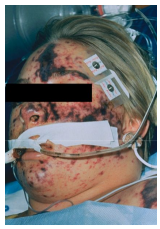
Absence of all 3 signs of the **classic triad** virtually eliminates a diagnosis of meningitis, we can't eliminate completely but bacterial meningitis would be unlikely, could be viral.

1- Sometimes it's difficult to differentiate between meningitis and encephalitis as they occur together usually. **Focal neurologic deficit and seizures are more common in encephalitis.**

2- we will focus more on clinical signs and symptoms. and patient who is older than 65 usually develop atypical presentation.

Bacterial Meningitis

◀ S&S of Acute Bacterial Meningitis (ABM) *cont.*



- **Vital signs: Fever**
- **Papilledema** (swelling of the optic nerve) due to increased ICP
- **Nuchal rigidity** = Neck stiffness
- Neurological deficit esp when there's pus.
- **Don't forget source of infection:** ears, sinuses, chest..etc
- Petechiae, ecchymosis[1] In pediatrics, esp with N.meningitidis
- Changes in mental status are more common in bacterial than viral meningitis
- Bacterial infections are more severe than viral

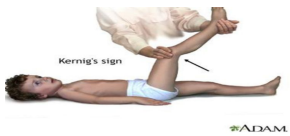
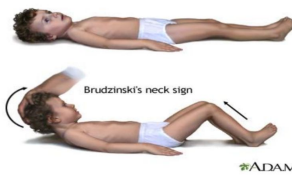
Focal neurologic signs

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

Clinical signs [2]

Table 22.20 Clinical clues in meningitis

Clinical feature	Possible cause
Petechial rash	Meningococcal infection
Skull fracture Ear disease Congenital CNS lesion	Pneumococcal infection
Immunocompromised patients	HIV opportunistic infection
Rash or pleuritic pain	Enterovirus infection
International travel	Malaria
Occupational (work in drains, canals, polluted water, recreational swimming) Clinical: myalgia, conjunctivitis, jaundice	Leptospirosis

Kernig's sign[3]	Brudzinski's neck sign
While patient is lying supine, with the hip and knee flexed to 90 degrees pain limits passive extension of the knee. Should perform on both sides.	Flexion of the neck causes involuntary flexion of the knee and hip.
	
The Kernig sign	Brudzinski sign

- In both tests you're stretching the meninges so the pt will flex the neck or the knee to minimize the stretch.
- These signs were useful in the past when they didn't have LP (Lumbar Puncture) and CT-scan etc. So they used to depend on these classic signs. However, these signs occur late in the course of the disease, 3 days or 1 week, because the meninges are very sensitive, so when we flex the hip,extending the knee or bending the neck we are actually stretching the meninges. and any stretch can trigger severe pain. They are rarely seen nowadays, usually happens in a pt with untreated bacterial meningitis for days or weeks but nowadays we put patients on antibiotics from the first day.
- They have **Low sensitivity, High specificity**

What's the most useful sign?

- **Jolt accentuation maneuver:** ask patient to rapidly rotate his or her head horizontally: Headache worsens, In healthy individuals it might be uncomfortable but a pt with meningitis will avoid doing it.
- **Sensitivity of 100%, specificity of 54% (Low, unlike kernig and Brudzinski signs),** positive likelihood ratio of 2.2, and negative likelihood ratio of 0 for the diagnosis of meningitis

1- In meningococcal septicaemia there is a non-blanching petechial and purpuric skin rash and signs of shock.
2- General physical examination is not that useful, we just want you to know some findings eg. focal deficit , hemiplegia. etc. It cannot diagnose meningitis, diagnosis is based on CSF study
3- Patient with spontaneous intracranial hypotension can have chronic headache and one of the treatments is subdural blood patch, this can cause irritation of the meninges usually at the lumbosacral area so they can have a +ve Kernig's sign

Bacterial Meningitis *cont.*

◀ Chronic Bacterial Meningitis

- **Tuberculous meningitis** (TBM) and **cryptococcal meningitis** commence typically with vague headache, lassitude, anorexia and vomiting.
- Acute meningitis can occur but is unusual.
- Meningitic signs often take some weeks to develop.
- Drowsiness, focal signs (e.g. diplopia, papilloedema, hemiparesis) and seizures are common. **Syphilis, sarcoidosis and Behçet's also cause chronic meningitis.**
- In some cases of chronic meningitis, an organism is never identified.

◀ Bacterial pathogens

Neonates	• **Group B Streptococci (MOST COMMON, and occurs ONLY in neonates) 49%** B=Babies • **Gram-negative bacilli (Escherichia coli** (2nd most common cause) **, Proteus)** • Others : Enterococci, Klebsiella, Enterobacter, Salmonella, Serratia and Listeria monocytogenes
Older infants and children	• **Neisseria meningitidis*** (subtypes B, C, Y, W) • **S. pneumoniae (Most common)** • M.tuberculosis **Less common** • H. influenzae (Less common than before)
Adults	• **Streptococcus pneumonia (MOST common)**.....37% • **Neisseria meningitidis** (subtypes B, C, Y, W) .....13% • **Listeria monocytogenes** ....10% • Other strept.species (7%), Gram negative (4%), H. influenzae (4%) • TB, Brucella (common in saudiarabia)

Keep in mind:

- Global emergence and prevalence of **Penicillin- Resistant Streptococcus pneumoniae**
- Dramatic Reduction in invasive Haemophilus influenzae disease secondary to use of conjugate Haemophilus Type B- vaccine.
- **Group B – Streptococci**: previously in neonate: **now emerging as disease of elderly**

1- Pneumococcal meningitis

- **The most common cause**
- **Highest mortality** 20 – 30%
- May be associated with other Focus:
  - Pneumonia, Otitis Media, Sinusitis
- Head Trauma & CSF Leak
- Splenectomy and Sickle cell disease
- Global emergence of Penicillin – Resistant

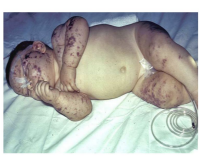
1- Same as adult, but in children has higher mortality and accompanied with complications.

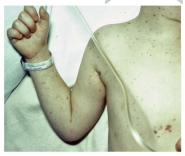
Bacterial Meningitis *cont.*

2- *Meningococcal meningitis and meningococcaemia

- **(Medical emergency)**
- Caused by Neisseria Meningitidis
- Fulminate meningococcemia with purpura:
  - Overwhelming sepsis, DIC
- **Classic: Meningitis with rash (Petechiae)** + Headache + Fever
- Meningitis without rash
- Mortality 3 - 10 %
- Lumbar puncture **should not be performed** if meningococcal sepsis is suspected because coning of the cerebellar tonsils may follow – the organism is confirmed by blood culture.

- **Treatment and prophylaxis:**
  - **Droplet Isolation:** 48h post Abx
  - **Treatment: Ceftriaxone or Pen G** 7 days
  - **Eradicate nasopharyngeal carriage:**
    - Household contact
    - Health care providers who examined patient closely
  - **Prophylaxis (Not done routinely):** Rifampin 600 mg for 2 d or Ciprofloxacin 500mg once or Ceftriaxone 125mg I.M once





Meningococcal meningitis and meningococcaemia: emergency treatment

Suspicion of meningococcal infection is a medical emergency requiring treatment immediately.

Clinical features:

- Petechial or nonspecific blotchy red rash
- Fever, headache, neck stiffness.

All these features may not be present – and meningococcal infection may sometimes begin like any apparently non-serious infection.

Immediate treatment for suspected meningococcal meningitis at first contact before transfer to hospital or investigation:

- Benzylpenicillin 1200 mg (adult dose) slow i.v. injection or intramuscularly
- Alternative if penicillin allergy – cefotaxime 1 g i.v.

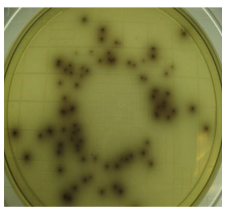
In meningitis, minutes count: delay is unacceptable. On arrival in hospital:

- Routine tests including blood cultures immediately
- Watch out for septicaemic shock.

Recall: Ceftriaxone is C.I in neonates, give cefotaxime instead.

3- Listeria Monocytogenes meningitis

- **Pathology:** It causes brain stem, cerebellum inflammation (Rhombencephalitis) and meningitis
- **Risk groups:**
  - Age <1y or >50y
  - Alcoholics
  - Pregnancy: up to 30%
  - Immunocompromised 70 %
- **Routes of transmission:**
  - **Mainly food borne:** survives refrigeration
    - linked to poultry, hotdogs, cold cuts, coleslaw, ice-cream
  - **Cheeses,** particularly soft cheeses, have been implicated in listeriosis outbreaks worldwide.
  - Transplacental /vertical
  - Cross contamination(nursery)
  - Inoculation(skin) farmers
  - Colo/ sigmoidoscopy → bacteremia / meningitis (up to 5% healthy: Normal flora)
  - Inform micro lab: special media **(Mueller-Hinton agar)**



Note: Whenever you see a pt with changing signals in brain stem and cerebellum MRI , think of Listeria.

- **Treatment:**
  - **Ampicillin** 2gm IV Q4h +/- Gentamicin 2mg/kg loading dose then 1.7mg/kg Q8h
  - **21 day** duration
  - Penicillin allergy patients: **TMP-SMX or Meropenem**

Bacterial Meningitis *cont.*

◀ Investigations:

How to manage a patient with meningitis?

