433 Teams

# MEDICINE

## 14 | CNS Infections

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COLOR INDEX

Slides - Step-Up medicine - Kaplan Notes - Extre explanation - Doctor Notes

# Objectives:

| |
|---|
| Be familiar with clinical presentation of disease |
| Appreciate different causative organisms |
| Approach to management |
| Utilization of antimicrobial therapy |
| How to prevent disease |
| Role of Steroids |
| Case discussion |

# Meningitis

## Definitions

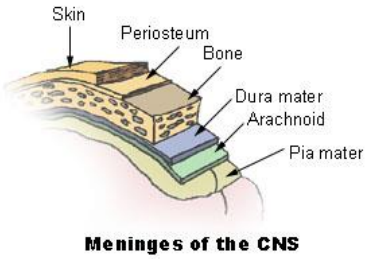
**Meningitis:** This refers to inflammation of the meningeal membranes that envelop the brain and spinal cord.

Or inflammation of the pia mater and the arachnoid mater, with suppuration of the cerebrospinal fluid .

It is usually associated with infectious causes, but non-infectious causes (such as medications, SLE, sarcoidosis, and carcinomatosis) also exist.

**Meningoencephalitis:** inflammation of brain and meninges .

**Aseptic meningitis:** inflammation of meninges with sterile CSF.



Meninges of the CNS

## Pathophysiology

Infectious agents frequently colonize the nasopharynx and respiratory tract.These pathogens typically enter the CNS via one of the following:

- Invasion of the bloodstream, which leads to hematogenous seeding of CNS
- Retrograde transport along cranial (e.g., olfactory) or peripheral nerves
- Contiguous spread from sinusitis, otitis media, surgery, or trauma

## Classification

| depending on onset of symptoms | |
|---|---|
| Acute meningitis | Chronic meningitis |
| onset within hours to days | onset within weeks to months<br>commonly caused by mycobacteria, fungi, Lyme disease, or parasites |

Or it can be classified according to the cause

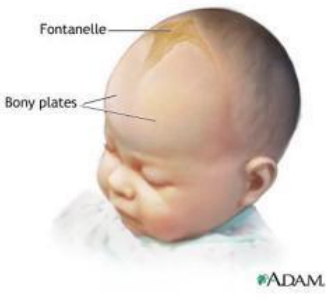
| dependingon the cause | |
|---|---|
| INFECTIOUS | NON-INFECTIOUS |
| Viral | Aseptic Meningitis |
| Bacteria | Malignancy |
| Mycobacterial | Sarcoid |
| Brucella | Behcet disease |
| Fungal | SLE and Subarachnoid hemorrhage |

## Etiology

<table>
<tr><th colspan="2">bacterial Vs aseptic</th></tr>
<tr><th>Acute bacterial meningitis</th><th>Aseptic meningitis</th></tr>
<tr><td rowspan="3">Causes :<br>Neonates:<br>Group B streptococci 49%, Escherichia coli, Listeria monocytogenes<br>Enterococci, Klebsiella, Enterobacter, Samonella, Serratia<br>Children >3 months:<br>Neisseria meningitidis, Streptococcus pneumoniae, H.influenzae<br>Adults (ages 18 to 50):<br>S.pneumoniae37%, N.meningitidis13%, L.monocytogenes10%,H.influenza4%<br>Elderly (>50):<br>S.pneumoniae, N.meningitidis, L.monocytogenes<br>Other strept.species , Gram negative Haemophillus influenza ,TB, Brucella<br>Immunocompromised<br>:L.monocytogenes, gram-negative bacilli, S.pneumoniae</td><td>CSF: pleocytosis 100s, Norm G&P, -ve Culture<br>Causes :<br>Frequently viruses like:<br>Enterovirus 80% and herpes simplex virus (HSV).<br>Certain bacteria, parasites, and fungi.<br>Partially treated bacterial meningitis<br>Drugs:<br>Metronidazole, TMP-SMX, NSAIDs, carbamazapine, IVIG<br>Rare: leptospirosis</td></tr>
<tr><td>It may be difficult to distinguish it clinically from acute bacterial meningitis.</td></tr>
<tr><td>If there is uncertainty in diagnosis, treat for acute bacterial meningitis.</td></tr>
<tr><td>Keep in mind :-Group B Streptococci: previously in neonate, now emerging as disease of elderly.<br>-Dramatic Reduction in invasive Hemophillus influenza disease secondary to use of conjugate Haemophillus Type B- vaccine.</td><td>It is associated with a better prognosis than acute bacterial meningitis.</td></tr>
</table>

