Microbiology of CNS infections - 2

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- A 40 year old patient presented to the ward with severe headache, vomiting and high fever for 5 days duration. On examination he looked ill, and had neck stiffness.
  - Probable Diagnosis?
  - Etiology?
  - Diagnosis?
    - Samples
    - Method
    - CSF profile
  - Management?

- A three weeks old neonate was admitted with excessive crying, irritability, and poor feeding.
  Meningitis was suspected.
  - Etiology?
  - Diagnosis?
    - Samples
    - Method
    - CSF profile
  - Management?

Objectives

- Types of CNS infections
- Aetiological agents
- Pathogenesis
- Presentations
- Laboratory diagnosis
- Management

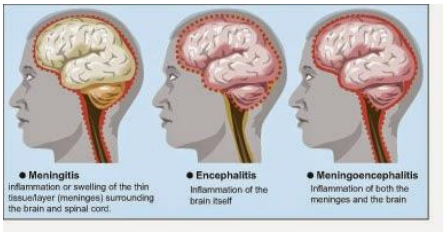
CNS infections

- Meningitis
- Encephalitis
- Brain/spinal abscess

CNS infections

- Bacterial
- Viral
- Fungal
- Parasitic

Meningitis Vs Encephalitis



MENINGITIS

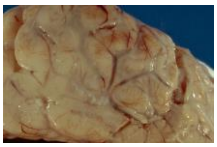
A medical emergency!

Meningitis

- Inflammation of meninges due to an infection
- Pathogens enter meninges
  - Via Blood/ lymphatics
  - Following trauma/ surgery
  - Via peripheral nerves
- Symptoms can be
  - Acute
  - Chronic

Bacterial meningitis

- Purulent infection within the subarachnoid space
  - Acute
  - Chronic



Acute Bacterial meningitis

- Aetiological agents
  - *Streptococcus pneumoniae*
  - *Haemophilus influenzae B*
  - *Neisseria meningitidis*
  - *Streptococcus agalactiae*
  - *Listeria monocytogenes*
  - Coliforms
    - *E. coli*
    - *Klebsiella*

Aetiologies according to age and risk factors

- <1 month
  - .....
- 1–23 months
  - .....
- 2–50 years
  - .....
- >50 years
  - .....
- Immuno-compromised

.....

Basilar skull fracture- .....
Penetrating trauma- .....
Post-neurosurgery- .....
CSF shunt- .....

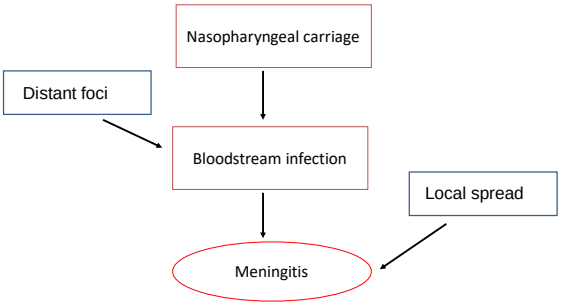
Reference: IDSA guidelines for meningitis

Bacterial meningitis - pathogens

- Acute
  - Neonates
    - Group B Streptococcus, *E.coli, Listeria*
  - Children and adults
    - *Streptocccus pneumoniae, Haemophilus influenzae, Neisseria meningitidis*
- Chronic
  - TB (*Mycobacterium tuberculosis*)

Entry of bacteria into meninges

- Haematogenous
  - Distant foci - e.g lung (Streptococcus pneumoniae)
  - Nasopharyngeal carriage (carriers) (Neisseria, Haemophilus)
- Local spread
  - middle ear, nasal sinus, osteomyelitis (*Haemophilus, S. pneumoniae*)
- Abnormal routes
  - Trauma –fractures
  - Surgery - shunts



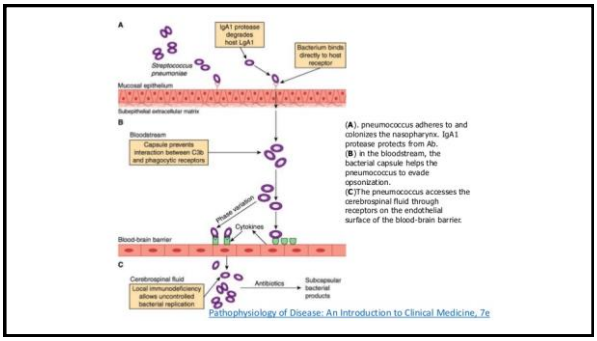



Fig. 110 Haemorrhagic rash (adult with meningitis).