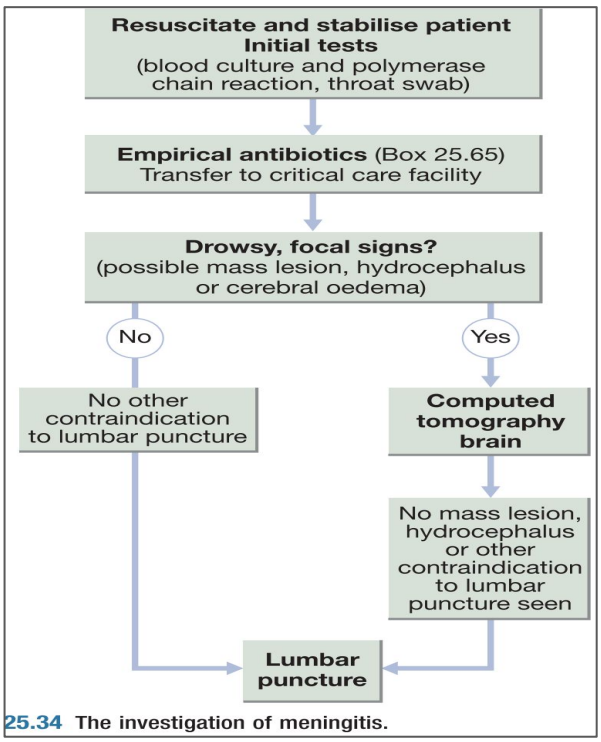
- **Step 1: Give empirical therapy**!! Whenever you suspect meningitis or encephalitis, start empirical therapy! (In real life the pt will be started on empirical therapy in the ER, before you see him)
- **Step 2: CT** (To exclude herniation, supratentorial tumor, bleeding, pus collection (Subdural empyema) before doing LP bc it may kill the pt). **NEVER do LP before CT.**
- **Step 3: LP**.
  - **Contraindications to LP:** Herniation, Infection at the site of LP (e.g. Cellulitis), bleeding disorders, Low platelet count <100, anticoagulants . If one of these contraindication is present you can delay LP but **NEVER delay the treatment**

1 Radiological

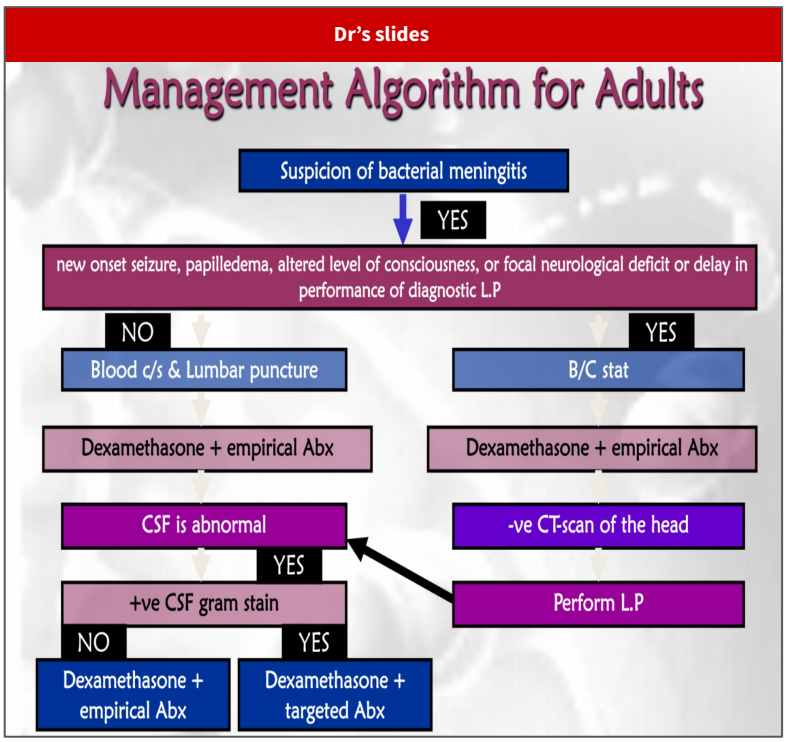
- **CXR** (To look for the source bc sometimes the pt may have pneumonia → Sepsis → Meningitis)
- **CT Head[1] Without contrast : Generally, patients with suspected meningitis require brain imaging before the LP, warning signs that mandate an image:**
  - Has altered consciousness
  - Has focal neurological deficits
  - Has seizures
  - Has papilledema [2] or cranial nerve palsies
  - Immunosuppressed, has undergone recent neurosurgery or has suffered a head injury.

2 Blood tests

- CBC, Creatinine, electrolytes: Na (to check kidney function for waterhouse-Friderichsen syndrome
- Blood Culture



25.34 The investigation of meningitis.



1- Initial test. But before it, start empirical treatment.

2- Swelling of optic disc due to elevated intracranial pressure, can present with loss of visual acuity due to enlargement of blind spot. Do fundoscopy, you will see edematous, poorly defined, prominent optic disc with blurry margins, widened blind spot and radial hemorrhage around the disc margin.

Bacterial Meningitis *cont.*

3 Lumbar puncture

- **Start empirical antibiotics on suspicion and don't wait for the results of LP!** If lumbar puncture is deferred or omitted, it is essential to take blood cultures and to start empirical treatment [4].
- **CSF analysis, remember to be careful:**
  - Increased ICP may increase risk of herniation Lowering of CSF pressure from withdrawal of CSF could precipitate herniation of the brain.
  - Cellulitis at area of lumbar puncture
  - Bleeding disorder

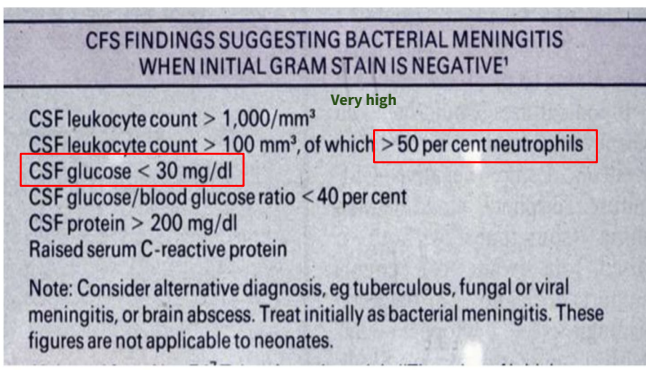
CSF analysis :

Tests from 1-6 are the standard tests, the rest are ordered based on suspicion. Although, in real life we ask for all of them.

1. **Appearance[1], opening pressure[2]**	2. **Cell count with differential**	3. **Glucose, protein**
4. **CSF appearance**	5. **Gram stain**	6. **Culture**
7. **TB AFB smear PCR and culture**	8. **Brucella serology and PCR** -Imp in our area-	9. **HSV PCR** -If you suspect encephalitis-
10. **Multiplex viral PCR** -for enterococcus-	11. **Cryptococcus antigen** -in DM and immunocompromised-	

***Any of these features is high likely for bacterial meningitis[3]:**
Low glucose <0.2 , High WBC >200 , Elevated PMN >1200 , Protein >2.2g

Females' slides	Typical CSF changes in viral, pyogenic and TB meningitis			
	Normal	Viral	Bacterial	Tuberculosis
Appearance	Crystal clear	Clear/turbid	Turbid/purulent	Turbid/viscous
Mononuclear cells	<5/mm^3	10-100/mm^3	<50/mm^3	100-300/mm^3
Polymorph cells	Nil	Nil	200-300/mm^3	0-200/mm^3
Protein	0.2-0.4 g/L	0.4-0.8 g/L	0.5-2.0 g/L	0.5-3.0 g/L
Glucose	⅔ - ½ blood glucose	> ½ blood glucose	< ½ blood glucose	< ½ blood glucose



- **Bacterial meningitis** the predominant cells will be neutrophils
- **Viral meningitis:** they will be lymphocytes.
- **Partially treated meningitis:** there will be elevated white cells (mainly neutrophils but may have elevated lymphocytes as well), but glucose and protein may be normal or near borderline (Can be confusing with viral meningitis).
- **How to differentiate between partially treated bacterial meningitis and viral meningitis?** By history (e.g. if the pt has visited a hospital recently and taken abx considered partially treated meningitis) or by gram stain, you may get positive results in partially treated meningitis
- **Protein:** can be high in other inflammatory causes such as MS. It is not specific.

No need to remember the numbers as they vary from reference to another, just understand the picture

1- If it's turbid it indicate most likely bacteria
2- Not useful in meningitis, but helpful in cases of idiopathic intracranial hyper/hypotension
3- these numbers can differ based on different resources, but take the general idea.
4- The treatment approach is to start broad spectrum empirical antibiotics, until culture result appear then you can adjust treatment accordingly.

