CNS/SPINAL INFECTIONS

BACTERIAL MENINGITIS:

- The most common causes of bacterial meningitis are Streptococcus pneumoniae, Neisseria meningitides, Group B streptococcus, Haemophilus influenzae and Listeria monocytogenes (descending order of frequency)>
- Median ago of illness has risen to 39 and incidence has declined
- Expect changes in epidemiological pattern due to rise of immunisation against pneumococcus and meningococcus

PATHOPHYSIOLOGY:

- Pneumococcus, meningococcus and H. influenzae are all ENCAPSULATED → invade the host through the upper airway, survive bloodstream dissemination and then gain access to the subarachnoid space
- The capsule elements are PRO-INFLAMMATORY
- CSF drainage is reduced due to interference with flow and absorption by the arachnoid granulations from inflammatory milieu
- Eventually due the combination of ↑d CSF volume (from ↓d drainage), vasogenic oedema and cytotoxic oedema → ↑ ICP → ISCHAEMIC INJURY EVENTUALLY RESULTS
- Organisms can also gain entry to the CSF by DIRECT CONTIGUOUS SPREAD → brain abscess, otitis media and sinusitis or via TRAUMA/NEUROSURGERY
- Immunosuppression are increasingly common and predispose to yet other organisms
- List of risk factors shown below:

Table 168-1 Important Risk Factors for Bacterial Meningitis
Acute or chronic otitis media
Sinusitis
Immunosuppression/splenectomy
Alcoholism
Pneumonia
Diabetes mellitus
Cerebrospinal fluid leak
Pneumonia
Endocarditis
Neurosurgical procedure/head injury
Indwelling neurosurgical device/cochlear implant
Advanced age
Malignancies
Liver disease
Unvaccinated to *Haemophilus influenzae* type b, *Neisseria meningitidis*, or *Streptococcus pneumoniae*

- Special historical factors should raise your suspicion for meningitis and deserve special mention:
    - Liver disease
    - Trauma → Staph more common (includes neurosurgery)
    - Immunocompromise
    - Immunisation

- Antibiotics use → alters clinical course and findings
- Sinusitis or otitis

CLINICAL FINDINGS:

- Definitive diagnosis is based on demonstration of bacterial organisms and related inflammatory response in the CSF
- CLASSIC SIGNS AN SYMPTOMS:
  - Fever
  - Neck stiffness
  - Headache
  - Altered mental state → if only altered mental state → risk of meningitis is low
    - All of above usually present BUT THEIR ABSENCE DOES NOT EXCLUDE MENINGITIS
  - Seizures in 25%
  - Focal neuro signs → usually cranial nerve palsies
- EXAMINATION:
  - Assess for meningeal irritation:
    - Resistance to passive neck flexion
    - BRUDZINSKI SIGN → flexion of hips and knees in response to passive neck flexion
    - KERNIG SIGN → contraction of hamstrings in response to knee extension while hip is flexed
  - Look for purpura/petechiae
  - Fundi examination for papilloedema

TREATMENT AND DIAGNOSIS:

- When bacterial meningitis is suspected, TREATMENT SHOULD PRECEDE METHODS FOR DIANGOSIS (LP, IMAGING ETC)
- EMPIRIC TREATMENT FOR PRESUMED MENINGITIS:
  - First priority is administration of antibiotic that GAINS RAPID ENTRY TO THE SUBARACNOID SPACE and should be initiated ASAP without delay for imaging or LP

In **children 3 months or more and adults**, use:

dexamethasone 10 mg (child: 0.15 mg/kg up to 10 mg) IV, starting before or with the first dose of antibiotic, then 6-hourly for 4 days. Antibiotics should not be delayed if corticosteroids are not available [Note 1]

PLUS EITHER

1 **ceftriaxone 4 g (child: 100 mg/kg up to 4 g) IV, daily**
or ceftriaxone 2 g (child: 50 mg/kg up to 2 g) IV, 12-hourly

OR

2 **cefotaxime 2 g (child: 50 mg/kg up to 2 g) IV, 6-hourly.**

- Dexamethasone is given to suppress CNS inflammation and if given prior to or at the time of the first antibiotic dose it effectively reduces the MORBIDITY FROM BACTERIAL MENINGITIS from H. influenzae (less evidence for other organisms).

