CNS infections

Objectives:

- Definition
- Types of meningitis
- Clinical features of suspected CNS infection.
- Appreciate different causative organisms.
- CSF analysis.
- Approach to management.
- Utilization of antimicrobial therapy
- Role of steroids.
- Prevention.

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this draft is based on doc slides+cases from 435

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- Editing file
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CNS infections

Introduction :

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

1- Primarily involving the meninges.

2- Primarily confined to the parenchyma.

- 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.

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

• Bacterial (pyogenic)

• Viral

• Granulomatous(Sarcoidosis)

• Aseptic

Approach to meningitis
(Female slides)

• 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.
• 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.

Clinical evaluation of adults with suspected meningitis (Clin Inf Diseases 2002; 35:46–52)	**Limited info available on literature searches,** often conflicting results. In summary: Meningitis is characterised by acute onset of headache, fever, neck stiffness and photophobia, often accompanied by nausea and vomiting. **One cannot reliably differentiate bacterial and viral meningitis clinically**, so all possible cases have to be referred to hospital (some bacterial forms are 'indolent' and some viral forms, e.g. Enterovirus, cause high fever + severe headache requiring morphine …) Features in the history make us think about the possibility of meningitis, but the clinical exam (in one meta-analysis) is more reliable in assessing pre-test probability. Bacterial meningitis is far less common than viral. (Nearly all junior drs I work with have never seen a sick pt with meningitis). But it has a mortality of 25% and delay in antibiotic treatment worsens outcome. I have chosen just one study to show you in detail because it was 'real world', prospective, and looked at patients with **suspected meningitis** in the ED (and included viral as well as bacterial cases after LP). Other studies just look at bacterial meningitis which we do not see a lot of. The study looked ad adults (>16yrs) who presented to one US hospital's ED over a 4 year period with symptoms compatible with meningitis such that they had an LP. 301 pts enrolled, 297 went on to have LP (4 had SOL on CT head). Clinical info about history and exam was recorded by the attending dr before the LP. They were not given instructions on how to perform the clinical examination and management decisions were at their discretion.

	Patient without meningitis	**Patient with meningitis**		**Patient without meningitis**	**Patient with meningitis**
Presenting symptoms	Headache (81%)	**Headache (92%)**	**Presenting Signs**	Temperature >38oC (52%)	Temperature >38oC (43%)
	Fever (67%)	Fever (71%)		Neck stiffness (32%)	Neck stiffness (30%)
	n&v (53%)	n&v (70%)		Kernig's sign (5%)	Kernig's sign (5%)
	Photophobia (51%)	Photophobia (57%)		Brudzinski's sign (5%)	Brudzinski's sign (5%)
	Stiff neck (45%)	Stiff neck (48%)		GCS <13 (7%)	GCS <13 (10%)
	Focal symptoms/seizure (21%)	Focal symptoms/seizure (18%)		Mean wbc in CSF 1	Mean wbc in CSF 359

★ Doctor Notes: “regarding research”

1- Regarding the presenting symptoms :

Baseline characteristics (age/gender etc) and clinical presentation were similar in both groups.

I was interested to see how common n&v was in meningitis.

Progressive deterioration in mental status occurs in untreated cases of bacterial meningitis

Whereas in viral cases there is spontaneous recovery.

2- Regarding the presenting Signs :

Baseline characteristics (age/gender etc) and clinical presentation were similar in both groups.

These are just the frequencies of symptoms and signs in people with suspected meningitis who went on to have an LP

We are going to drill down the diagnostic accuracy of clinical findings in a minute … (but note the low frequency in “traditional” signs you have been taught).

Ask the group – how do you (and how should you) test for:

1)Neck stiffness

2)Kernig’s sign

3)Brudzinski’s sign?

Main message here is that meningitis commonly occurs without neck stiffness!

What about inflammatory markers in the blood – do they help?

(probably like everything else normal inflamm markers help exclude in a low clinical prob pt but by themselves are not helpful in diagnosis).