Bacterial Meningitis Management [1]

◀ Bacterial Meningitis - Empiric Treatment (Gram stain Negative)

(no need to know the doses)

- Droplet precautions
- ABCs, vitals, IV, oxygen, monitored setting
- STAT antibiotics:
  - **Ceftriaxone** 2 gm **IV** Q12h
    - High CSF levels
  - **AND Vancomycin** 500-750 mg IV Q6h (for highly penicillin resistant pneumococcus)
  - **+/- Ampicillin** IV (if **Listeria** suspected) :
    - Age <3 months or > 50 yrs,
    - Immunosuppressed patient
  - **Metronidazole** (500 mg **IV** Q6h) :
    - If otitis media, sinusitis as source – anaerobes may be involved
  - **Dexamethasone (to suppress acute inflammation not used in chronic)** (0.15mg/kg IV Q6h) for 2-4 days:
    - 1st dose 15-20 min prior to or concomitant with 1st dose antibiotic to block TNF production
    - Continue only if S. pneumo is isolated
    - Reduces hearing loss and neurological sequelae
- Continue Abx for **7 days** (H. flu/N.men); **14 days** (S. pneumo); **21 days** (Listeria)
- Management of ↑ICT : mannitol, glycerine, acetazolamide

◀ Bacterial Meningitis - Empiric Treatment of unknown cause (Gram stain Negative)

- **Ceftriaxone and vancomycin should always be administered**

Comment	Recommended Treatment
Adults aged **18–50 years** with or without a typical meningococcal rash	• **Cefotaxime** 2g IV QID or • **Ceftriaxone** 2g IV Q12h (**High CSF levels)**
Patients in whom **highly penicillin resistant pneumococcus is suspected** , or in areas with a significant incidence of penicillin resistance in the community	As for (1) but add: • **Vancomycin** 500-750 mg IV Q6h or • Rifampicin 600 mg IV twice daily
Adults aged > 55 years and If **Listeria** suspected (brainstem signs, **immunosuppression**, diabetic, alcoholic)	As for (1) but add: • **Ampicillin** 2 g IV 6 times daily or • Co-trimoxazole 5 mg/kg IV daily in two divided doses
Patients with a clear history of anaphylaxis to **β-lactams**	• Chloramphenicol 25 mg/kg IV QID plus • Vancomycin 1 g IV twice daily
Adjunctive treatment (see pg7 management)	• **Dexamethasone** (to suppress acute inflammation not used in chronic**) (0.15mg/kg IV Q6h) for 2-4 days:**
- Management of ↑ICT : mannitol, glycerine, acetazolamide. - Tt of Seizures, pyrexia. - Treat shock, DIC if present. - Add Acyclovir for herpes Encephalitis. - Add amphotericin B or fluconazole for fungal infections.	

1- Early endotracheal intubation and mechanical ventilation protect the airway and may prevent the development of the acute respiratory distress syndrome.
Adverse prognostic features include: hypotensive shock, a rapidly developing rash, a haemorrhagic diathesis, multisystem failure and age over 60 years.

Bacterial Meningitis Management

Chemotherapy of bacterial meningitis when the cause is known

Pathogen	Regimen of choice	Alternative agents
Neisseria meningitidis	• **Benzylpenicillin** 2.4 g IV 6 times daily for 5–7 days	- **Cefuroxime**, **ampicillin** - **Chloramphenicol**[1]
Streptococcus pneumoniae (sensitive to β-lactams, MIC < 1 mg/L)	• **Cefotaxime** 2 g IV QID or • **Ceftriaxone** 2 g IV twice daily for 10–14 days	- **Chloramphenicol**[1]
Strep. pneumoniae (resistant to β-lactams)	As for sensitive strains but add: • **Vancomycin** 1 g IV twice daily or • **Rifampicin** 600 mg IV twice daily	- **Vancomycin** + **rifampicin**[1] - **Moxifloxacin** - **Gatifloxacin**
Haemophilus influenzae	• **Cefotaxime** 2 g IV QID or • **Ceftriaxone** 2 g IV twice daily for 10–14 days	- **Chloramphenicol**[1]
Listeria monocytogenes	• **Ampicillin** 2 g IV 6 times daily plus • **Gentamicin** 5 mg/kg IV daily	- **Ampicillin** 2 g IV 4-hourly plus - **Co-trimoxazole** 50 mg/kg daily in two divided doses
Streptococcus suis	• **Cefotaxime** 2 g IV 4 times daily or • **Ceftriaxone** 2 g IV twice daily for 10–14 days	- **Chloramphenicol**[1]

Prevention of meningitis

Vaccination

- Vaccinate all adults >65 years for S. pneumoniae.
- Vaccinate asplenic patients for S. pneumoniae, N. meningitidis, and H. influenzae (encapsulated organisms).
- Vaccinate immunocompromised patients for N. meningitidis.
- Vaccines are available for most meningococcal subgroups but not group B, which is one of the most common serogroups isolated in many countries.
- Prophylaxis (e.g., rifampin or ceftriaxone)—for all close contacts of patients with meningococcus.

25.67 Chemoprophylaxis following meningococcal exposure

Close contacts warranting chemoprophylaxis

- Household contacts (including persons who ate or slept in the same dwelling as the patient during the 7 days prior to disease onset)
- Child-care and nursery-school contacts
- Persons having contact with patient's oral secretions during the 7 days prior to disease onset:
  - Kissing
  - Sharing of toothbrushes
  - Sharing of eating utensils
  - Mouth-to-mouth resuscitation
  - Unprotected contact during endotracheal intubation
- Aircraft contacts for persons seated next to the patient for >8 hrs

Persons at low risk in whom chemoprophylaxis is not recommended

- Casual contact (e.g. at school or work) without direct exposure to patient's oral secretions
- Indirect contact only (contact with a high-risk contact and not a case)
- Health-care worker without direct exposure to patient's oral secretions

Complications of meningitis

- **Hydrocephalus** (in pediatrics) cerebral edema and increased ICP
- Seizures
- Syndrome of inappropriate ADH secretion (SIADH)
  - present with refractory hyponatremia)
- Subdural effusions, empyema and abscess
- Septic sinus or cortical vein thrombosis
- (Stroke) Arterial ischemia / infarction (inflammatory vasculitis)
  - VZV and aspergillus infections can cause stroke with meningitis or encephalitis.
- **Most common:** CN Palsies (esp. **sensorineural deafness**)
- **Septic shock / multi-organ failure from bacteremia (esp meningococcus & pneumococcus)**
- Risk of adrenal hemorrhage with hypo-adrenalism **(Waterhouse-Friderichsen syndrome)**

25.64 Complications of meningococcal sepsis

- Meningitis
- Rash (morbilliform, petechial or purpuric)
- Shock
- Intravascular coagulation
- Renal failure
- Peripheral gangrene
- Arthritis (septic or reactive)
- Pericarditis (septic or reactive)

1- For patients with a history of anaphylaxis to β-lactam antibiotics.

Tuberculous Meningitis

Introduction

- **Most dreaded and dangerous form of TB**
- It is now uncommon in developed countries except in immunocompromised individuals, although it is still seen in those born in **endemic areas** and in **developing countries**. It is seen more frequently as a secondary infection in patients with the acquired immunodeficiency syndrome **(AIDS).**
- **Risk factors:**
  - Malnutrition
  - Young age
  - Household contact
  - Recent infection
  - Measles
  - Alcoholism
  - Malignancy
  - HIV
  - Immunosuppressive therapy

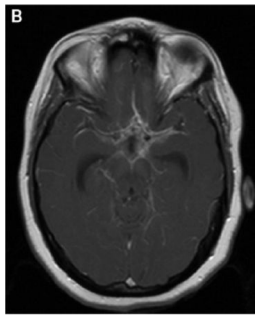
Pathophysiology:

- Mycobacterium tuberculosis (M. TB) is inhaled (lungs) → Disseminates through blood to the brain → Disseminated granulomas can remain dormant for months to years then reactivation occurs
- TB meningitis occurs when a granuloma ruptures into subarachnoid space.
- Primary infection → bacillemia → hematogenous seeding of meninges (Rich's foci) → rupture.
- Thick exudates in basal cisterns, Arteritis.
- Most commonly occurs shortly after a primary infection in childhood or as part of miliary TB.
- The usual local source of infection is a caseous focus in the meninges or brain substance adjacent to the CSF pathway.
- **The brain is covered by a greenish, gelatinous exudate, especially around the base, and numerous scattered tubercles (granuloma) are found on the meninges.**

Clinical features of tuberculous meningitis[1]

Symptoms	• **Immunocompetent:** -Headache, fever, **CN deficits (CN 6,7,2 most common)**, vomiting, meningeal signs, increased ICP, apathy • **Immunocompromised/HIV:** -More subtle, altered mental status, fever • **Vessels can be infected → vasculitis, stroke, hemorrhage:** -Strokes often in BG/MCA branches • Delirium, Behaviour changes • Decerebrate posturing, optic atrophy, extrapyramidal signs, hydrocephalus (communicating or obstructive) more common.

Signs	• **Hallmark feature = thick exudate over basilar meninges;**
	  ○ Cranial nerve palsies – CN VII, VIII
	  ○ Hydrocephalus
	  ○ Stroke
	• TB abscess
	• Cerebral tuberculomas = Granulomas.
	• Meningism (may be absent), Oculomotor palsies, Papilloedema
	• Depression of conscious level, Focal hemisphere signs



1- **Onset** is much slower than in other bacterial meningitis – over 2–8 weeks. If untreated, tuberculous meningitis is fatal in a few weeks but complete recovery is usual if treatment is started at stage I When treatment is initiated later, the rate of death or serious neurological deficit may be as high as 30%.

