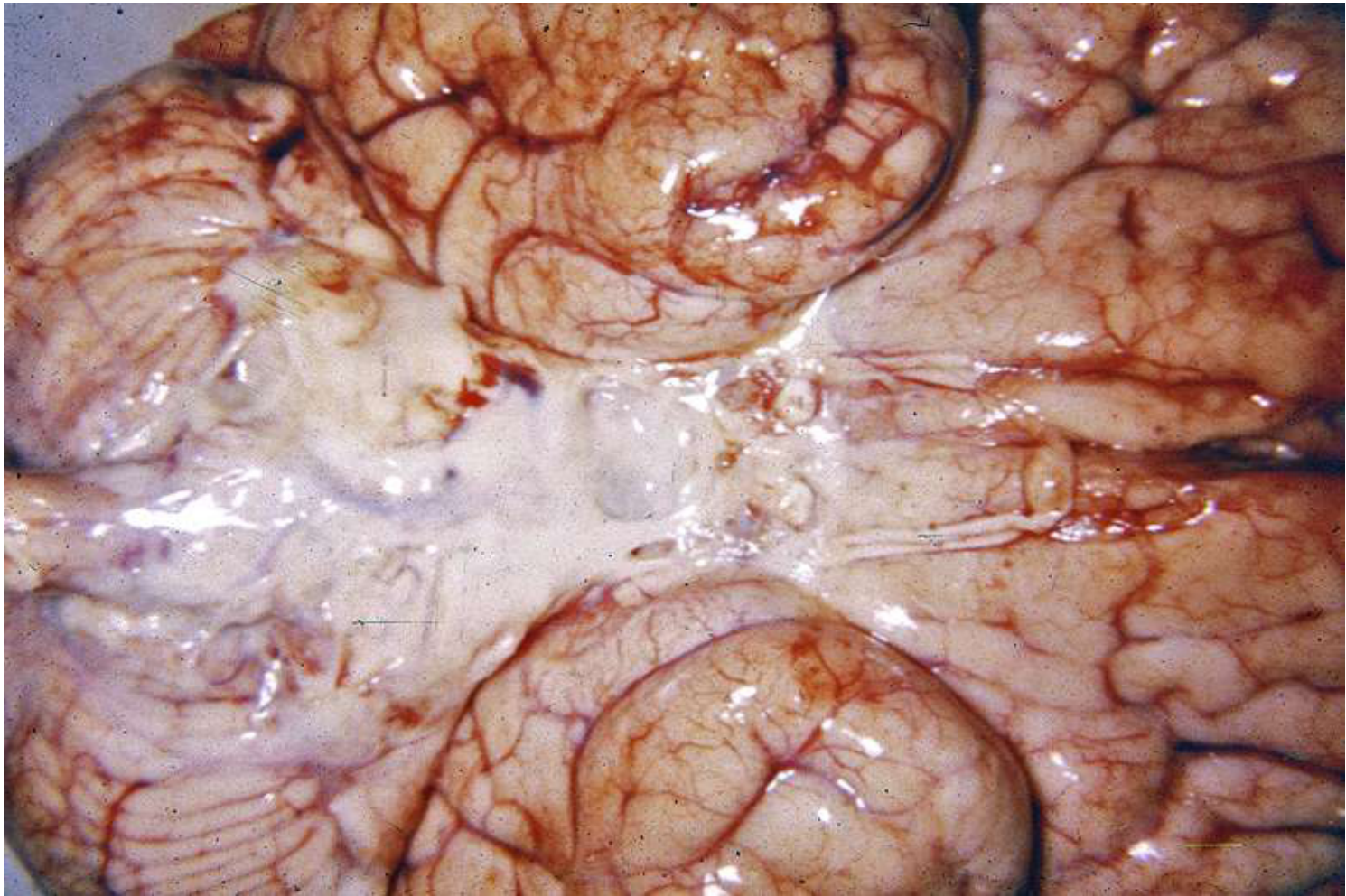


CNS Infections

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Meningitis

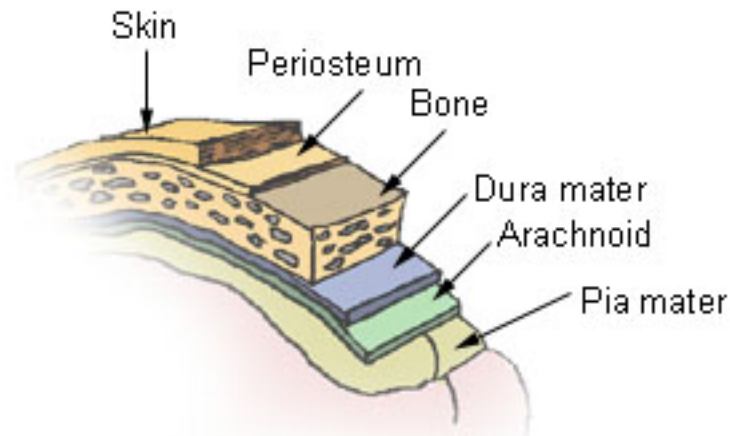


Definitions

- Meningitis – inflammation of the meninges
- Encephalitis – infection of the brain parenchyma
- Meningoencephalitis – inflammation of brain + meninges
- Aseptic meningitis – inflammation of meninges with sterile CSF
- Meninges?

Meninges

- Meningitis: inflammation of the pia mater and the arachnoid matter, with suppuration of the cerebrospinal fluid



Meninges of the CNS

CAUSES OF MENINGITIS

INFECTIOUS	NON-INFECTIOUS
Viral	Aseptic Meningitis
Bacteria	Malignancy
Mycobacterial	Sarcoidosis
Brucella	behcet disease
Fungal	SLE

Encephalitis/Encephalopathy

- Herpes simplex: PCR, Acyclovir
- Arboviruses: e.g dengue
- Rabies
- Rare: *Listeria*, cat scratch disease, amebic



Aseptic Meningitis

- **CSF: pleocytosis 100s, Norm G &P, Neg Culture**
- Enteroviruses: most common cause 80%
- HSV-2
- Dengue, Zika, Chikungunya, yellow fever
- HIV
- Partial Rx Bacteria
- Drugs: Metronidazole, TMP-SMX, NSAIDs, carbamazepine, IVIG
- Rare: leptospirosis (spirochaete)

Symptoms of Bacterial Meningitis

- High grade sudden fever
- Severe Headache
- Altered level consciousness, irritability, photophobia
- Vomiting
- Seizures
- Stiff neck
- Bulging fontanel in infants

Signs

- Vital signs: **Fever**
- Nuchal rigidity
- Kerning's sign: while patient is lying supine, with the hip and knee flexed to 90 degrees pain limits passive extension of the knee
- Brudzinski's sign: flexion of the neck causes involuntary flexion of the knee and hip
- Papilledema
- Neurological deficit
- Don't forget source of infection: ears, sinuses, chest..etc
- Petechiae, ecchymosis

Signs