Chronic meningitis

- Bacterial
  - *Mycobacterium tuberculosis*
- Fungal
  - *Cryptococcus neoformans*

TB meningitis

- Has a high frequency of neurologic sequelae and mortality if not treated promptly
- Increased risk for TBM
  - young children with primary TB
  - patients with immunodeficiency caused by aging, malnutrition, HIV, cancer

Presentation

- low-grade fever, malaise, headache, dizziness, vomiting, and/or personality changes

↓

persist for few weeks

↓

- then develop more severe headache, altered mental status, stroke, hydrocephalus, and cranial neuropathies
- seizures are commonly seen in children (50%)
- Classic features of bacterial meningitis, such as stiff neck and high fever may be absent.

Cryptococcal meningitis

- Acquired by inhalation
- Cryptococcus shows a predilection for the central nervous system
- Commonly seen in immuno-compromised patients

Clinical presentations

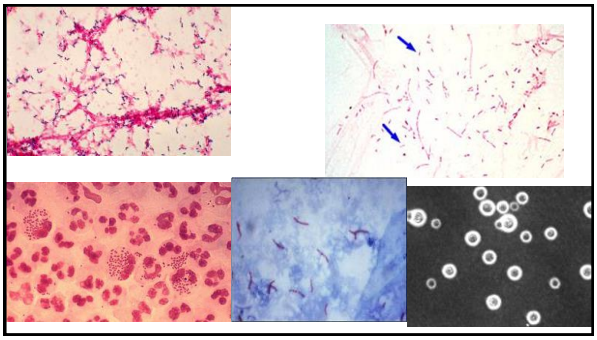
- Meningitis, meningoencephalitis or expanding cryptococcoma
- Symptoms usually develop slowly over several months
- Cryptococcoma is characterized by localized, solid, tumor-like masses, usually found in the cerebral hemispheres or cerebellum

Laboratory diagnosis of meningitis

- Specimens- CSF, Blood
- Collection
  - Aseptic procedure – Ex. skin decontamination, sterile equipment/drapes
  - Container – Ex. sterile, screw capped for culture
    - sugar bottle, full count, protein
  - Labelling, request form
- Transport
  - Room temp, ASAP, inform lab
- Storage – room temp

Laboratory diagnosis of meningitis

- Methods
  - Direct smear and gram stain of CSF and blood
    - ICGND – Neisseria
    - GPC in chains – Pneumococci(Diplo) , Group B Strep
    - GNCB – *H. influenzae*
    - GNB- Coliforms
  - AFB stain - TB
  - India ink stain
    - Cryptococcus
  - CSF full report
    - Turbidity, cells, proteins, glucose (compare with serum glucose)