Tuberculous Meningitis *cont,*

◀ Clinical features of TB *cont,*

- **Staging of severity:**
  - **Stage I (early):** prodromal stage with nonspecific symptoms 1-4 weeks **(without alteration of consciousness)**
  - **Stage II (intermediate):** altered consciousness **without coma** or delirium plus neurological manifestations – seizures, deficits, meningeal signs
  - **Stage III (advanced):** stupor or **coma**, severe neurological deficits, seizures or abnormal movements

◀ Diagnosis

1 CSF[1,2] examination

- ↑pressure[3], **cells up to 500 /cu mm**, mostly lymphocytes but **can contain neutrophils.**
- ↑protein, sugar ↓upto ½ of concomitant blood sugar (**marked fall in glucose).**
- Mononuclear pleocytosis, low glucose, high protein

2 Brain imaging

- **MRI or enhanced CT :**
  - Tuberculoma
  - Subcortical infarcts
  - Hydrocephalus
  - Enhancement of basilar meninges

3 Skin test , Newer Tests

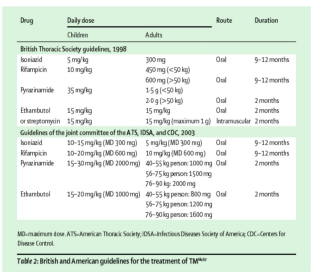
- Tuberculostearic acid
- Adenosine deaminase test
- ELISA for antibody/antigen
- Interferon gamma release assays
- Tuberculin test

4 Other

- CSF AFB smear : diagnostic yield increase to 87% when four serial specimens examined
- Use last fluid & large volume (10-15mL)
- **Culture[4] : gold standard**
- **PCR: NAAT sensitivity 56 % and specificity 98%**
- **Hyponatremia (45%) —>** Cerebral salt wasting

◀ Treatment [5]

- Empiric treatment should be started if CNS TB suspected before getting confirmation
- **First 8 weeks -** 4 drugs : RIPE (first line Meds), **Continue for 12 months -** 2 drugs
  - **Know that it's the same treatment as pulmonary TB but prolonged for up to a year.**
- CSF concentrations:
  - **INH**, **Pyrazinamidine**, **pass freely into the CSF**
  - **Rifampin** has 10% the concentration as in Plasma
  - **Streptomycin** or **Ethionamide** do not pass BBB in absence of Inflammation.
  - **Supplemental Pyrodoxine** (Vit B6) **with INH Therapy** (Because it leads to vit B6 deficiency)
- **Dexamethasone** (12 to 16 mg /day) for 3 weeks then tapered off over 3 weeks
- Shunt surgery for hydrocephalus



Drug	Daily dose		Route	Duration
	Children	Adults		
British Thoracic Society guidelines, 1998				
Isoniazid	5 mg/kg	300 mg	Oral	9–12 months
Rifampicin	10 mg/kg	450 mg (<50 kg) 600 mg (≥50 kg)	Oral	9–12 months
Pyrazinamide	35 mg/kg	1·5 g (<50 kg) 2·0 g (>50 kg)	Oral	2 months
Ethambutol	15 mg/kg	15 mg/kg	Oral	2 months
or streptomycin	15 mg/kg	15 mg/kg (maximum 1 g)	Intramuscular	2 months
Guidelines of the joint committee of the ATS, IDSA, and CDC, 2003				
Isoniazid	10–15 mg/kg (MD 300 mg)	5 mg/kg (MD 300 mg)	Oral	9–12 months
Rifampicin	10–20 mg/kg (MD 600 mg)	10 mg/kg (MD 600 mg)	Oral	9–12 months
Pyrazinamide	15–30 mg/kg (MD 2000 mg)	40–55 kg person: 1000 mg 56–75 kg person: 1500 mg 76–90 kg: 2000 mg	Oral	2 months
Ethambutol	15–20 mg/kg (MD 1000 mg)	40–55 kg person: 800 mg 56–75 kg person: 1200 mg 76–90 kg person: 1600 mg	Oral	2 months

MD=maximum dose. ATS=American Thoracic Society; IDSA=Infectious Diseases Society of America; CDC=Centers for Disease Control.

Table 2: British and American guidelines for the treatment of TM[44]

1- Lumbar puncture should be performed if the diagnosis is suspected.
2-The tubercle bacillus may be detected in a smear of the centrifuged deposit from the CSF but a negative result does not exclude the diagnosis.
3- **usually clear but, when allowed to stand, a fine clot ('spider web') may form.**
4- The CSF should be cultured but, as this result will not be known for up to 4 weeks.
5- treatment must be started without waiting for confirmation.

Aseptic Meningitis

Males' slides

- **Definition:**
  - Inflammation of meninges with sterile CSF
  - **CSF: pleocytosis 100s,** Normal Glucose, Protein normal, -ve Culture
  - **Note:** Pleocytosis is the hallmark of aseptic meningitis, since it's sterile inflammation usually it has **neutrophilic** pleocytosis (there might be some lymphocytes, but the main cells are neutrophils)

- **Causes:**
  - **Enteroviruses:** most common cause 80%
  - HSV-2 (HSV-1 can cause it but it usually causes encephalitis)
  - HIV
  - Dengue, Zika (can also cause PNS infections), Chikungunya, yellow fever.
  - **Partially treated bacteria** (Think of it when the pt has taken abx in the past 2-3 days. When you suspect viral meningitis it is important to verify that the patient has not received antibiotics (for whatever cause) prior to the lumbar puncture, as CSF lymphocytosis can also be found in partially treated bacterial meningitis.)
  - **Drugs: Metronidazole**, TMP-SMX, NSAIDs, carbamazepine (Given to epileptic pts), **IVIG-** headache is very common (Given to pts with myasthenia gravis and Guillain barre syndrome (GBS)
  - Rare: leptospirosis (spirochaete)

- **Clinical Features:**
  - Fever
  - Headache
  - Irritability
  - Vomiting
  - Convulsion (rare)
  - Meningeal signs

? Box 26.60 Causes of sterile CSF pleocytosis

- Partially treated bacterial meningitis
- Viral meningitis
- Tuberculous or fungal meningitis
- Intracranial abscess
- Neoplastic meningitis
- Parameningeal foci, e.g. paranasal sinus
- Syphilis
- Cerebral venous thrombosis
- Cerebral malaria
- Cerebral infarction
- Following subarachnoid haemorrhage
- Encephalitis, including HIV
- Rarities, e.g. cerebral malaria, sarcoidosis, Behçet's syndrome, Lyme disease, endocarditis, cerebral vasculitis

- **Treatment:**
  - No specific therapy other than supportive care is required. The disease is self-limited.
  - **Analgesics and fever reduction may be appropriate.**

Viral Meningitis [1]

◀ Introduction

- is most commonly caused by a variety of non bacterial pathogens, Also called "Aseptic Meningitis" **Viruses are the most common cause of meningitis**, usually resulting in a benign and self-limiting illness requiring no specific therapy.
- It is much **less serious** than bacterial meningitis **unless** there is associated encephalitis.
- A number of viruses can cause meningitis, the most common being **enteroviruses**.
- Where specific immunisation is not employed, the **mumps** virus is a common cause.
- Can be self limiting or more severe if accompanied by encephalitis.
- Every viral meningitis is considered aseptic meningitis, but not every aseptic meningitis is caused by viruses (could be caused by variety non-bacterial pathogens)

1-How to differentiate viral meningitis from viral encephalitis clinically?
- Viral meningitis: called Aseptic meningitis, usually cause headache, photophobia, not so much neurological deficits and it's usually self limiting.

Viral Meningitis *cont.*

Clinical features

- **Acute onset of headache**
- **Irritability**
- **The rapid development of meningism.**
- There may be a high **pyrexia** but focal neurological signs are rare.
- Other signs of specific viral infection can aid in diagnosis:
  - Pharyngitis (enteroviral infections)
  - Skin manifestation (VZV,HSV,Measles etc)
  - Lymphadenopathy and Splenomegaly (EBV)
  - Parotitis and orchitis (Mumps)

Viral Pathogens

- Viral meningitis occurs mainly in children or young adult

children And young adults

- **Enteroviruses** (echo, Coxsackie, polio) (most common - 85%) a life threatening virus.
- **Mumps**
- Influenza
- **Herpes simplex** (usually causes encephalitis)
- Varicella zoster
- Epstein–Barr
- **HIV**
- Lymphocytic choriomeningitis
- **Mollaret's meningitis (herpes simplex virus type 2)**

Investigations

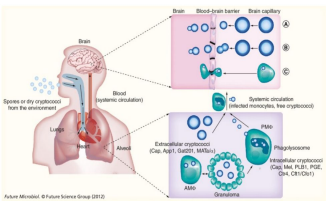
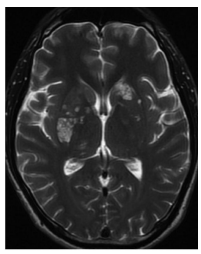
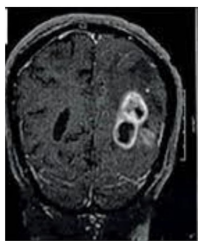
- The diagnosis is made by **lumbar puncture.**
- CSF usually contains an **excess of lymphocytes (pleocytosis)**
- CSF : viral PCR.
- While **glucose** and **protein levels** are commonly normal, they latter may be raised.
- It is important to verify that the patient has not received antibiotics (for whatever cause) prior to the lumbar puncture, as CSF lymphocytosis can also be found in partially treated bacterial meningitis.

Management[1]

- There is no specific treatment and the condition is usually benign and self-limiting.
- The patient should be treated symptomatically in a quiet environment.
- Recovery usually occurs within days, although a lymphocytic pleocytosis may persist in the CSF.
- Meningitis may also occur as a complication of a systemic viral infection such as mumps, measles, infectious mononucleosis, herpes zoster and hepatitis.
- **Whatever the virus, complete recovery without specific therapy is the rule.** (only treat the symptoms)
- Herpes virus: Antivirals (Acyclovir).
- Other: supportive (rest, IV hydration. antipyretics etc…)

1- Clinically when someone comes with clinical picture that is suspicious for meningitis, if you are not really sure what they have or what the organism is, you can start empirical therapy on treating bacterial and viral together.