- 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 and Brudzinski signs have low sensitivity but high specificity

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**

JAMA Does this adult patient have acute meningitis?

Complications

- Hydrocephalus
- Seizures
- SIADH
- Subdural effusions & empyema
- Septic sinus or cortical vein thrombosis
- Arterial ischemia / infarction (inflammatory vasculitis)
- CN Palsies (esp deafness)
- Septic shock / multi-organ failure from bacteremia (esp meningococcus & pneumococcus)
- Risk of adrenal hemorrhage with hypo-adrenalism (Waterhouse-Friderichsen syndrome)

Investigations

- CBC, Creat, lytes: Na
- Blood Culture
- CXR
- CT Head
- **CSF analysis**

Remember to be careful:

- ↑ ICP may increase risk of herniation
- Cellulitis at area of lumbar puncture
- Bleeding disorder

Before a lumbar puncture.....

- Generally, patients with suspected meningitis require brain imaging before the LP
 - Warning signs that mandate an image:
 - Altered consciousness
 - Focal neurological deficits
 - Papilledema or cranial nerve palsies
 - Seizure
 - Neurological deficits

CSF analysis

- Appearance, opening pressure
- Cell count with differential
- Glucose, protein
- CSF appearance
- **Gram stain**
- **Culture**

- TB AFB smear PCR and culture
- Brucella serology and PCR
- HSV PCR
- Multiplex viral PCR
- Cryptococcus antigen

Bacterial Meningitis

TABLE IV

CFS FINDINGS SUGGESTING BACTERIAL MENINGITIS
WHEN INITIAL GRAM STAIN IS NEGATIVE¹

CSF leukocyte count $> 1,000/\text{mm}^3$

CSF leukocyte count $> 100 \text{ mm}^3$, of which > 50 per cent neutrophils

CSF glucose $< 30 \text{ mg/dl}$

CSF glucose/blood glucose ratio < 40 per cent

CSF protein $> 200 \text{ mg/dl}$

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.