One study of 623 pts in Egypt found: “The plasma inflammatory markers showed highly significant difference between people with bacterial and non-bacterial meningitis (value <0.01). Leukocytosis (>10,000/mm3) was encountered in bacterial meningitis in 47.9% of patients, while only in 24.1% of patients with non bacterial meningitis. Positive CRP result (≥6) was significantly higher in patients with bacterial (47.9%) than non bacterial meningitis (15.7%)”. This study did not compare people who did not have meningitis.

★ Clinical manifestation :

- 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.symptoms for more than 1 week, without history of antibiotics>TB, Brucella.

partially treated meningitis(acute bacterial with history of antibiotic use)can presents as chronic meningitis.

- Fever and changes in level of alertness or mental status are less common in partially treated meningitis than in untreated meningitis.
- 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).
- 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.
- Certain bacteria, particularly N. meningitidis, can cause characteristic skin manifestations, such as petechiae and palpable purpura. Arthritis occurs in some patients with bacterial meningitis.
- 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

Symptoms ● some patients don't have clear symptoms(don't present in the classical picture):1-antibiotics use in some RTI(sinusitis) 2-immunocompromised patients 3-extreme age groups 4-analgesics use.	**Importance of early recognize CNS infection**
● - Early meningitis symptoms may mimic the flu (influenza). Symptoms may develop over several hours or over a few days. ● Possible signs and symptoms: - Sudden high fever - Stiff neck - Severe headache that seems different than normal - Headache most common with nausea or vomiting - Confusion or difficulty concentrating - Seizure or delirium or coma - Sleepiness or difficulty waking - **Sensitivity to light** (photophobia) - No appetite or thirst - Skin rash (sometimes, such as in meningococcal meningitis) ● The classic triad consists of fever, nuchal rigidity, and neck stiffness	● High mortality ● Permanent disability ● Features of both meningeal and brain involvement to various degrees ● Common features in presentation and sequelae - Bacterial meningitis - Tuberculous meningitis - Viral meningoencephalitis - Brain abscess - Fungal - polio

★ Important meningeal signs /Examination

• No focal neurologic deficits in the majority of cases. you can find patients that are completely normal by exam.

Focal neurologic signs

• Isolated cranial nerve abnormalities (principally of cranial nerves III, IV, VI, and VII).common example is 6th nerve.

• Focal cerebral signs as a result of ischemia from vascular inflammation and thrombosis.depends on location affected.

• Papilledema

Examination for nuchal rigidity

• Brudzinski sign

• The Kernig sign

Kernig's sign	Brudzinski's neck sign trying to flex neck > withdrawal+knee flexion
	

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.

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.

• Endotoxic shock with vascular collapse is characteristic of severe N meningitidis (meningococcal) infection

• Non Blanching 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.

Differential Diagnosis

- Infectious encephalopathies
  - Cerebral malaria
  - Enteric encephalopathy
  - Shigella encephalopathy
  - Sepsis
- Structural lesions with fever eg stroke/ tumour
- Non infectious encephalopathy with fever eg Reye's, electrolyte encephalopathy

Acute bacterial Meningitis (ABM)

- Very common & serious
- Medical emergency one of the top top medical emergency
- 100% curable if treated adequately or 100% fatal
- High index of suspicion important, Hx and Physical examination
- Dx by CSF examination

Etiology:

- **Streptococcus pneumoniae (pneumococcus).** This bacterium is the most common cause of bacterial meningitis in infants, young children and adults in the United States. It more commonly causes pneumonia or ear or sinus infections. A vaccine can help prevent this infection.
- **Neisseria meningitidis (meningococcus).** This bacterium is another leading cause of bacterial meningitis. These bacteria commonly cause an upper respiratory infection but can cause meningococcal meningitis when they enter the bloodstream. This is a highly contagious infection that affects mainly teenagers and young adults. It may cause local epidemics in college dormitories, boarding schools and military bases. A vaccine can help prevent infection we see it in Al Hajj or crowded places
- **Haemophilus influenzae (haemophilus).** Haemophilus influenzae type b (Hib) bacterium was once the leading cause of bacterial meningitis in children. But new Hib vaccines have greatly reduced the number of cases of this type of meningitis.
- **Listeria monocytogenes (listeria)**. These bacteria can be found in **unpasteurized cheeses**, hot dogs and lunch meats. Pregnant women, newborns, older adults and people with **weakened immune systems** are most susceptible. Listeria can cross the placental barrier, and infections in late pregnancy may be fatal to the baby. The Rx here is different so becareful
- Anatomic defects (# base of skull, pilonidal sinus), immunodeficiency, others...