Fungal Meningitis

General info,	
Epid.	❖ The most common opportunistic infection of the CNS ❖ Mostly seen in **immunocompromised** patients **and is a recognised complication of HIV infection.** ❖ High mortality rate – near 100% if untreated
Etiology	❖ **Cryptococcus neoformans is the most common cause.**
Pathogenesis	❖ "Cryptococcus neoformans" ⟶ encapsulated yeast ❖ Respiratory system (Lung) ⟶ Hematogenous spread ⟶ Brain. 
Clinical Presentation	❖ Insidious onset typical over 2-4 weeks ❖ Fever ❖ Headache (Severe, with high ICP signs – vomiting, double vision, papilledema etc.) ❖ Neck stiffness ❖ Encephalopathy ❖ Cranial neuropathies[1] ⟶ affecting one or more CNs (II, VII, VIII, IX, X, XII)
Diagnosis	❖ Brain imaging: ➢ Should be performed before LP ⟶ to R/O Cryptococcomas ❖ CSF (The findings are similar to those of tuberculous meningitis, but the diagnosis can be **confirmed by microscopy or specific serological tests**) : ➢ Lymphocytosis ➢ Glucose ⟶ Low ➢ Protein ⟶ High ➢ CSF fungal culture (highly sensitive) ➢ CSF cryptococcal antigen **(highly sensitive and specific)**  
Treatment	❖ Induction: **Amphotericin B + flucytosine** x 2 weeks ❖ Consolidation: **Fluconazole** 400mg/day x 8 weeks ❖ Maintenance: **Fluconazole** 200mg/day x 1 year
Complications	❖ Seizures ❖ Strokes[2] ❖ Persistent hydrocephalus ❖ Herniation

1- It could be due to Cryptococcoma or high pressure in the brain pressing on the nerve in the subarachnoid space.
2- Stroke can happen due to compression of the vessels and blocking them Or indirect effect by vasculitis that causes blockage and stroke.

Brucellosis

Epid.		❖ Brucellosis is an enzootic infection (i.e. endemic in animals) ❖ Common in the middle east
Transmission		❖ Consumption of: ➢ Undercooked meat, or ➢ **Unpasteurized dairy products.** ❖ Via: ➢ Inhalation, or ➢ Direct contact with skin, mucus membranes or wounds
Etiology		❖ Brucella, a Gram-negative bacteria. ❖ **B. melitensis causes the most severe disease** ❖ B. suis is often associated with abscess formation.
Clinical Presentation	**Brucellosis**	❖ Acute phase illness: ➢ Fevers, migratory arthralgia, and excessive sweating ❖ Systemic involvement: ➢ MSK (Back pain), genitourinary, and hepatic.
	Neurobrucellosis	❖ Rare (less than 5% of cases). ❖ Meningitis or meningoencephalitis (Acute or chronic). ❖ **Peripheral and cranial neuropathies*** ➢ **Has predilection to involving the brain stem**
Diagnosis		❖ **CSF** → lymphocytosis, increased protein, and decreased glucose ❖ **Serology** → **Anti-Brucella antibodies** ❖ Blood or CSF culture
Treatment		❖ **Doxycycline** (100mg IV/po bid) **or** Ceftriaxone (2gm IV q12h) ❖ **Plus** Rifampin (600-900mg po od) ❖ **Duration:** ➢ For at least 2 months [1]. ➢ Continue until CSF is normal (3-12 months); duration vary based on symptoms and MRI changes

1- Depends on response to therapy.

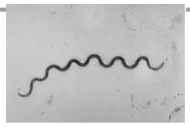
Syphilis

Neurosyphilis

Epid.

- Occurs in persons with untreated syphilis 10 - 20 years after they are first infected.
- Most commonly seen in patients with HIV infection.

Etiology



- By the bacteria spirochaete **Treponema pallidum.**
- Infects the brain and spinal cord.

Transmission

- by intimate contact or **vertical transmission.**

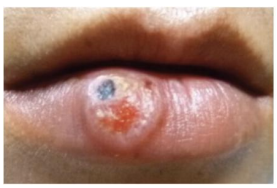
Clinical Presentation

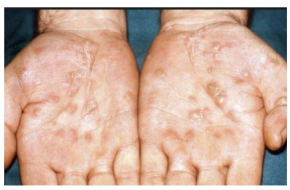
- Evolves within months of inoculation, but frequently is **asymptomatic.**
- Fever often is absent,
- But **headache** & **confusion** may be evident.
- **Major neurological complications occur in the "tertiary stage":**
  - Meningio-vascular syphilis
  - "Tabes dorsalis" = Posterior column involvement
  - "General paresis of the insane" = Dementia
  - Gummatous neurosyphilis = Brain lesions
  - Argyll Robertson pupils

Table 1

5 Stages of syphilis

Stage	Symptoms
Primary syphilis	Chancre in genitalia (often unnoticed)
Secondary syphilis	Maculopapular, non-tender rash; fever; lymphadenopathy; condyloma latum (genital)
Latent syphilis	Asymptomatic; serum nontreponemal and treponemal antibody tests are positive
Tertiary syphilis	Multiple organ-system involvement: Nerve involvement (deafness), aortic root dilation, aortitis, gummas (liver, bone, skin, spleen)
Neurosyphilis	Any stage can progress to neurologic involvement. Most common presentation is asymptomatic pupillary afferent defect (Argyll Robertson pupil). Focal symptoms include aphasia, paresis, blurry vision, hearing loss, seizures, ataxia, bowel or bladder incontinence, tabes dorsalis, loss of position and vibration senses, progressive ataxia, and sudden and severe pain, loss of balance, delirium, hydrocephalus, transverse myelitis, and stroke-like small vessel changes





Workup

- CSF (Aseptic profile):
  - WBC = lymphocytosis
  - Protein = increased
  - Glucose = Normal
  - Positive serologic tests → CSF VDRL & FTA-Abs

Treatment

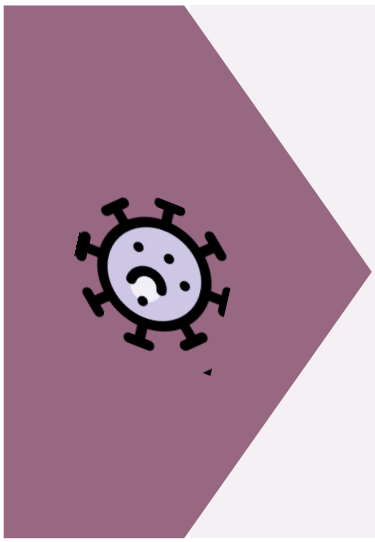
- **Penicillin G** (24 million units/day) IV x 14 days

Encephalitis / Encephalopathy

Introduction

- **Encephalitis**: means acute infection/inflammation of brain parenchyma, and is often seen simultaneously with meningitis, usually viral.
- In viral encephalitis, fever (90%) and meningism are usual; in contrast to meningitis, however, the clinical picture is dominated by brain parenchyma inflammation.
- Personality and behavioural change is a common early manifestation, which progresses to a reduced level of consciousness and even coma.
- **Seizures** (focal and generalized) are very common and focal neurological deficits, such as speech disturbance, often occur (especially in herpes simplex encephalitis).

Viral encephalitis Causes

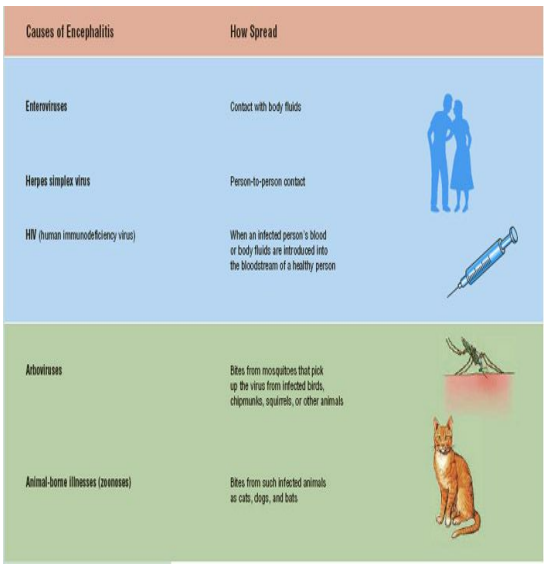


- **Most common: Herpes simplex[1] (Either type 1 or 2)**:
  - How to confirm? Perform LP and PCR. MRI is also helpful (**The limbic system** and the medial temporal are its favourable place)
  - Treated with Acyclovir
- **Varicella zoster**
- Rabies
- Arboviruses[2]: e.g dengue
- **Zika virus**
- **HIV** [3]
- Nonviral infectious causes:
  - Toxoplasmosis
  - Cerebral aspergillosis
- Rare: Listeria, cat scratch disease, amebic

Case of viral encephalitis: Elderly, coming with new onset focal seizure, impaird memory, and personality changes.

Pathophysiology

- The infection provokes an inflammatory response that involves the cortex, white matter, basal ganglia and brainstem.
- The distribution of lesions varies with the type of virus.
- For example, in herpes simplex encephalitis, the temporal lobes are usually primarily affected, whereas cytomegalovirus can involve the areas adjacent to the ventricles (ventriculitis).
- Inclusion bodies may be present in the neurons and glial cells, and there is an infiltration of polymorphonuclear cells in the perivascular space.
- There is neuronal degeneration and diffuse glial proliferation, often associated with cerebral oedema.