Bacterial Pathogens

Neonates

- Group B *Streptococci* 49%, *E coli*, enterococci, *Klebsiella*, *Enterobacter*, *Samonella*, *Serratia*, *Listeria*

Older infants and children

- *Neisseria meningitidis*, *S. pneumoniae*, *M.tuberculosis*, *H. influenzae*

Causes of Bacterial meningitis in Adults

- ▣ *Streptococcus pneumoniae*.....37%
- ▣ *Neisseria meningitides*.....13%
- ▣ *Listeria monocytogenes*....10%
- ▣ Other strept.species.....7%
- ▣ Gram negative.....4%
- ▣ *Haemophilus influenzae*.....4%
- ▣ TB, Brucella

Keep in mind

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

Bacterial Meningitis - Empiric Treatment (Gram stain Negative)

- **Remember MENINGEAL DOSES**
- Ceftriaxone 2gm IV Q12h
 - High CSF levels
- Vancomycin 500-750mg IV Q6h (highly penicillin resistant *pneumococcus*)
- Dexamethasone (0.15mg/kg IV Q6h) for 2-4 days :
1st dose 15-20 min prior to or con-comitant with
1st dose Abx to block TNF production
- Ampicillin (for *Listeria*)

Management Algorithm for Adults

Suspicion of bacterial meningitis

YES

new onset seizure, papilledema, altered level of consciousness, or focal neurological deficit or delay in performance of diagnostic L.P

NO

Blood c/s & Lumbar puncture

Dexamethasone + empirical Abx

CSF is abnormal

YES

+ve CSF gram stain

NO

Dexamethasone +
empirical Abx

YES

Dexamethasone +
targeted Abx

YES

B/C stat

Dexamethasone + empirical Abx

-ve CT-scan of the head

Perform L.P

Meningococcus

- **Fulminate meningococccemia 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

Epidemiological Features of *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

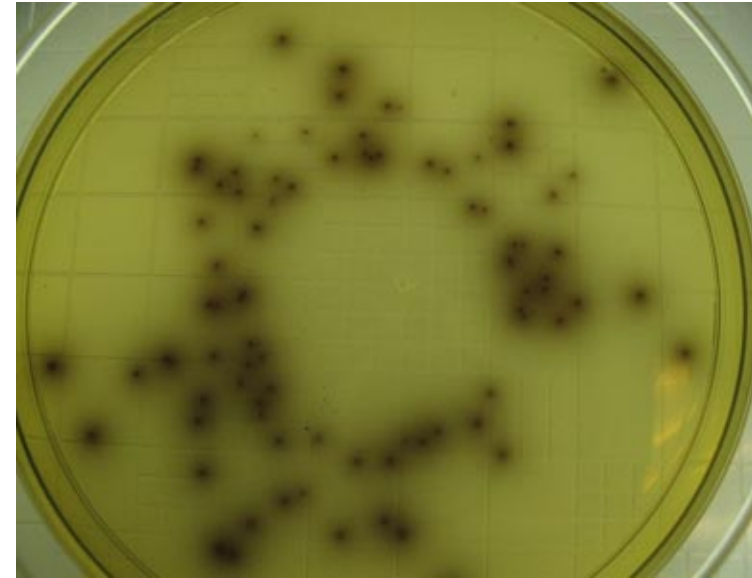
Listeria Monocytogenes

Risk groups:

- Age <1y or >50y
- Alcoholics
- Pregnancy: up to 30%
- Immunocompromised 70 %

Routes of transmission:

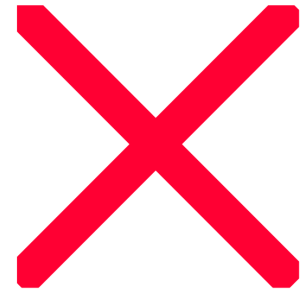
- Mainly food borne: survives refrigeration
linked to poultry, hotdogs, cold cuts, coleslaw, ice-cream
- Transplacental /vertical
- Cross contamination(nursery)
- Inoculation(skin) farmers
- Colo/ sigmoidoscopy → bacteremia / meningitis (up to 5% healthy:
Normal flora)
- Inform micro lab: special media (Mueller-Hinton agar)