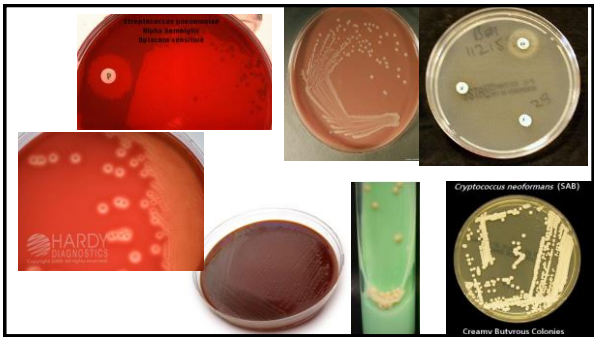


Laboratory diagnosis of meningitis

- Culture
  - Blood culture
  - CSF culture

  } on blood agar, chocolate agar, MacConkey agar

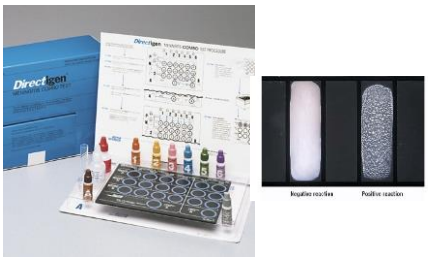
  - TB culture
  - Fungal culture



Laboratory diagnosis of meningitis ctd…

- CSF antigen detection – Latex agglutination
  - For Hib, *N. meningitidis*, *S. pneumoniae*, E.coli, Group B strep
- PCR
  - Multiplex PCR – acute viral and bacterial meningitis
  - TB PCR – (Sensitivity 54-100%, specificity 94-100%)

CSF Ag detection kit



CSF Abnormalities in Meningitis
CSF full report

Condition	Appearance	Cells/cu mm	Gram	Protein	Glucose
Normal	Clear, colourless	0-5 lymphocytes			
Bacterial	Cloudy, turbid	100-2000 polymorphs	Orgs	High	Low
'Aseptic' (viral)	Clear, slightly cloudy	10-500 lymphocytes		Normal	Normal
TB	Clear, slightly cloudy	10-500 lymphocytes		High	Low
Cryptococcal	Clear	10-200 lymphocytes		Normal, slightly elevated	Normal, slightly reduced

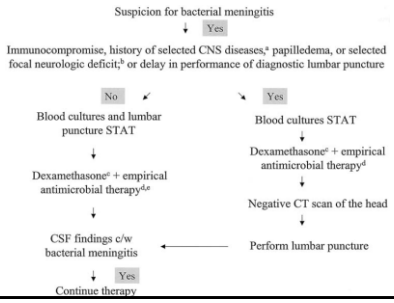
CSF abnormalities in Acute bacterial meningitis

- ↑ opening pressure
- ↑ WBC (>10000 wbc/mm^3, mainly PMN)
- ↓ glucose (less than 40% of serum glucose)
- ↑ Protein
- Positive gram stain/culture in 70-90%
  - Less if antibiotics are started before LP

Normal CSF glucose is about two thirds of the serum glucose measured during the preceding two to four hours in a normal adult

Protein concentration is falsely elevated by the presence of RBCs in a traumatic tap situation. This can be corrected by subtracting 1 mg per dL (0.01 g per L) of protein for every 1,000 RBCs per mm3

Management algorithm



Empirical antibiotics for acute bacterial meningitis

Age group	Antibiotic
0-3 months	Penicillin/ Ampicillin + cefotaxime
3 months to 65 years	Cefotaxime/ Ceftriaxone +/- Vancomycin
>65 years & other risk factors	Ampicillin + Cefotaxime/ ceftriaxone +/- vancomycin
Trauma/ surgery/ shunt	Ceftazidime + Vancomycin
Dexamethasone 8-10mg (child:0.15mg/kg up to 10mg) IV, starting before or with the first dose of antibiotic, then 6 hourly for 2-4 days	

Antibiotic treatment

- *S. pneumoniae*- IV penicillin
  - 3rd gen ceph +/- Vancomycin
  - x 10-14 days
- *Neisseria meningitidis* – IV Penicillin or
  - 3rd gen ceph
  - x 5-7 days
- *H. influenzae* – 3rd gen ceph
  - x 7 days
- *Listeria monocytogenes* - Ampicillin or IV penicillin
  - x>21 days
- Group B strep - Ampicillin or IV penicillin
  - x 14-21 days
- Coliform - 3rd gen ceph
  - x 21 days

Meningitis Prophylaxis

- **Meningococcal Infection**
  - only for close contacts in the preceding seven days:
    - 1st line: Rifampicin 600mg every 12 hours for 4 doses
      2nd line: Ciprofloxacin 500mg po stat (if on OCP)
    - Pregnant – Ceftriaxone
- Hib meningitis
  - Unvaccinated or incompletely vaccinated children or persons at increased risk (e.g. asplenia or complement deficiency) in the household
  - Rifampicin 20mg/kg once daily for 4 days up to max of 600mg/day