1- **Is the most serious cause of viral encephalitis In Europe ,which probably reaches the brain via the olfactory nerves.**
2- viruses transmitted by mosquitoes and ticks
3- may cause encephalitis with a subacute or chronic presentation but occasionally has an acute presentation with seroconversion.

Encephalitis / Encephalopathy

◀ Clinical features

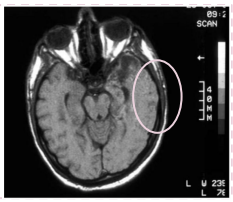
Viral encephalitis patients present with:

- acute onset of headache
- fever
- focal neurological signs (aphasia and/or hemiplegia, visual field defects) & seizures.
- Disturbance of consciousness ranging from drowsiness to deep coma supervenes early and may advance dramatically.
- Meningism occurs in many patients.

◀ Investigations

1 Radiological

- **CT scan** may show low-density lesions in the temporal lobes.
- But **MRI** is more sensitive in detecting early abnormalities.
- **Image:** This pt probably had encephalitis, MRI showing an old insult appearing dark. Usually we look for hyperintensity.



2 Lumbar puncture

- Should be performed once imaging has excluded a mass lesion.
- The CSF usually contains excess lymphocytes but polymorphonuclear cells may predominate in the early stages.
- The CSF may be normal in up to 10% of cases.
- Some viruses, including the West Nile virus, may cause a sustained neutrophilic CSF.
- The protein content may **be elevated** but the glucose is **normal**.
- **Virological investigations** of the CSF, including **PCR**, may reveal the causative organism but treatment initiation should not await this.

3 EEG

- **is usually abnormal in the early stages**, especially in herpes simplex encephalitis, with characteristic periodic slow wave activity in the temporal lobes.

◀ Management

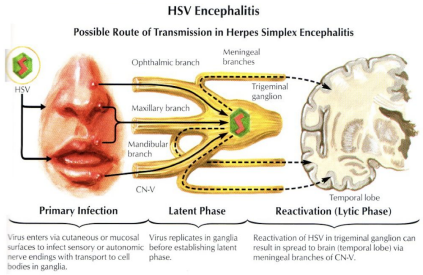
- Optimum treatment for **herpes simplex encephalitis** (**aciclovir** 10 mg/kg IV 3 times daily for 2–3 weeks) has reduced mortality from 70% to around 10%.
- This should be given early to all patients suspected of having viral encephalitis.
- Some survivors will have residual epilepsy or cognitive impairment.
- Antiepileptic treatment may be required and **raised intracranial pressure may indicate the need for dexamethasone.**

Herpes Simplex Virus Encephalitis

Epid.[1]

- HSV encephalitis is the most common cause of sporadic lethal encephalitis
- The mortality rate reaches up to 70% in patients who are not treated.
- Herpes simplex encephalitis (HSE) is an acute or subacute illness.

Pathogenesis



Clinical presentation

Causing both general and focal signs of cerebral dysfunction:

- Alteration of consciousness (97%)
- Fever (90%)
- Headache (81%)
- Psychiatric symptoms (71%)
- Seizures (67%)
- Hemiparesis (38%)
- Focal weakness (33%)
- Memory loss[2] (24%)

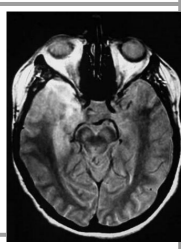
Investigations

Lumbar puncture (CSF)

- Viral **PCR** test → **HSV DNA (Gold standard)**
- Cells:
  - WBC → **lymphocyte cell predominance** (PMNs in the first ~24 hrs)
  - RBC → Can be elevated (necrotic process)
- Protein → Slightly elevated
- Glucose → Normal or mildly decreased

MRI Brain

- **Hemorrhage, necrosis,**
- **Edema in the medial temporal lobes → T2 hyperintensity**



Treatment

- Empiric treatment of patients with suspected is recommended pending confirmation of the diagnosis. Start with broad spectrum antibiotic, then add Acyclovir.
- **Acyclovir** 10 mg/kg IV every 8 hours for 14–21 days

Complications

- Motor deficits
- Seizures → Acute or chronic +/- Status Epilepticus
- Cognitive and memory deficits
- Kidney injury (so you **must** give them fluid).

Brainstem encephalitis

- This presents with ataxia, dysarthria, diplopia or other cranial nerve palsies.
- The CSF is lymphocytic, with a normal glucose.
- The causative agent is presumed to be viral.
- However, Listeria monocytogenes may cause a similar syndrome with meningitis (and often a polymorphonuclear CSF pleocytosis) and requires specific treatment with ampicillin (500 mg 4 times daily)

1- Most of the patients having the virus dormant in their nervous ganglia. and it can move to the brain causes reactivation.
2- Due to collection in the temporal lobe which is the memory center.

Cerebral abscess

Definition

- Bacteria may enter the cerebral substance through penetrating injury, by direct spread from paranasal sinuses or the middle ear, or secondary to sepsis. **Untreated congenital heart disease** is a recognised risk factor.
- Initial infection leads to local suppuration followed by loculation of pus within a surrounding wall of gliosis, which in a chronic abscess may form a tough capsule.
- Haematogenous spread may lead to multiple abscesses.
- **Organisms:**
  - **Streptococci (60-70%),** Bacteroides (20-40%), Enterobacteriacea (25-33%), S.Aureus (10-15%) (Post surgical) , S.Milleri.
  - Rare: Nocardia, Listeria

◀ Pathogenesis :

- **Direct spread** (From other infection)
  - Sinusitis
  - Mastoiditis
  - Otitis media
  - Dental infection etc.
- **Hematogenous spread** (Bacteremia)
  - Pneumonia
  - Skin infection
  - Intraabdominal infections
  - Endocarditis
  - Congenital heart disease etc.

◀ Clinical features :

The usual presenting features are:

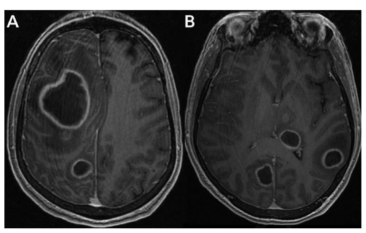
- Fever , but not all as this is a walled off infection
- Headache, Meningism (clinical syndrome of headache, neck stiffness and photophobia) and Drowsiness
- Papilledema, Seizures and Focal deficits - depends on location of abscess. But more commonly presents over days or weeks as a cerebral mass lesion with little or no evidence of infection.
- Seizures, raised intracranial pressure and focal hemisphere signs occur alone or in combination.

Note: Distinction from a cerebral tumour may be impossible on clinical grounds.

◀ Investigations :

1- Imaging

- **CT brain:** If abscess more than 2.5 cm then do **surgical drainage**. And if patient neurologically unstable or decrease LOC drain regardless of size.
- **CT with contrast:** reveals single or multiple low-density areas, which show ring enhancement with contrast and surrounding cerebral oedema
- **MRI:**
  - Grey/white junction and watershed areas most common location
  - **MCA territory**
  - Multifocal (25-50%)
  - Vasogenic edema
  - Ring enhancing lesions



Cerebral abscess

◀ Investigations *cont, :*

2- Others

- Lumbar puncture is potentially hazardous in the presence of raised intracranial pressure **and CT should always precede it.**
- WBC often normal
- Blood cultures positive in 30%
- ESR and CRP often elevated
- CSF cultures (Positive in 10%)
- Brain abscess culture (Positive in 100%)

◀ Management :

- **Medical:**
  - **Antimicrobials:**
    - empirically Ceftriaxone with metronidazole, otherwise according to susceptibility . Start antimicrobial therapy and refer the pt to neurosurgery.
    - **Vancomycin (15-20 mg/kg BID) + Metronidazole (500 mg TID) + Ceftriaxone (2g BID) = empiric treatment**
    - **Minimum 4-6 weeks if aspirated, 6-8 weeks if no surgery**
  - **Steroids —> Used early with edema and focal deficits/high ICP**
  - Duration until response by neuroimaging

- **Surgical management —> Aspiration/Resection**

i 25.69 Aetiology and treatment of bacterial cerebral abscess

Site of abscess	Source of infection	Likely organisms	Recommended treatment
Frontal lobe	Paranasal sinuses Teeth	Streptococci Anaerobes	Cefotaxime 2–3 g IV 4 times daily *plus* Metronidazole 500 mg IV 3 times daily
Temporal lobe	Middle ear	Streptococci Enterobacteriaceae	Ampicillin 2–3 g IV 3 times daily *plus* Metronidazole 500 mg IV 3 times daily *plus either*
Cerebellum	Sphenoid sinus Mastoid/middle ear	*Pseudomonas* spp. Anaerobes	Ceftazidime 2 g IV 3 times daily *or* Gentamicin* 5 mg/kg IV daily
Any site	Penetrating trauma	Staphylococci	Flucloxacillin 2–3 g IV 4 times daily *or* Cefuroxime 1.5 g IV 3 times daily
Multiple	Metastatic and cryptogenic	Streptococci Anaerobes	Benzylpenicillin 1.8–2.4 g IV 4 times daily if endocarditis or cyanotic heart disease Otherwise cefotaxime 2–3 g IV 4 times daily *plus* Metronidazole 500 mg IV 3 times daily

*Monitor gentamicin levels.