Listeria Monocytogenes Meningitis

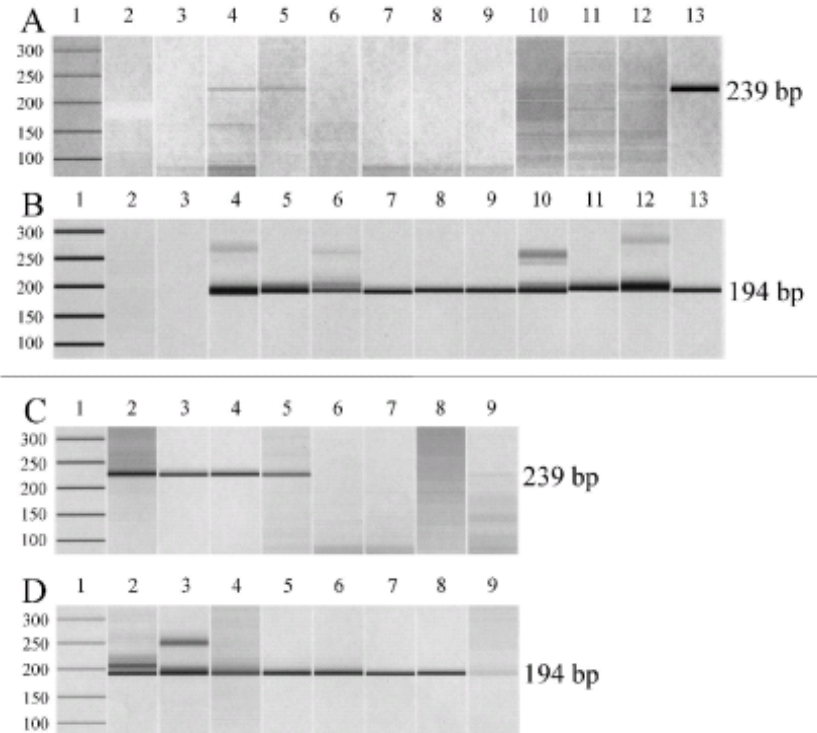
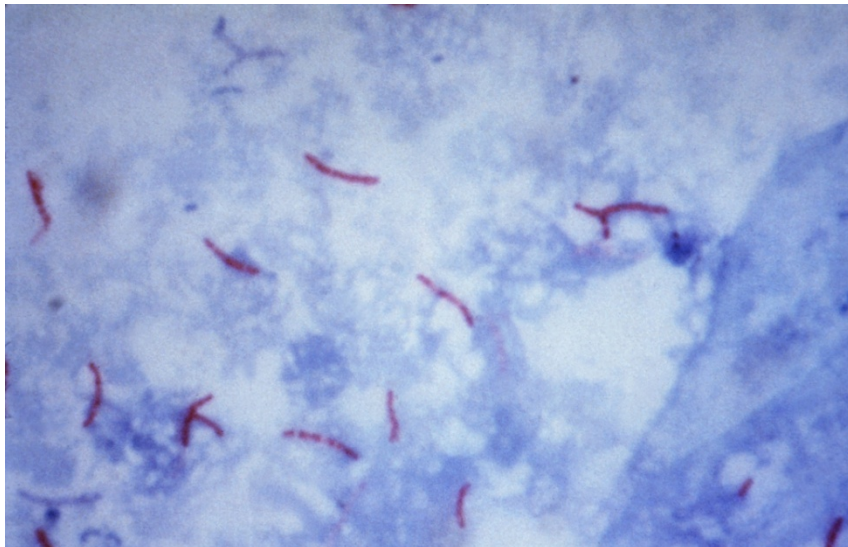
Treatment

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



What Other Test?

- AFB: diagnostic yield increase to 87% when four serial specimens examined
- Use last fluid & large volume (10 to 15 mL)
- Culture: gold standard
- PCR: NAAT sensitivity %56 percent and specificity 98%



Antibiotic Chemotherapy

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^{66,67}

CSF concentrations:

- INH, Pyrazinamide, 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 Pyridoxine with INH Therapy

Tuberculous meningitis: many questions, too few answers

Neurobrucellosis Treatment

- Doxycycline 100mg IV/po bid
- Rifampin 600-900mg po od
- Ceftriaxone 2gm IV q12h
- Duration?
 - Continue until CSF is normal (3-12 months)

CNS Toxoplasmosis in HIV/AIDS

- Treatment:
 - Pyrimethamine 200mg once po then 75mg od
 - Sulfadiazine 1.5gm po Q6h
 - Folinic acid 25mg po od
- Duration?
 - Minimum 6 wks after resolution of signs/symptoms

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

Primary Prophylaxis

- TMP-SMX-DS 1 tab po od
 - Sulfa allergy:
- Dapsone and pyrimethamine and folinic acid
- Atovaquone 1500mg po od
- Can stop if CD4 > 200 for 3 months

Brain Abscess

- Organisms:
 - *Streptococci* (60-70%), *Bacteroides* (20-40%), *Enterobacteriaceae* (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
- Abx same as brain abscess