## Symptoms

- Headache (may be more severe when lying down)
- Fevers (High grade sudden fever)
- Nausea and vomiting
- Stiff, painful neck
- Malaise
- Photophobia
- Alteration in mental status (confusion, lethargy, coma)
- Seizures
- Bulging fontanel in infants



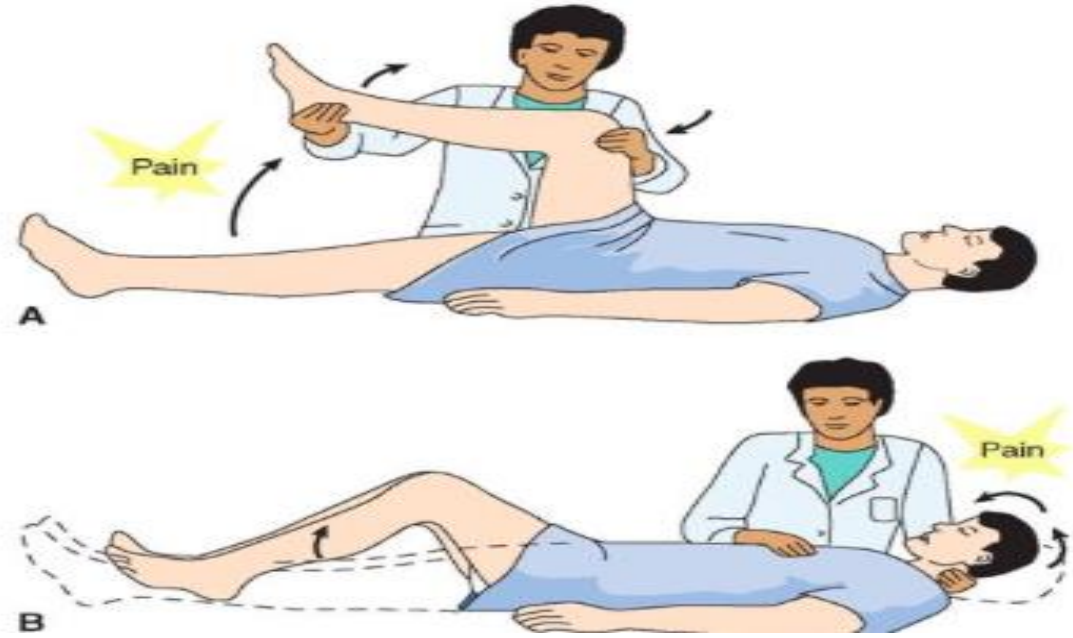
- **Signs**

❖ **Vital signs:** Fever
❖ Nuchal rigidity: stiff neck, with resistance to flexion of spine (may be absent)
❖ Rashes
  - ➢ Maculopapular rash with petechiae—purpura is classic for N. meningitidis.
  - ➢ Vesicular lesions in varicella or HSV.
  - ➢ ecchymosis.
❖ Increased ICP and its manifestations e.g. : papilledema, seizures
❖ Cranial nerve palsies
❖ **Kerning's sign (A):**inability to fully extend knees when patient is supine with hips flexed (90°)
  - ➢ Caused by irritation of the meninges.
❖ **Brudzinski's sign(B):**flexion of legs and thighs that is brought on by passive flexion of neck for same reason as above
❖ Neurological defecit
❖ Don't forget source of infection: ears, sinsuses, chest
❖ **Most useful Sign :**

Jolt accentuation maneuver: ask patient to rapidly rotate his or her head horizontally -Headache worsens

Sensitivity of 100%, specificity of 54%, positive likelihood ratio of 2.2, and negative likelihood ratio of 0 for the diagnosis of meningitis

✓ Absence of all 3 signs of the classic triad of fever, neck stiffness, and an altered mental status virtually eliminates a diagnosis of meningitis
✓ Changes in mental status are more common in bacterial than viral meningitis
✓ Kernig(A) and Brudzinski(B) signs have low sensitivity but high specificity.



## • Diagnosis and Investigations

CBC, creatinine, electrolytes: Na ,Blood Culture ,CXR ,CT Head , CSF analysis

The best initial test and most accurate test is an **LP (lumbar puncture).**

| cerebrospinal fluid evaluation | | | | |
|---|---|---|---|---|
| | **bacterial meningitis** | **cryptococcus, lyme ,rickettsia** | **tuberculosis** | **viral** |
| **Cell count** | 1000s, neutrophils | 10s-100s lymphocytes | 10s-100s lymphocytes | 10s-100s lymphocytes |
| **Protein level** | Elevated | Possibly elevated | Markedly elevated | Usually normal |
| **Glucose level** | Decreased | Possibly decreased | May be low | Usually normal |
| **Stain and culture** | Stain: 50-70%; culture: 90% | Negative | Negative | Negative |