Other parenchymal bacterial infections

Subdural Empyema

- A rare complication of frontal sinusitis, osteomyelitis of the skull vault or middle ear disease. A collection of pus in the subdural space spreads over the surface of the hemisphere, causing underlying cortical oedema or thrombophlebitis.
- **In adults 60-90% are extension of** Sinusitis or Otitis media
- **Clinical features:**
  - Severe pain in the face or head & pyrexia, often with a Hx of preceding paranasal sinus or ear infection. The patient then becomes drowsy, with seizures and focal signs such as a progressive hemiparesis.
- **Diagnosis:**
  - Rests on a strong clinical suspicion in patients with a local focus of infection.
  - Careful assessment with contrast-enhanced CT or MRI may show a subdural collection with underlying cerebral oedema.
- **Treatment:**
  - **Surgical emergency: Must drain;** requires aspiration of pus via a burr hole and appropriate parenteral antibiotics (Abx same as brain abscess)
  - If it's small and not causing seizures or cognitive impairment it will be absorbed by the body with time "no need for surgery"

Spinal Epidural abscess

Definition	• An infection in the space between the bones of your spine & the lining membrane of SC. • Main risk factor: IV drug misuse • **Neurological emergency!**
Pathogens	• **Staph. A (most common)**, streptococci, Gram -ve bacilli, anaerobes
Causes	• **Hematogenous dissemination** • **Contiguous spread from an adjacent local infection** (eg, vertebral osteomyelitis, psoas abscess, decubitus ulcer) • **Iatrogenic inoculation** (Spinal Surgery, LP, Epidural steroid injections etc.)
Clinical features	• **Fever, Back pain & Neurologic deficit;** (Depending on the location in the spinal cord). ○ Focal motor weakness, Sensory disturbance, Bowel/bladder dysfunction • Characteristic features are pain in a root distribution (Back pain) & progressive transverse spinal cord syndrome with paraparesis, sensory impairment & sphincter dysfunction.

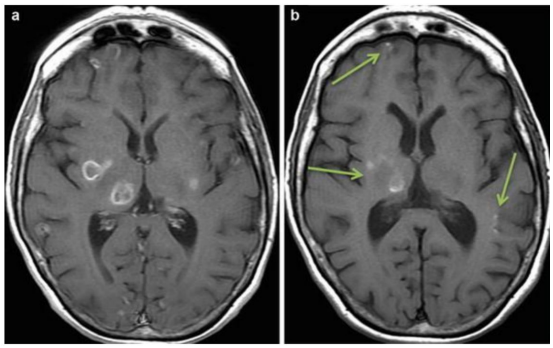
Diagnosis	• **MRI (Gold standard)** or myelography should precede urgent neurosurgical intervention.
	N.B **Lumbar Puncture is contraindicated in spinal epidural abscesses.**
	• **CSF:**
	  ○ WBC ⟶ Low (<100), both PMN and lymphocytes
	  ○ Protein ⟶ High
	  ○ Glucose ⟶ Normal

Treatment	• **Surgery, together with appropriate (broad spectrum) antibiotics**, may prevent complete and irreversible paraplegia. • Decompressive laminectomy with abscess drainage relieves the pressure on the dura. Organisms may be grown from the pus or blood.

CNS Toxoplasmosis in HIV/AIDS

◀ Overview :

- Toxoplasmosis is the leading cause of focal central nervous system (CNS) disease in AIDS. It tends to cause brain abscess. CNS toxoplasmosis in HIV-infected patients is usually a complication of the late phase of the disease. Happens with CD4 less than 100, on CT it will have a ring enhancement Appearance.
- Can happen in pregnancy



◀ Treatment and prevention :

Treatment	Prophylaxis

• **Pyrimethamine** 200mg once po then 75mg od
• **Sulfadiazine** 1.5 gm po Q6h
• Folinic acid 25 mg po od
• Duration? Minimum 6 wks after resolution of signs/symptoms
	Primary prophylaxis
	• **TMP-SMX-DS** 1 tab po od
	• Sulfa allergy:
	  ○ **Dapsone** and **pyrimethamine** and **folinic acid**
	  ○ **Atovaquone** 1500 mg po od
	• Can stop if CD4 > 200 for 3 month
	Secondary prophylaxis
	• Chronic Suppression (**secondary prophylaxis**):
	  ○ **Sulfadiazine** 2-4gm po divided in 2-4 doses/day
	  ○ **Pyrimethamine** 25-50mg po od
	  ○ Folinic acid 10-25mg po od
	• When to stop? CD4 > 200 for 6 months

◀ CSF results and type of organism :

Table 1. Typical CSF Findings in Patients With and Without Meningitis

Parameter	Normal	Bacterial Meningitis	Viral Meningitis	Fungal Meningitis	Tuberculous Meningitis
Opening pressure (mm H_2O)	<180	200-500	NA	>250 (*Cryptococcus* sp)	NA
WBC count (mm^3)	0-5	100-20,000 (mean 800)	5-500 (mean 80)	20-2,000 (mean 100)	5-2,000 (mean 200)
WBC differential	No predominance	>80% PMN	>50% L, <20% PMN	>50% L	>80% L
Protein (mg/dL)	15-50	100-500	30-150	40-150	>50
Glucose (mg/dL)	45-100 (2/3 of serum)	≤40 (<40% of serum)	30-70	30-70	<40
Gram stain (% +)	NA	60-90	–	–	37-87 (AFB smear)

+: positive; –: negative; AFB: acid-fast bacilli; CSF: cerebrospinal fluid; L: lymphocytes; NA: not applicable; PMN: polymorphonuclear cells; WBC: white blood cells. Source: References 9, 10.

70-year old male presented to the hospital with 2 days **abnormal behavior** and **lethargy**.

On presentation he was **febrile** and **confused,** and in the emergency department developed **seizure** (Generalized tonic-clonic). Before that, he was diagnosed with **UTI,** CT scan of the brain was **normal** at that time.

In the next two days of hospitalization he continued to get worse, mental status has worsened, he became **extremely confused and agitated**, and he required some **sedatives** like : Haloperidol, and lorazepam.

Q1: What causes his presentation?

- **Infection:** UTI → Septicemia → Encephalitis.
- **Medication effect :** it has more systemic symptoms not localized.

So he became more confused, looked ill, had mixed aphasia and visual field defect. Furthermore, he developed right sided weakness and right sided hyperreflexia.

Q2: Does that change his DDx?

Yes, The symptoms become more localised in the brain.

- **Encephalitis or Abscess**

Q3: What symptoms go more with Encephalitis?

- Seizure
- Confusion
- Multiple site involvement
- The course of history
- The Abscess is more acute.

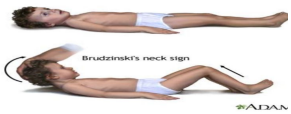
Bacterial meningitis

Definition

- Inflammation of the (meninges) pia mater and the arachnoid mater (dura mater is usually spared),with suppuration of the cerebrospinal fluid

Signs and Symptoms

- **Classic triad: fever, neck stiffness and confusion.**
- **Severe Headache, Photophobia**
- Bulging fontanel in infants, sometimes with hydrocephalus

Kernig's sign	Brudzinski's neck sign
While patient is lying supine, with the hip and knee flexed to 90 degrees pain limits passive extension of the knee.  The Kernig sign	Flexion of the neck causes involuntary flexion of the knee and hip.  Brudzinski sign

What's the most useful sign?

- **Jolt accentuation maneuver:** ask patient to rapidly rotate his or her head horizontally: Headache worsens.
- **Sensitivity of 100%, specificity of 54%**

Management (Based on Dr notes)

How to manage a patient with meningitis?

- **Step 1:** Give empirical therapy!! Whenever you suspect meningitis or encephalitis, start empirical therapy! (In real life the pt will be started on empirical therapy in the ER, before you see him)
- **Step 2: CT** (To exclude herniation, supratentorial tumor, bleeding, pus collection (Subdural empyema) before doing LP bc it may kill the pt). **NEVER do LP before CT.**
- **Step 3:** LP.

What antibiotics should be given?

- **Ceftriaxone + Vancomycin (**to cover highly penicillin resistant pneumococcus)
- Add ampicillin if there's suspicion of listeria
  Note: **Dexamethasone should be given** concomitant with 1st dose Abx to block TNF production

Special cases of bacterial meningitis

Meningococcal meningitis (Emergency)

- Fulminant meningococcemia with purpura caused by **Neisseria meningitidis**
  - Overwhelming sepsis, DIC
- **Classic: Meningitis with rash (Petechiae) + Headache + Fever**
- Lumbar puncture **should not be performed** if meningococcal sepsis is suspected
  - **Droplet Isolation:** 48h post Abx
  - **Treatment: Ceftriaxone or Pen G** 7 days
  - **Eradicate nasopharyngeal carriage:**
    - Household contact and Healthcare providers who examined patient closely

Listeria Monocytogenes meningitis

- **Pathology:** It causes brainstem, cerebellum inflammation (Rhombencephalitis) and meningitis
- **Risk groups:**
  - Age <1y or >50y , Alcoholics, Pregnancy and Immunocompromised
- **Routes of transmission:**
  - **Mainly food borne, Cheeses**, Inform micro lab: special media **(Mueller-Hinton agar)**
- **Treatment:**
  - **Ampicillin** +/- Gentamicin for **21 days**
  - Penicillin allergy patients: **TMP-SMX or Meropenem**

Important

- **What's the most common organism in neonates?**
  - Group B Streptococci (occurs ONLY in neonates)
- **What's the most common organism in older infants and children?**
  - Streptococcus pneumonia
- **What's the most common organism in adults?**
  - **Streptococcus pneumonia**
- **What's the most common complication?**
  - CN palsies (esp. deafness)

Tuberculous meningitis

Overview

- **Pathophysiology:**
  - Primary infection → bacillemia → hematogenous seeding → rupture.
  - The brain is covered by a greenish, gelatinous exudate, especially around the base, and numerous scattered tubercles are found on the meninges.
- **Symptoms:**
  - **Immunocompetent:** Headache, fever, CN deficits (CN 6,7,2 most common), vomiting
  - **Immunocompromised/HIV:** More subtle, altered mental status, fever
- **Signs :**
  - **Hallmark feature :** thick exudate over basilar meninges;
- **Tx:**
  - **First 8 weeks**- 4 drugs : RIPE (first line Meds), Continue for 12 months - 2 drugs
  - Know that it's the same treatment as pulmonary TB but prolonged for up to a year.