Prevention of Bacterial Meningitis

Vaccination
- BCG
- Hib – incidence decreased by > 99%
- Polyvalent pneumococcal
- Meningococcal A & C

Perinatal Screening
- HVS for Group B Strep.
- Antepartum penicillin

Chemoprophylaxis

Brain abscess

- Begins as localized cerebritis (1-2 wks)
- Evolves into a collection of pus surrounded by a well-vascularized capsule (3-4 wks)

Pathogenesis

- Direct spread from contiguous foci (40-50%)
  - Infected bone, Otitis media/mastoiditis ,Sinusitis, Dental infection
- Hematogenous (25-35%)
  - Empyema, lung abscess, bronchiectasis, endocarditis, wound infections, pelvic infections, intra-abdominal source
- Penetrating trauma/surgery (10%)

MICROBIOLOGY OF BRAIN ABSCESS

AGENT	FREQUENCY (%)
Streptococci (*S. intermedius*,*S. milleri*)	60–70
Bacteroides and *Prevotella* spp.	20–40
Enterobacteriaceae	23–33
Staphylococcus aureus	10–15
Fungi*	10–15
Streptococcus pneumoniae	<1
Haemophilus influenzae	<1
Protozoa, helminths† (vary geographically)	<1

*Yeasts, fungi (*Aspergillus* Agents of mucor *Candida* Cryptococci Coccidiodoides *Cladosporium trichoides Pseudallescheria boydii)*
†Protozoa, helminths (*Entamoeba histolytica*, Schistosomes Paragonimus Cysticerci)

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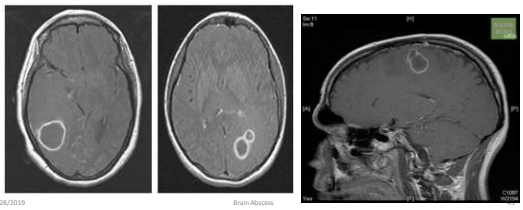
Presentation

- Non-specific symptoms
- Mainly due to the presence of a space-occupying lesion
  - H/A, fever, altered mental status, focal neuro signs, N/V, lethargy, seizures
- Signs/symptoms influenced by
  - Location
  - Size
  - Virulence of organism
  - Presence of underlying condition

Laboratory tests

- **Aspirate:** Gram/AFB/fungal stains & cultures, cytopathology (+/-PCR for TB)
- **WBC** Normal in 40% (only moderate leukocytosis in ~ 50% & only 10% have WBC >20,000)
- **CRP** elevated
- **ESR** Usually moderately elevated
- **BC** Often negative BUT *Should still be done*
- **LP** ***Contraindicated in patients with known/suspected brain abscess***
  Risk of herniation 15-30%
  If done, may have normal CSF findings, but:
  Usually elevated CSF protein & cell count (lymphs)
  Unremarkable glucose & CSF cultures rarely positive

Imaging



Treatment

- Combined medical & surgical
  - Aspiration or excision
  - empirical abx
- Empirical antibiotics are selected based on:
  - Likely pathogen (consider primary source, underlying condition, & geography)
  - Antibiotic characteristics: usual MICs, CNS penetration, activity in abscess cavity
- Duration: usually 6-8 wks

CSF shunt associated infections

- Pathogens
  - Biofilm forming organisms
    - CONS, MSSA, MRSA, *Pseudomonas aeruginosa*, Coliforms, Propionibacterium, Enterococci
  - Presentations
    - minimal ventriculitis without meningeal involvement /only mechanical blockage as a result of biofilm formation
    - Symptoms of meningitis +/-, more subtle with a longer duration of symptoms
    - peritonitis or pleuritis (VP shunts), Bacteraemia (VA shunts)
  - Diagnosis - CSF cultures from the shunt, CSf full report
  - Antibiotics- Vancomycin plus ceftazidime/ meropenem

Summary

- Types of CNS infections
- Aetiological agents
- Pathogenesis
- Presentations
- Laboratory diagnosis
- Management