Remember to be careful:

- ❖ Cellulitis at area of lumbar puncture
- ❖ Bleeding disorder
- ❖ CSF appearance

### When Is a Head CT the Best Initial Test?

Head CT is necessary prior to an LP only if there is the possibility that a space occupying lesion may cause herniation. (Increase ICP)
Answer head CT first when any of the following is present:

- ❖ Papilledema
- ❖ Seizures
- ❖ Focal neurological abnormalities
- ❖ Confusion interfering with the neurological examination

***If there is a contraindication to immediate LP, giving antibiotics is the best initial step in management.**

**-Bacterial Antigen Detection (Latex Agglutination Tests)**

These tests are similar to a Gram stain. If antigen detection methods are positive,they are extremely specific. If they are negative, the person could still have the infection. These tests by themselves are not sufficiently sensitive to exclude bacterial meningitis.

**When is a bacterial antigen test indicated?**

When the patient has received antibiotics prior to the LP and the culture may be falsely negative.

## Organism Specific Diagnostic Tests

### Tuberculosis:

PCR, Acid fast stain and culture on 3 high-volume lumbar punctures. Centrifuge the specimen to concentrate the organisms. TB has the highest cerebrospinal fluid (CSF) protein level. An acid fast stain of a single, uncentrifuged sample of CSF has only 10% sensitivity.

### Brucella:

Serology and PCR

### Lyme and Rickettsia:

Specific serologic testing, ELISA, western blot, PCR .

### Cryptococcus:

India ink is 60% to 70% sensitive. Cryptococcal antigen is more than 95% sensitive and specific.

### Herpes simplex virus (HSV):

PCR

### Viral:

Generally a diagnosis of exclusion.

**TABLE IV**

**CFS FINDINGS SUGGESTING BACTERIAL MENINGITIS WHEN INITIAL GRAM STAIN IS NEGATIVE[1]**

CSF leukocyte count > 1,000/mm³
CSF leukocyte count > 100 mm³, of which > 50 per cent neutrophils
CSF glucose < 30 mg/dl
CSF glucose/blood glucose ratio < 40 per cent
CSF protein > 200 mg/dl
Raised serum C-reactive protein

Note: Consider alternative diagnosis, eg tuberculous, fungal or viral meningitis, or brain abscess. Treat initially as bacterial meningitis. These figures are not applicable to neonates.

- **Treatment**

**Remember MENINGEAL DOSES"big dose"**

The best initial treatment for bacterial meningitis is **ceftriaxone** (High CSF levels),**vancomycin** (highly penicillin resistant *pneumococcus)* and steroidsdexamethasone (block TNF production)

: 1st dose 15-20 min prior to or concomitant with 1st dose

You will base your treatment on the cell count. Culture takes 2 to 3 days and is never available at the time that a treatment decision made. Gram stain is good if it is positive; however, the false negative rate is 30% to 50%.

Empiric antibiotic therapy—Start immediately after LP is performed. If a CT scan must be performed or if there are anticipated delays in LP, give antibiotics first.

Protein and glucose levels are too nonspecific to allow for atreatment decision.

Although steroids (dexamethasone) have been proven to lower mortality only in S. pneumoniae infection, you must give them when you see thousands of neutrophils because you will not know the culture results for several days.

**Listeria Monocytogenes**

Listeria is resistant to all cephalosporins but sensitive to penicillins. You must add ampicillin to ceftriaxone and vancomycin if the case describes risk factorsfor Listeria. These risk factors are:

- Elderly
- Neonates
- Steroid use
- AIDS or HIV
- Immunocompromised, including alcoholism
- Pregnant

**Keep in mind:** global emergence and prevalence of Penicillin Resistant Streptococcus pneumonia

**Neisseria meningitides**

Additional Management:

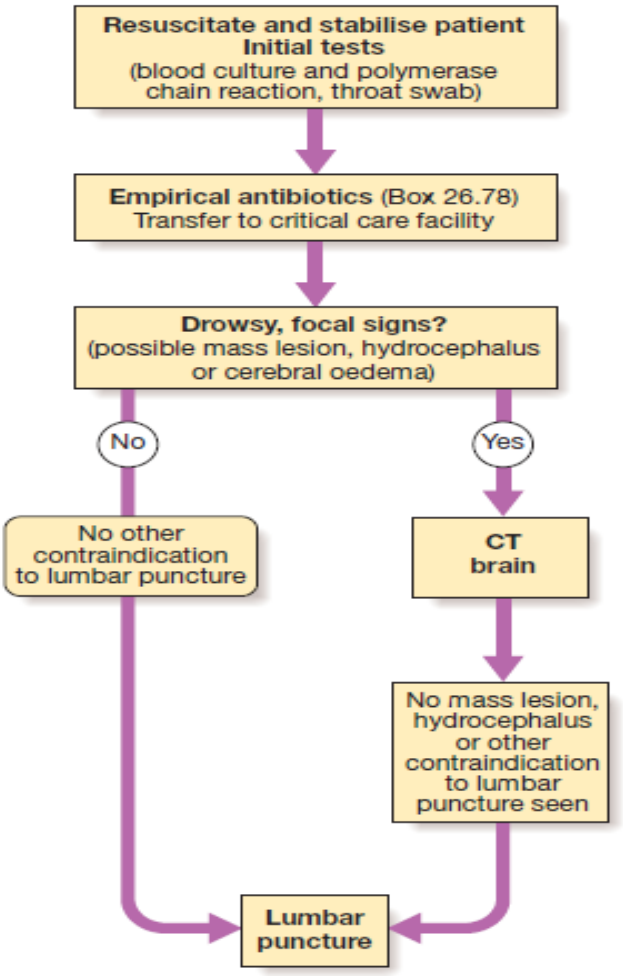
Respiratory isolation

Rifampin, ciprofloxacin, or ceftriaxone to the close contacts to decrease nasopharyngeal carriage

Close contacts: means those who have major respiratory fluid contact,such as household contacts, kissing, or sharing cigarettes or eating utensils. Routine school and work contacts are not close contacts.

Sitting in class with someone with Neisseria infection does not make them a close contact.

Healthcare workers qualify only if they intubate the patient, performsuctioning, or have contact with respiratory secretions.




| Pathogen | Regimen of choice | Alternative agents |
|---|---|---|
| *N. meningitidis* | Benzylpenicillin 2.4 g IV 6 times daily for 5–7 days | Cefuroxime, ampicillin Chloramphenicol* |
| *Strep. pneumoniae* (sensitive to β-lactams, MIC < 1 mg/L) | Cefotaxime 2 g IV 4 times daily *or* ceftriaxone 2 g IV twice daily for 10–14 days | Chloramphenicol* |
| *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 *plus* rifampicin* Moxifloxacin Gatifloxacin |
| *H. influenzae* | Cefotaxime 2 g IV 4 times daily *or* ceftriaxone 2 g IV twice daily for 10–14 days | Chloramphenicol* |
| *L. 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 |
| *Strep. suis* | Cefotaxime 2 g IV 4 times daily *or* ceftriaxone 2 g IV twice daily for 10–14 days | Chloramphenicol* |

*For patients with a history of anaphylaxis to β-lactam antibiotics.
(MIC = minimum inhibitory concentration)

**26.78 Treatment of pyogenic meningitis of unknown cause**

**1. Adults aged 18–50 yrs with or without a typical meningococcal rash**

- Cefotaxime 2 g IV 4 times daily *or*
- Ceftriaxone 2 g IV twice daily

**2. Patients in whom penicillin-resistant pneumococcal infection is suspected, or in areas with a significant incidence of penicillin resistance in the community**

As for (1) but add:

- Vancomycin 1 g IV twice daily *or*
- Rifampicin 600 mg IV twice daily

**3. Adults aged > 50 yrs and those in whom *Listeria monocytogenes* infection is suspected (brainstem signs, immunosuppression, diabetic, alcoholic)**

As for (1) but add:

- Ampicillin 2 g IV 6 times daily *or*
- Co-trimoxazole 50 mg/kg IV daily in two divided doses

**4. Patients with a clear history of anaphylaxis to β-lactams**

- Chloramphenicol 25 mg/kg IV 4 times daily *plus*
- Vancomycin 1 g IV twice daily

**5. Adjunctive treatment (see text)**

- Dexamethasone 0.15 mg/kg 4 times daily for 2–4 days

## Complications

- Seizures
- Coma
- Brain abscess
- Subdural empyema & effusions
- DIC
- Respiratory arrest
- SIADH
- Septic sinus or cortical vein thrombosis
- Arterial ischemia / infarction (inflammatory vasculitis)
- Septic shock / multi-organ failure from bacteremia (meningococcus & pneumococcus)
- Risk of adrenal hemorrhage with hypo-adrenalism (Waterhouse-Friderichsen syndrome)
- Permanent sequelae :
  - Deafness
  - Brain damage
  - Hydrocephalus

The most common neurological deficit of untreated bacterial meningitis is 8th cranial nerve deficit or deafness.