Epidemiology:

- Max in 1st 5 yrs
- Risk Factors:
  - Colonization
  - **Crowding**: person to person droplet infection
  - Poverty
  - Male
  - Absence of breast feeding

Pathology :

- **Bacterial colonization of nasopharynx** -->bacteremia -->choroid plexus--> meninges.
- Meningeal exudates, ventriculitis, perivascular inflammatory exudates, venous occlusion, infarction, necrosis, ↑ICT
- Role of cytokines.

Clinical Features:

- Sudden onset
- high fever, headache, anorexia, myalgia, photophobia, meningeal signs, convulsions, stupor, coma
- ↑ICP: hypertension, bradycardia, bulging AF, 3rd/6th cranial nerve palsy, posturing, breathing abnormalities.
- Papilledema, Purpuric rash s/o meningococcus and Septic foci.

Other things that cause a petechial rash:

- Strep and staph bacteraemias
- Hemorrhagic viral fevers e.g. Dengue
- Low platelets
- Vasculitis (e.g. Henoch-Schönlein purpura)
- Spotted fevers (e.g. Mediterranean Spotted Fever)
- Trauma (e.g. violent coughing/vomiting especially around the eyes)

DDx

- TBM
- Viral meningoencephalitis
- Aseptic meningitis
- Other

Diagnosis

- High index of suspicion very important
- Confirm by CSF examination
- LP deferred if there is contraindication e.g. Skin infection near the site or raised ICP or bleeding tendency.
- Start empirical antibiotics on suspicion and don't wait for the results of LP! (give ceftriaxone+vancomycin)
- **CSF:** ↑Pressure, color's turbid, ↑cells (mostly polys), ↑protein, ↓sugar to < 40% of blood sugar. notice that CSF is for confirmation.
- Gram stain, culture.
- Latex.
- Imaging.

Table 1 | Typical cerebrospinal fluid (CSF) findings in infectious meningitis[1 3 14]

Cause of meningitis	White blood cell count (cells/mm³/10⁶ cells/l)	Predominant cell type	CSF: serum glucose (normal ≥0.5)	Protein (g/l) (normal 0.2-0.4)
Viral	50-1000	Mononuclear (may be neutrophilic early in course)	>0.5	0.4-0.8
Bacterial	100-5000	Neutrophilic (mononuclear after antibiotics)	<0.5	0.5-2.0
Tuberculous	50-300	Mononuclear	<0.3	0.5-3.0
Cryptococcal	20-500	Mononuclear	<0.5	0.5-3.0

*sequela is very specifically something that is leftover after a disease - IT IS NOT A COMPLICATION

Complications	Sequelae
- Subdural effusion - Subdural empyema - **Ventriculitis** - Abscess - SIADH - Hydrocephalus - **Infarcts** - Septic shock and (DIC) - Focal neurologic deficits (eg, cranial nerve palsy, hemiparesis) - Coma - Seizures - Cerebral edema - Septic arthritis - Pericardial effusion(especially with viral) - Hemolytic anemia (H influenzae)	- Neurological deficits - Deafness (brucella common to cause hearing loss) - MR mental retardation - Epilepsy - hydrocephalus(with acute bacterial)

Treatment for bacterial meningitis:

- IV **ceftriaxone** 2g BD (or cefotaxime 2g QDS) **Vancomycin (**due to ceftriaxone resistance) 500-750 mg q6hrs (highly penicillin resistant pneumococcus). - **Dexamethasone** 0.15mg QDS for 4 days started with first dose of antibiotics (especially if pneumococcal meningitis is suspected); stop if non-bacterial cause is identified - **Plus** IV ampicillin 2g 4 hourly if **Listeria** suspected (age >55 yrs, immunosuppressed) - Consult with Microbiology if returning traveller (?penicillin resistance) or immunocompromised host (Dr. notes : Important to liaise with Micro/ID re duration of treatment and treatment may be guided by culture results as well)	• Subsequent therapy according to sensitivity • Repeat LP/ imaging indicated if poor response • Supportive Rx - IV Fluids ? Restrict - Management of ↑ICT : mannitol, glycerine, acetazolamide - Tt of Seizures, pyrexia - Dexamethasone - Treat shock, DIC if present - Nutrition - Nursing • **we treat BM for 14DAYS IV ANTIBIOTICS !!!!**

Advice for relatives:

- Prophylaxis is only indicated for meningococcal cases - The risk for a contact is low and highest in the first 7 days - Regardless of immunisation status, household contacts, people exposed to droplets when the person got ill (e.g. healthcare workers) and the patient should be treated. - The guidelines have changed . (we either give single dose of ciprofloxacin or rifampicin)	- All ages including pregnant women should receive a single dose of ciprofloxacin - Adults and children over 12 yrs 500mg PO 

Prevention:

- Vaccines
  Hib, Pneumococcal vaccine and Meningococcal vaccine during outbreaks.
- Chemoprophylaxis for contacts: rifampicin 10 mg/kg/d every 12 hrs x 2 days
- Wash your hands.
- Practice good hygiene.
- Cover your mouth.

*patient should be isolated if we highly suspected BM

Chronic meningitis

- Slow-growing organisms (such as fungi and Mycobacterium tuberculosis) that invade the membranes and fluid surrounding your brain cause chronic meningitis.
- Chronic meningitis develops **over two weeks or more.**
- The signs and symptoms of chronic meningitis — headaches, fever, vomiting and mental cloudiness — are similar to those of acute meningitis.

Tuberculous meningitis (TBM)

Most dreaded and dangerous form of TB **Risk Factors:** - Young age - Household contact - Recent infection - **Measles** **Pathophysiology** - Primary infection bacillemia hematogenous seeding of meninges (Rich's foci) rupture - Thick exudates in basal cisterns - Arteritis	**Clinical Features**	**DDx**	**Dx**
	*3 stages - Stage 1: prodromal stage with nonspecific symptoms 1-4 weeks - Stage 2 : neurological manifestations – **seizures**, deficits, meningeal signs and ptosis - Stage 3: coma *Decerebrate posturing, cranial nerve palsies, optic atrophy, extrapyramidal signs, hydrocephalus (communicating or obstructive) more common	- Partially treated bacterial meningitis - Other CNS infections	- CSF examination - ↑pressure, cells upto 500 /cu mm, mostly lymphos, ↑protein, sugar ↓upto ½ of concomitant blood sugar - AFB - Culture - CXR - Skin test - Newer Tests: 1- Tuberculostearic acid 2- Adenosine deaminase test 3- Bromide partition test 4- NBT 5- ELISA for antibody/antigen 6- PCR 7- Interferon gamma release assays

Complications & sequelae:

- Hydrocephalus
- Focal deficits
- MR
- Endocrine
- Optic neuritis
- Epilepsy
- Spinal block/ arachnoiditis

Treatment:

- 4 anti TB drugs for initial 2 months + 3 drugs for 6-7 months total 9Months to a year
- DOTS ??
- Steroids initially for 6 weeks
- Shunt surgery for hydrocephalus

Tuberculous meningitis (Female slides)

•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(usually occurs with chronic meningitis).

• Other symptoms include Lymphadenopathy, Papilledema and tuberculomas during funduscopy

• Meningismus

Viral meningitis

- Viral meningitis is usually mild and often clears on its own.
- Most cases in the United States are caused by a group of viruses known as enteroviruses, which are most common in late summer and early fall.
- Viruses such as herpes simplex virus, HIV, mumps, West Nile virus and others also can cause viral meningitis.