Aseptic meningitis

Overview

- Inflammation of meninges with sterile CSF
- **CSF: pleocytosis 100s** (hallmark of aseptic meningitis), Normal Glucose, Protein normal, -ve Culture

Causes

- **Enteroviruses:** most common cause 80%
- HSV-2 (HSV-1 can cause it but it usually causes encephalitis)
- **Partially treated bacteria**
- **Drugs: Metronidazole**, TMP-SMX, NSAIDs, carbamazepine, **IVIG**

Fungal meningitis

General info

- The **most common opportunistic infection of the CNS.**
- Mostly seen in **immunocompromised** patients and is a recognised complication of HIV infection.
- **Cryptococcus neoformans is the most common cause.**
- Cranial neuropathies → affecting one or more CNs (II, VII, VIII, IX, X, XII)
- CSF (The findings are similar to those of tuberculous meningitis, but the diagnosis can be **confirmed by microscopy or specific serological tests**) :
  - CSF fungal culture (highly sensitive)
  - **CSF cryptococcal antigen (highly sensitive and specific)**

Management

- Induction: **Amphotericin B + flucytosine** x 2 weeks
- Consolidation: **Fluconazole** x 8 weeks
- Maintenance: **Fluconazole**

Viral encephalitis

General info

- **Encephalitis**: means acute infection/inflammation of brain parenchyma, and is often seen simultaneously with meningitis, usually viral.
- **Meningoencephalitis:** inflammation of brain + meninges
- In viral encephalitis, fever (90%) and meningism are usual; in contrast to meningitis, however, the clinical picture is dominated by brain parenchyma inflammation.
- **Personality and behavioural change** is a common early manifestation, which progresses to a reduced level of consciousness and even coma.
- **Seizures** (focal and generalized) are very common and focal neurological deficits, such as speech disturbance, often occur (especially in herpes simplex encephalitis).

What's the most common organism?

- **Most common: Herpes simplex (Either type 1 or 2)**:
  - How to confirm? Perform LP and PCR. MRI is also helpful (**The limbic system** and the medial temporal are its favourable place)
  - Treat with Acyclovir

Brucellosis

Definition

- **Gram-negative bacteria**, **B. melitensis**, From Undercooked meat, or **Unpasteurized dairy products**.

Neurobrucellosis

- **Meningitis or meningoencephalitis (Acute or chronic).**
- Peripheral and cranial neuropathies*
  - **Has predilection to involving the brain stem**
- **Serology → Anti-Brucella antibodies**
- **Tx → Doxycycline or** Ceftriaxone **Plus** Rifampin

Syphilis

General info

- By the bacteria spirochaete **Treponema pallidum**.
- Untreated syphilis 10 - 20 years after they are first infected.
- Most commonly in patients with HIV infection.
- Frequently is asymptomatic. But **headache & confusion** may be evident.
- **Neurological complications "tertiary stage":**
  - **Meningio-vascular syphilis**
  - **"Tabes dorsalis" = Posterior column involvement**
  - **"General paresis of the insane" = Dementia**
  - **Gummatous neurosyphilis = Brain lesions**
  - **Argyll Robertson pupils**
- **Tx → Penicillin G** x 14 days

Cerebral abscess

General info

- Bacteria may enter the cerebral substance through penetrating injury, by direct spread from paranasal sinuses or the middle ear, or secondary to sepsis. **Untreated congenital heart disease** is a recognised risk factor.
- Initial infection leads to local suppuration followed by loculation of pus within a surrounding wall of gliosis, which in a chronic abscess may form a tough capsule.
- **Organisms:**
  - **Streptococci (60-70%),** Bacteroides (20-40%), Enterobacteriacea (25-33%),
- **S&S:**
  - Fever, Headache, Meningism, Drowsiness
  - Seizures, raised intracranial pressure and focal hemisphere signs occur alone or in combination.

Management

- Lumbar puncture is potentially hazardous in the presence of raised intracranial pressure **and CT should always precede it.**
- **CT with contrast:** reveals single or multiple low-density areas, which show ring enhancement with contrast and surrounding cerebral oedema
- **CT brain:** If abscess more than 2.5cm then **surgical drainage**. And if patient neurologically unstable or decrease LOC drain regardless of size
- **Antimicrobials:** empirically Ceftriaxone with metronidazole, otherwise according to susceptibility

Lecture Quiz

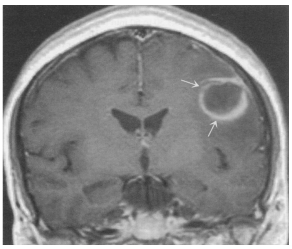
1- A man comes to the emergency department with fever, severe headache, neck stiffness, and photophobia. On physical examination he is found to have weakness of his left arm and leg. What is the most appropriate next step in the management of this patient?

A- Ceftriaxone, vancomycin, and steroids.
B- Head CT.
C- Ceftriaxone.
D- Neurology consultation.
E- Steroids.

2- A 52-year-old previously healthy woman presents with behavioral abnormalities and aphasia. Her husband reports that her symptoms began 3 days ago with fever and headache. On examination, she has a temperature of 38.4°C (101°F), mild nuchal rigidity, and agitation. When questioned, she repeats the question or responds with nonsense words. CT scan shows mild temporal hypodensity on the right; CSF examination shows 354 WBC with 75% lymphocytes. The CSF protein is elevated at 167 mg/dL, but the CSF glucose is normal at 112 (simultaneous peripheral glucose 142).

A- Pneumococcal meningitis
B- Cryptococcal meningitis
C- Coxsackievirus (aseptic) meningitis
D- Listeria monocytogenes meningitis
E- Herpes simplex encephalitis

3- A 28-year-old alcoholic has recently been treated for lung abscess. Three days before this admission, the patient develops headache, fever, and mild right-sided weakness. His MRI scan is shown in the following figure.



A- Pneumococcal meningitis
B- Coxsackievirus (aseptic) meningitis
C- Pyogenic brain abscess
D- Herpes simplex encephalitis
E- Cerebral cysticercosis

4- An 18 year old male student has been home from university for 3 days, during which time he has become increasingly drowsy. He is able to be roused but is disorientated. He has a temperature of 39°C, has marked neck stiffness and a positive Kernig's sign. He has developed a spotting, non-blanching rash over his anterior chest wall. He has no focal neurological deficit. What is the most appropriate next course of action?

A. Administer intravenous (IV) benzylpenicillin
B. Arrange for a computed tomography (CT) brain scan
C. Carry out a lumbar puncture
D. Puncture one of the purpuric lesions for microscopic analysis
E. Take blood for viral polymerase chain reaction (PCR) test

5- With regard to the patient in Question 4, IV benzylpenicillin has now been administered and his cerebral imaging has been shown to be normal. A lumbar puncture has been carried out. What is the most likely pattern of abnormality to emerge in cerebrospinal fluid (CSF)?

A- Normal white cells, normal protein, low glucose
B- Normal white cells, raised protein, normal glucose
C- Raised white cells (90% lymphocytes), raised protein, low glucose
D- Raised white cells (90% neutrophils), normal protein, normal glucose
E- Raised white cells (90% neutrophils), raised protein, low glucose

6- A 35 year old female presents with a 6-day history of delirium and disorientation. She is pyrexial but aside from being unable to answer questions or follow direction, exhibits no neurological deficit. After normal imaging has been carried out, a lumbar puncture is done, which shows the following results: white cell count 35 × 109/L; blood film – 90% lymphocytes; CSF protein 0.65 g/L; CSF glucose 4.2 mmol/L (76 mg/dL); serum glucose 6.0 mmol/L (108 mg/dL) (normal CSF glucose is > 60% of contemporary serum glucose). Which process would be a likely cause of this?

A- Brainstem encephalitis
B- Meningococcal meningitis
C- Subarachnoid haemorrhage
D- Tuberculous meningitis
E- Viral encephalitis

Answers: Q1:A | Q2:E | Q3:C | Q4:A | Q5:E | Q6:E

Answers Explanation File!

GOOD LUCK !

***This work was originally done by* 438 Medicine team:**

Team Leaders

- *Raghad AlKhashan*
- *Amirah Aldakhilallah*
- *Mashal AbaAlkhail*
- *Nawaf Albhijan*

Member : Mohammed Aljarem

Note taker : Khalid Alharbi

***Edited by* 439 Medicine team:**

Team Leaders

- *Shaden Alobaid*
- *Ghada Alabdi*
- *Hamad Almousa*
- *Naif Alsulais*

Member : Majed Alaskar

Note taker : Abdulaziz Alghuligah

CONTACT US THROUGH OUR EMAIL :
MEDICINE439@GMAIL.COM