## Prognosis

Depend on:

- Different etiological organisms
- Time of starting appropriate therapy

## Vaccination

- ✓ Vaccinate all adults>65 years for *S. pneumoniae.*
- ✓ Vaccinate asplenic patients for *S. pneumoniae, N. meningitidis,* and *H. influenzae* (organisms with capsules).
- ✓ Vaccinate immunocompromised patients for meningococcus.

## Prophylaxis

(e.g., rifampin or ceftriaxone)—For all close contacts of patients with meningococcus, give 1 dose of IM ceftriaxone.

# Encephalitis

## Definition

**Encephalitis:**is a diffuse inflammation of the brain parenchyma and is often seen simultaneously with meningitis.

## Causes

It is usually viral in origin. Non-viral causes, however, must also be considered.

**Viral causes:**

- Herpes (HSV-1) : do PCR, give Acyclovir
- Arbovirus e.g.: Eastern equine encephalitis, West Nile virus , dengue
- Enterovirus e.g.: polio
- Less common causes e.g.: measles, mumps, EBV, CMV, VZV, rabies, and prion diseases such as Creutzfeldt–Jakob disease

The overall mortality associated with viral encephalitis is approximately 10%.

**Non-viral infectious causes:**

- Toxoplasmosis
- Cerebral aspergillosis
- Rare: Listeria, cat scratch disease, amebic

**Noninfectious causes:**

- Metabolic encephalopathies
- T-cell lymphoma

## Risk factors

- Patients with AIDS are especially at risk for toxoplasmosis when the CD4 count is<200.
- Other forms of immunosuppression.
- Travel in underdeveloped countries
- Exposure to insect (e.g., mosquito) vector in endemic areas
- Exposure to certain wild animals (e.g., bats) in an endemic area for rabies

## Clinical features

- Patients often have a prodrome of headache, malaise, and myalgias.
- Within hours to days, patients become more acutely ill.
- Patients frequently have signs and symptoms of meningitis (e.g., headache, fever, photophobia, nuchal rigidity).
- In addition, patients have altered sensorium, possibly including confusion, delirium, disorientation, and behavior abnormalities.
- Focal neurologic findings (e.g., hemiparesis, aphasia, cranial nerve lesions) and seizures may also be present

## Diagnosis and Investigations

- head CT
- PCR

## Treatment

- ✓ Acyclovir is the best initial therapy for herpes encephalitis.
- ✓ Foscarnet is used for acyclovir-resistant herpes.

# Brain Abscess

**Organisms:**

Streptococci (60-70%), Bacteroides (20-40%), Enterobacteriacea (25-33%), S.Aureus (10-15%), S.Milleri.

**Rare:**

Nocardia, Listeria

**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
Duration until response by neuroimaging

# Subdural Empyema

In adults 60-90% are extension of:

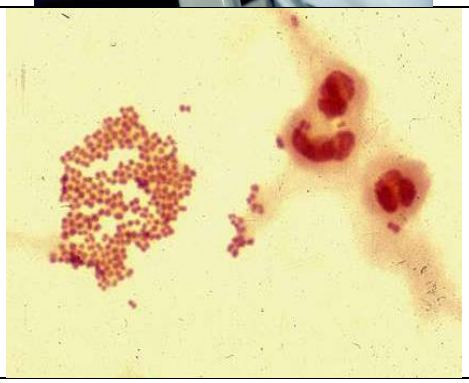
- Sinusitis
- Otitis media

Surgical emergency: must drain
Antibiotics same as brain abscess

# Doctor's cases

**These cases are important because it contain information not present in the lecture above**

## Case 1

<table>
<tr><td colspan="2">34 years old man returning from Hajj<br>Fever, severe headache, neck stiffness, vomiting for two days<br>Found confused by family</td></tr>
<tr><td>In ER :<br>Temp 38.4, HR 110, BP 100/70<br>Obtunded, Nuchal rigidity, Kerning's and brudzinski'ssigns ,Petechiae</td><td>  </td></tr>
<tr><td>CSF examination:<br>Opening pressure: 260 mm H20 &cloudy<br>WBC: 1500/ ml: 96% polymorphs<br>Glucose: 24mg / dl<br>Protein: 200 mg<br>Gram negative diplococci: meningococcus</td><td>  </td></tr>
<tr><td>N. meningitidis</td><td>Vaccination: Pre Hajj vaccination in 90's<br>serogroups A, C<br>Up to 3 years in adult : Does not affect nasopharyngeal carriage and does not provide herd immunity</td></tr>
</table>