Viral Meningoencephalitis more serious than meningitis

- Encephalitis and meningitis are 2 ends of the spectrum
- Neurotropic & non neurotropic viruses can cause VME
  - Arbo: JE/ west nile/ dengue
  - Entero
  - Herpes:HSV1, EBV, CMV, HHV-6, Varicella zoster
  - Myxo
  - Paramyxo
  - Adeno
  - Rhabdo

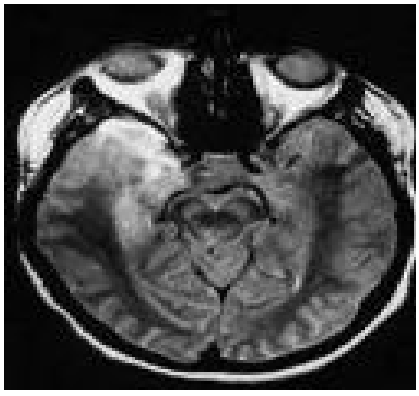
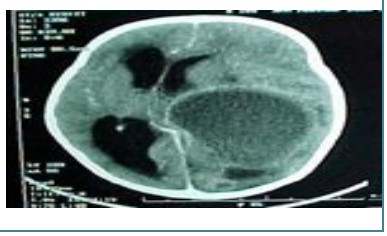
Clinical features	Dx	DDx very wide
3 stages - Prodromal: fever, vomiting, diarrhea, anorexia, malaise - Acute encephalitis stage: **convulsion**. Coma, neuro deficits, raised ICT, death - Convalescent stage: improving coma, extrapyramidal	- Neutrophilia +/- - CSF clear, pleocytosis +/-. Normal or ↑protein, normal sugar - Specific Dx by PCR - Imaging: normal/ edema/ patchy hypodensity/ specific changes - EEG: nonspecific diffuse slowing	- Other CNS infections - Enteric encephalopathy - Reye's - Cerebral malaria - Vascular - Abscess - Metabolic

Treatment

- Specific Treatment only for Herpes:HSV1 (HSE)
- Supportive
  - Treat pyrexia
  - Treat seizures
  - Treat ↑ICP by :

1- Raise head end
2- Mannitol
3- Diuretics
4- Diamox
5- Glycerine
5- Ventilation

- Fluids & electrolytes
  Nutrition
  Nursing
  Treatment of movement disorder
  Physiotherapy & rehabilitation

Herpes Encephalitis	Viral (Aseptic) Meningitis	Brain Abscess
- Commonest sporadic encephalitis in west - Severe, fulminant course - Focal deficits - Focal features on EEG - Imaging: temporal hypodensities - Specific antiviral Treatment available: **acyclovir** 10 mg/kg/d x 14-21 days 	- Mild, self limited **- Etiology:** Mumps Entero EBV Arbo M pneumoniae **- Clinical features:** Fever Headache Irritability Vomiting Convulsion (rare) Meningeal signs **- Lab:** CSF clear, pleocytosis, ↑protein, normal sugar **- Tt:** supportive only	◆ **Predisposing features:** - Congenital cyanotic heart disease - Meningitis - Penetrating head injury - Local extension from mastod, otitis, sinusitis, soft tissues of face and scalp ◆ **Etiology:** - S aureus - Micro aerophilic strep - Other aerobic & anaerobics - Mixed infections in 35% ◆ **Clinical Features:** - Fever - Headache - Vomiting - Focal deficits - ↑ICT ◆ **Lab** - Blood counts non specific - EEG: focal slowing - CT scan diagnostic ◆ **Treatment:** - IV antibiotics – cover anaerobes (CP + Chloro) - Surgical drainage  

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

The rest is from female's slides only ...

Investigations (Female slides)	
Blood Studies	**Lumbar puncture**
• complete blood count (CBC) with differential • Serum electrolytes(SIADH can occur with CNS infections> hyponatremia) • Serum glucose(to compare csf glucose) • Blood urea nitrogen (BUN) or creatinine and liver profile, to assess organ function and adjust antibiotic dosing • A coagulation profile and platelet count(for LP) • 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(if it is elevated it directs to bacterial infection)	• 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. **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 **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.