***Meningococcus:***

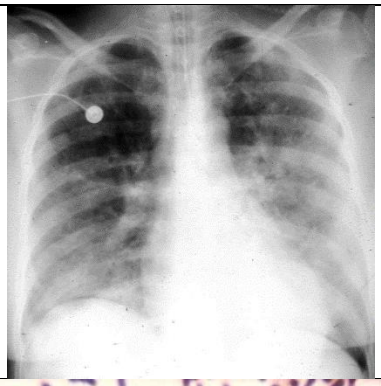
- ✓ **Fulminate meningococcemia with purpura: Overwhelming sepsis, DIC**
- ✓ **Meningitis with rash (Petechiae)**
- ✓ **Meningitis without rash**
- ✓ **Mortality 3 - 10 %**

**Treatment & Chemoprophylaxis:**

- ✓ **Droplet Isolation: 48h post Abx**
- ✓ **Treatment: Ceftriaxone or Pen G 7 days**
- ✓ **Eradicate nasopharyngeal carriage: house hold contact**
- ✓ **Health care providers who examined patient closely**

**Rifampin 600 mg for 2 d or Ciprofloxacin 500mg once**
**or Ceftriaxone 125mg I.M once**

## Case 2

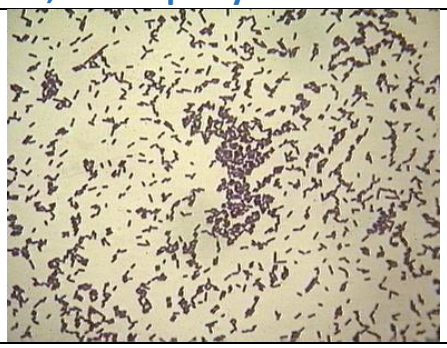
<table>
<tr><td colspan="2">26 year old Saudi female presents with fever, cough and headache for the last 3 days</td></tr>
<tr><td>Examination revealed ill – looking woman with sign of consolidation over lower lungs</td><td>  </td></tr>
<tr><td>Six hours after admission, her headache became worse and rapidly became obstunded.<br>CSF: WBC: 3000 : 99% PML<br>Sugar: Zero<br>Protein: 260 mg/dl.<br>Gram positive diploccoci pneumococcus</td><td>  </td></tr>
<tr><td>Pneumococcal meningitis</td><td>The most common Cause<br>Highest mortality 20 – 30%<br>May be associated with other Focus: Pneumonia, Otitis Media, Sinusitis , Head Trauma & CSF Leak , splenectomy and Sickle cell disease<br>Global emergence of Penicillin Resistant</td></tr>
</table>

**Treatment & prevention of *Pnemococcus*meningitis:**

- **Penicillin G (MIC< 0.1mcg/ml)**
- **Ceftriaxone 14 days**
- **Vancomycin if Highly penicillin resistance (MIC>=2mcg/ml)**
- **Steroids (pre Abx)**

- **Vaccination:**
  - Pneumococcal conjugate vaccine PCV (Prevnar 13): is a vaccine used to protect infants and young children
  - Pneumococcal polysaccharide vaccine PPSV (Pneumovax): 23 serotypes of *Streptococcus* ,PPSV is recommended (routine vaccination)

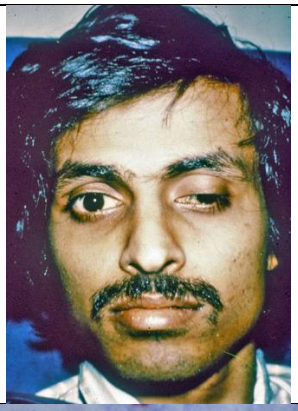
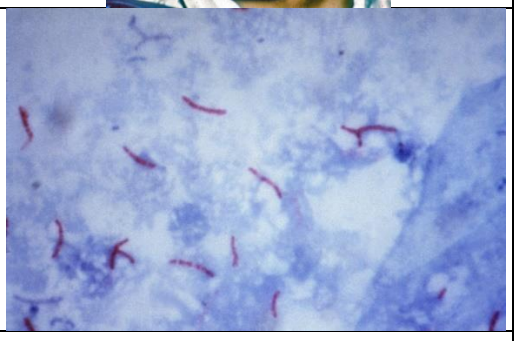
## Case 3

<table>
<tr><td colspan="2">70 year old man with malaise, anorexia loss of weight of 7kg over 1 month<br>Underwent Colonoscopy prior to symptoms onset, Watery diarrhea 4 times a day for 1 wk</td></tr>
<tr><td colspan="2">Fever, chills and headache for 3 days<br>Double vision for 2 days<br>Neck stiffness, jolt accentuation, 6th CN palsy</td></tr>
<tr><td>CSF<br>Cloudy<br>WBC: 1000 70% lymphocytes<br>Glucose: 50mg / dl<br>Protein: 170 mg<br>Gram positive bacilli</td><td>  </td></tr>
<tr><td>Listeria Monocytogenes</td><td>Risk groups:<br>age <1y or >50y<br>Alcoholicspregnancy: up to 30%<br>immunocompromised 70 %<br>Routes of transmission:<br>-mainly food borne<br>-transplacental /vertical<br>-Cross contamination(nursery)<br>-inoculation(skin) farmers<br>-<br>colo/sigmoidoscopy→bacteremia / meningitis ( up to 5% healthy :N flora)</td></tr>
</table>

***Listeria Monocytogenes*Meningitis Treatment:**

- **Ampicillin 2gm IV Q4h +/- Gentamicin 2mg/kg loading dose then 1.7mg/kg Q8h21 day duration**
- **Penicillin allergy patients: TMP-SMX or Meropenem**

## Case 4

<table>
<tr><td colspan="2">56 year old Indian man presented to the infectious disease clinic with low grade fever and night sweats for 6 wks and headache for 4 wks</td></tr>
<tr><td>T: 38.2 C, speaking well<br>Opthalmoplegia<br>Neck stiffnes<br>bilateralpapillodema</td><td>  </td></tr>
<tr><td>CSF:<br>xanthocromic<br>wbc 340 L: 85 %<br>protein 1.5g<br>sugar 25 mg<br>+ve AFB</td><td>  </td></tr>
<tr><td>TB meningitis</td><td>AFB: diagnostic yield increase to 87% when four serial specimensexamined<br>use last fluid & large volume (10 to 15 mL)<br>Culture: gold standard<br>PCR: NAAT sensitivity %56 percent and specificity 98%)</td></tr>
</table>

**Antibiotic Chemotherapy:**

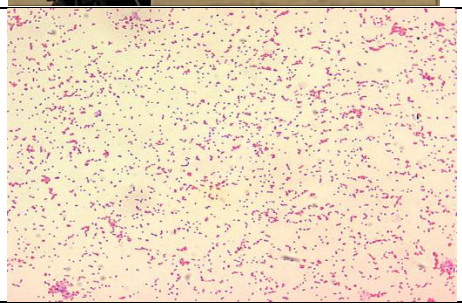
CSF concentrations:

- INH, Pyrazinamidine, pass freely into the CSF
- Rif has 10% the concentration as in Plasma
- Streptomycin or ethionamide do not pass BBB in absence of inflammation.

Dexamethasone in TB meningitis:

- Dexamethasone was started as soon as possible after the start of antituberculosis treatment
- Treatment with dexamethasone is associated with a reduced risk of death

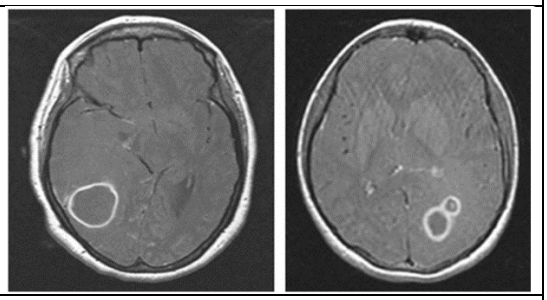
## Case 5

<table>
<tr><td colspan="2">30 y Saudi sheep herder with 3 weeks headache blurred vision</td></tr>
<tr><td>Looks uncomfortable, Temp 38.1<br>Jolt accentuation present</td><td>  </td></tr>
<tr><td>CSF<br>pleocytosis 105 mostly lymphocytes<br>Blood culture grew Brucella spp<br>Brucella titre 1:320<br>Brucella PCR in CSF poistive</td><td>  </td></tr>
<tr><td>Brucella</td><td>Treatment: Doxycycline, Rifampin, TMP-SMX</td></tr>
</table>

## Case 6

<table>
<tr><td colspan="2">32 HIV positive gentleman with 3 weeks history of forgetfulness change in personality , Presents with generalized seizure to ER</td></tr>
<tr><td>After ABC and stabilization CT done</td><td>  </td></tr>
<tr><td colspan="2">CD4: 77, VL 1 340 324<br>Toxoplasma IgG poitive<br>Brain Bx: ToxplasmaGondii</td></tr>
<tr><td>ToxplasmaGondii</td><td>Treatment: Pyrimethamine + sulfadiazine + folinic acid</td></tr>
</table>

## Case 7

<table>
<tr><td colspan="2">46 gentleman with fever for 1 weekHeadache for 3 days , Prosthetic AVR 6 years ago</td></tr>
<tr><td colspan="2">Fever 39.1, Stiff neck</td></tr>
<tr><td>Blood Culture: staphylococcus Aureus<br>TEE: vegetation aortic valve<br>Drainage of brain abscess: MSSA</td><td>  </td></tr>
<tr><td>staphylococcus Aureus</td><td>Treatment: Cloxacillin, flagyl</td></tr>
</table>