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
CSF characteristics of acute <u>bacterial meningitis</u>
• 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(< ⅔ of serum)
• CSF WBC count of 500/µL or higher
• CSF lactate level of 31.53 mg/dL or higher
CSF characteristics of <u>viral meningitis</u>
• WBC count is 10-300/µL.
• Glucose is typically normal
• Protein concentration slightly elevated
CSF characteristics of <u>tuberculous meningitis</u>
• Lymphocytic pleocytosis
• Elevated protein level
• Low glucose level (< 40 mg/dL).
• PCR testing can provide a rapid diagnosis

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

Treatment of meningitis (Female slides)		
Antibiotic regimen	**Community-acquired meningitis**	**Healthcare-associated meningitis**
- 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	-Mostcommonorganisms: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 4hours ampicillin is added when atypical bacteria is suspected(listeria)	-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. **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 **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	**<u>Vaccination</u>** - 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. - In October 2014, the FDA approved the first meningococcal vaccine for serogroup B (Trumenba) **<u>Chemoprophylaxis</u>** • 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. • 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. meningitidi**<u>s</u>**

<u>These are extra cases from female dr's slides last year</u>

<u>(not in her slides this year)</u>

link

Summary

Meningitis: is an inflammation of the membranes (meninges) surrounding your brain and spinal cord.	
Symptoms	- Sudden high fever - Stiff neck - Severe headache - nausea or vomiting - No appetite or thirst - Skin rash (sometimes, such as in meningococcal meningitis) - **Sensitivity to light** - Sleepiness or difficulty waking - Seizures - Confusion or difficulty concentrating
signs	**- Kernig's sign.** **- Brudzinski's neck sign**
DDx	- Infectious encephalopathies - Structural lesions with fever eg stroke/ tumour - Non infectious encephalopathy with fever eg Reye's, electrolyte encephalopathy
Acute bacterial Meningitis (ABM)	
Etiology	- Streptococcus pneumoniae (pneumococcus). - Neisseria meningitidis (meningococcus). - Haemophilus influenzae (haemophilus). - Listeria monocytogenes (listeria) - Anatomic defects
Clinical Features	- Sudden onset - high fever, headache, photophobia, - ↑ICP - Papilledema, Purpuric rash.
Diagnosis	- High index of suspicion very important - LP - Start empirical antibiotics on suspicion **- CSF:** ↑Pressure, turbid, ↑cells (mostly polys), ↑protein, ↓sugar to < 40% of blood sugar. - Gram stain, culture. - Latex. - Imaging.
Treatment	- IV **ceftriaxone** - **Vancomycin** - **Dexamethasone** i - **Plus** IV ampicillin if **Listeria** suspected (age >55 yrs, immunosuppressed)

<table>
<tr><th colspan="2">Chronic meningitis:</th></tr>
<tr><td colspan="2">Slow-growing organisms (fungi ,Mycobacterium tuberculosis)
- Chronic meningitis develops over two weeks or more.
- signs and symptoms are similar to those of acute meningitis.</td></tr>
<tr><th colspan="2">Tuberculous meningitis (TBM)</th></tr>
<tr><td>Clinical Features</td><td>3 stages
- Stage 1: prodromal stage with nonspecific symptoms 1-4 weeks
- Stage 2 : neurological manifestations – seizures, deficits, meningeal signs and ptosis
- Stage 3: coma</td></tr>
<tr><td>Diagnosis</td><td>CSF examination - ↑pressure, cells upto 500 /cu mm, mostly lymphos, ↑protein, sugar ↓upto ½ of concomitant blood sugar
- AFB
- Culture
- CXR
- Skin test
-Tuberculostearic acid
- Adenosine deaminase test
- Bromide partition test
- NBT
- ELISA for antibody/antigen
-- PCR
- Interferon gamma release assays</td></tr>
<tr><td>treatment</td><td>- 4 anti TB drugs for initial 2 months + 3 drugs for 6-7 months
- DOTS
- Steroids initially for 6 weeks
- Shunt surgery for hydrocephalus</td></tr>
<tr><td colspan="2">Viral meningitis
Viral meningitis is usually mild and often clears on its own.</td></tr>
<tr><th colspan="2">Viral Meningoencephalitis</th></tr>
<tr><td>Clinical features</td><td>3 stages
- Prodromal: fever, vomiting, diarrhea, anorexia, malaise
- Acute encephalitis stage: convulsion. Coma, neuro deficits, raised ICT, death
- Convalescent stage: improving coma, extrapyramidal</td></tr>
<tr><td>Diagnosis</td><td>- Neutrophilia +/-
- CSF clear, pleocytosis +/-. Normal or ↑protein, normal sugar
- PCR
- Imaging: normal/ edema/ patchy hypodensity/ specific changes
- EEG: nonspecific diffuse slowing</td></tr>
<tr><td></td><td>● Specific Treatment only for Herpes:HSV1 (HSE)
● Supportive
- Treat pyrexia
- Treat seizures
- Treat ↑ICP</td></tr>
</table>