# MCQs

**1-** A 35-year-old previously healthy man develops cough with purulent sputum over several days. On presentation to the emergency room, he is lethargic. Temperature is 39°C, pulse 110, and blood pressure 100/70. He has rales and dullness to percussion at the left base. There is no rash. Flexion of the patient's neck when supine results in spontaneous flexion of hip and knee. Neurologic examination is otherwise normal. There is no papilledema. A lumbar puncture is performed in the emergency room. The cerebrospinal fluid (CSF) shows 8000 leukocytes/µL, 90% of which are polys. Glucose is 30 mg/dLwith a peripheral glucose of 80 mg/dL. CSF protein is elevated to 200 mg/dL. CSF Gram stain is pending. Which of the following is the correct treatment option?

a. Begin acyclovir for herpes simplex encephalitis.

b. Obtain emergency MRI scan before beginning treatment.

c. Begin ceftriaxone and vancomycin for pneumococcal meningitis.

d. Begin ceftriaxone, vancomycin, and ampicillin to cover both pneumococci and Listeria.

e. Begin high-dose penicillin for meningococcal meningitis.

**2-**A 50-year-old woman is on high-dose corticosteroids and immunosuppressives because of renal transplant rejection. She presents with a 10-day history of fever, headache, and confusion. Lumbar puncture reveals 25 lymphocytes per microliter and a very high CSF protein. India ink stain is positive. What is the most likely diagnosis?

a. Pneumococcal meningitis
b. Cryptococcal meningitis
c. Coxsackievirus (aseptic) meningitis
d. Pyogenic brain abscess
e. Listeria monocytogenes meningitis
f. Herpes simplex encephalitis
g. Cerebral cysticercosis

**3-** what is the most accurate test of herpes encephalitis?

a. brain biopsy
b. PCR of CSF
c. MRI
d. Viral culture of CSF
e. Tzanck prep
f. Serology for herpes (IgG, IgM)

**4-**A woman is admitted for herpes encephalitis confirmed by PCR. After 4 days of acyclovir her creatinine level begins to rise. What is the most appropriate next step in management?

a. Stop acyclovir.
b. Reduce the dose of acyclovir and hydrate.
c. Switch to oral famciclovir or valacyclovir.
d. Switch to foscarnet.

Answers: 1-C 2-B 3-B 4-B

# Answers

**1-The answer is c**.This previously healthy male has developed acute bacterial meningitis as evident by meningeal irritation with a positive Brudzinski sign, and a CSF profile typical for bacterial meningitis (elevated white blood cell count, high percentage of polymorphonuclear leukocytes, elevated protein, and low glucose). The patient likely has concomitant pneumonia. This combination suggests pneumococcal infection. Because of the potential for beta-lactam resistance, the recommendation for therapy prior to availability of susceptibility data is ceftriaxone and vancomycin. Though herpes simplex can be seen in young healthy patients, the clinical picture and CSF profile are not consistent with this infection. The CSF in herpes simplex encephalitis shows a lymphocytic predominance and normal glucose. Listeria monocyto-genes meningitis is a concern in immunocompromised and elderly patients. Gram stain would show gram-positive rods. Neisseria meningitidis is the second commonest cause of bacterial meningitis but rarely causes pneumonia (the portal of entry is the nasopharynx). Although penicillin G still kills the meningococcus, empiric therapy should cover all likely pathogens until Gram stain and culture results are available. Because the patient has no papilledema and no focal neurologic findings, treatment should not be delayed to obtain an MRI scan.

**2- The answer is b**. The patient on high-dose corticosteroids with a positive CSF India ink stain has cryptococcal meningitis. Cryptococcal meningitis patients usually have a lymphocytic meningitis, with a very high CSF protein and low CSF sugar. Cryptococcal meningitis usually begins insidiously with headache and mental status changes. Bacterial or viral (aseptic) meningitis and herpetic encephalitis typically have a more acute onset.

**3- The answer is b.** PCR is more accurate than a brain biopsy. Serology for herpes is useless; 95% of the population will be positive, since blood serology cannot distinguish oral herpes from a routine cold sore, genital herpes, or encephalitis. Tzanck prep can be done as the initial test on a genital ulcerative lesion. Viral culture is the most accurate test of genital or skin lesions, but not of CSF or the brain.

**4- The answer is b.** Oral medications such as famciclovir and valacyclovir are insufficient for herpes encephalitis. Although acyclovir may occasionally be renal toxic because the medication precipitates in the renal tubules, foscarnet has far more renal toxicity.

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