Questions

1. A 12-year-old boy presented to the ER with headache, nausea, vomiting and photophobia. On examination, his temperature was 39.3 C and he has positive Kering's sign. He has history of URTI. The treatment team suspected meningitis and the diagnosis was confirmed. Which of the following is the most common bacterial organism that causes meningitis?
    a. Streptococcus pneumoniae.
    b. Haemophilus influenzae.
    c. Listeria monocytogenes.
    d. Neisseria meningitidis.

2. A 35-year-old female in her 25th week of gestation presented to the ER with sudden high fever and severe headache. She was diagnosed with meningitis. Which of the following regimens is the best to be used empirically in this case?
    a. IV Ceftriaxone and Vancomycin.
    b. IV Ampicillin, Penicillin and Vancomycin.
    c. IV Ampicillin, Gentamycin and Cephalosporin.
    d. IV Ampicillin, Ceftriaxone and Vancomycin.

3. A 27-year-old male presented to the ER with headache, fever and ptosis. In which of the following stages of tuberculous meningitis he is?
    a. Stage 1.
    b. Stage 2.
    c. Stage 3.
    d. Stage 4.

4. A 18-year-old male presented with fever and headache and a seizure attack. CT revealed temporal hypodensities. Which of the following is best confirmatory test?
    a. Electroencephalogram.
    b. CSF cytology.
    c. Temporal lobe biopsy.
    d. CSF Cytology and PCR.

5. A 10-year-old girl presented to the ER with Headache, fever and vomiting. On examination, she was confused with papilledema. What is the best initial step in managing this patient?
    a. Lumbar puncture.
    b. Call neurologist.
    c. Head CT scan.
    d. Empirical treatment for meningitis.

6. A 25-year-old male known case of hemophilia, DM type 1 and HTN presented to the ER with mental cloudiness, headache and fever. Which of the following is best initial step initial step in managing such cases?
    a. Start empirical treatment for meningitis after LP.
    b. Head CT scan to rule out space occupying lesion.
    c. Start empirical treatment for meningitis.
    d. Head and spine CT scan and call neurologist.

7. Which of the following bacterial etiology of meningitis that can't be prevented by vaccination?
    a. Streptococcus pneumoniae.
    b. Neisseria meningitidis.
    c. Haemophilus influenzae.
    d. Listeria monocytogenes.

8. A 22-year-old female in her 1st trimester presented to the ER by her family unconscious. She has been recently in LA, America. On examination the patient had a rash on her face shown in the picture below and vitally unstable.

Which of the following is the causative organism of her presentation?
    a. Streptococcus pneumoniae.
    b. Neisseria meningitidis.
    c. Haemophilus influenzae.
    d. Listeria monocytogenes.

9. Which of the following etiology of meningitis will cause the highest protein in CSF analysis?
    a. Herpes virus.
    b. Neisseria meningitidis.
    c. Mycobacterium tuberculosis.
    d. EBV.

Answers: 1-A. 2- D. 3-B. 4-D. 5-C. 6-C. 7-D. 8-B. 9-C.