Listeria monocytogenes is resistant to cephalosporins. In patients who are immunocompromised, adults more than 50 years of age, patients with a history of alcohol abuse or patients who are pregnant or debilitated, to cover *Listeria*, **add** to the above regimen:

benzylpenicillin 2.4 g (child: 60 mg/kg up to 2.4 g) IV, 4-hourly.

- Beware penicillin in suspected pneumococcus as there are high levels of resistance (25-35%)

Add vancomycin if Gram-positive diplococci are seen or a pneumococcal antigen assay in CSF is positive, or if the patient has known or suspected otitis media or sinusitis or has been recently treated with a beta lactam [Note 2]. This is to ensure that *Streptococcus pneumoniae* isolates that display intermediate or higher resistance to penicillin and/or cephalosporins are adequately covered prior to the availability of culture and susceptibility results. Consider vancomycin also if Gram-positive cocci resembling staphylococci are seen, or if neutrophils are present but organisms are not seen, and if viral meningitis or meningococcal disease are unlikely. **Add**:

vancomycin 1.5 g (child less than 12 years: 30 mg/kg up to 1.5 g) IV, 12-hourly (adjust initial dosage for renal function and monitor blood concentrations, see Dosing and monitoring of vancomycin; slow infusion required).

- Note from above that the addition of vancomycin is recommended in patients with GRAM POSITIVE DIPLOCOCCI (I.E. PNEUMOCOCCUS) → high levels of intermediate sensitivity to cephalosporins

For patients with immediate penicillin or cephalosporin hypersensitivity (see Table 2.2), use:

1 **vancomycin 1.5 g (child less than 12 years: 30 mg/kg up to 1.5 g) IV, 12-hourly (adjust initial dosage for renal function and monitor blood concentrations, see Dosing and monitoring of vancomycin; slow infusion required)**

PLUS

ciprofloxacin 400 mg (child: 10 mg/kg up to 400 mg) IV, 12-hourly

OR

2 **moxifloxacin 400 mg (child: 10 mg/kg up to 400 mg) IV, daily.**

- CT SCAN BEFORE LP?
  - This practice has arisen due to the concern for BRAIN HERNIATION after LP in those with a space-occupying lesion → the incidence is UNKNOWN
  - NEXUS II CT database identified a prevalence of herniation or brain shift in those with documented normal neurologic examination
  - Recommendations for when to obtain a CT first are shown below:

Table 168-3 Some Suggested Criteria for Obtaining Head CT before Lumbar Puncture for Suspected Meningitis
Altered mental status or deteriorating level of consciousness[28]
Focal neurologic deficit
Seizure
Papilledema
Immunocompromised state
Malignancy
History of focal central nervous system disease (stroke, focal infection, tumor)
Concern for mass central nervous system lesion
Age >60 y[7]

- LUMBAR PUNCTURE:

- The diagnosis of meningitis is based upon CSF results → however any contraindication or impediment to performing an immediate LP requires initiation of empiric antibiotic therapy → THE THERAPEUTIC GUIDELINES ADVOCATE LP FIRST IF IT CAN BE PERFORMED WITHIN 30 MINUTES
- Typical findings of CSF for meningeal processes are shown below:

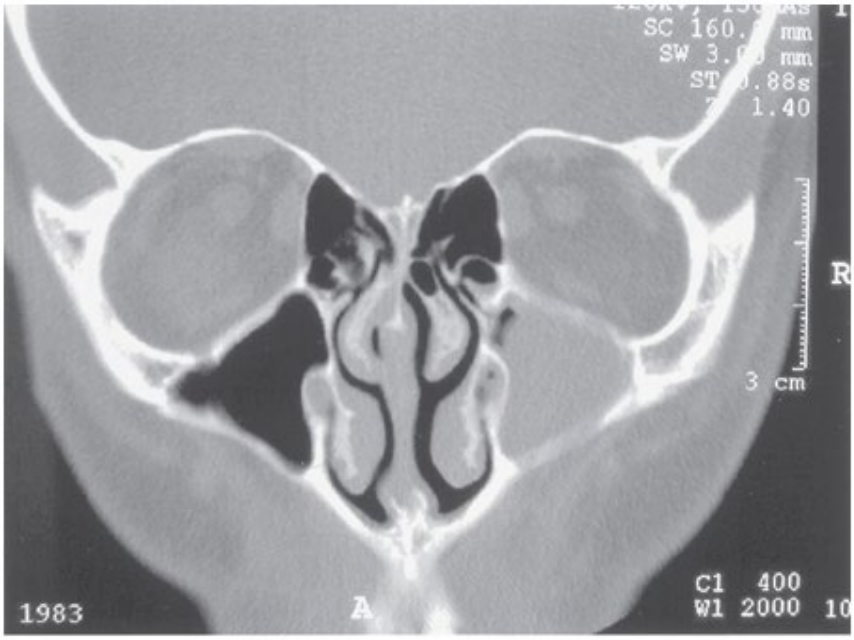
Table 168-4 Typical Spinal Fluid Results for Meningeal Processes

Parameter (Normal)	Bacterial	Viral	Neoplastic	Fungal
Opening pressure (<170 mm cerebrospinal fluid)	>300 mm	<300 mm	200 mm	300 mm
White blood cell count (<5 mononuclear)	>1000/mm3	<1000/mm3	<500/mm3	<500/mm3
% Polymorphonuclear cells (0)	>80%	1%–50%	1%–50%	1%–50%
Glucose (>40 milligrams/dL)	<40 milligrams/dL	>40 milligrams/dL	<40 milligrams/dL	<40 milligrams/dL
Protein (<50 milligrams/dL)	>200 milligrams/dL	<200 milligrams/dL	>200 milligrams/dL	>200 milligrams/dL
Gram stain (–)	+	–	–	–
Cytology (–)	–	–	+	+

- An aseptic profile can also be found in cases of partially treated bacterial meningitis (as well as viral)
- Sterilization of CSF if possible within 2 hours of initiating appropriate antibiotics → without antibiotics gram stain is ~60-90% sensitive and 97% specific for identifying the causative organism
- PCR now available has sensitivities and specificities of >90% for detection of the common bacterial pathogens
- Other tests:
  - INDIA INK FOR CRYPTOCOCCUS IN IMMUNOCOMPROMISED
  - Acid fast staining if TB considered

SPECIAL SITUATIONS:

- BACTERIAL MENINGITIS FROM OTITIS OR SINUSITIS:
  - About 10% cases overall thought to be due to sinusitis
  - SUBDURAL EMPYEMA AND CAVERNOUS SINUS THROMBOSIS can coexist with bacterial meningitis
  - These infections are POLYMICROBIAL → third generation cephalosporin and metronidazole as well as urgent ENT referral



Acute maxillary sinusitis on CT

- ADJUNCTIVE TREATMENTS IN MENINGITIS:
  - SEIZURES
  - Hyponatraemia → SIADH or cerebral salt wasting can develop
  - Hydrocephalus
  - Hyperpyrexia
  - ↑'D ICP → mannitol 0.5-1g/kg
- CHEMOPROPHYLAXIS TO THOSE EXPOSED TO BACTERIAL MENINGITIS:
  - HIGH RISK → those exposed to confirmed meningococcus within the preceding 7 days → RIFAMPICIN 10MG/KG (UP TO 600MG) BD FOR FOUR DOSES, ALTERNATIVE IS CIPROFLOXACIN
  - Seek advice from public health

VIRAL MENINGITIS:

- A number of viruses can cause meningitis → non-polio enteroviruses, mumps, CMV, HSV, adenovirus, HIV
  - Non-polio enteroviruses (echovirus, coxsackie and enterovirus) account for ~85% of cases of viral meningitis
- Although CSF findings often make the diagnosis straightforward, there is considerable overlap in CSF findings
- Prudent to treat with empiric antibiotics until culture results return
- TREAT WITH ACYCLOVIR 10MG/KG Q8H

VIRAL ENCEPHALITIS:

- Viral encephalitis is a viral infection of brain parenchyma that produces an inflammatory response (often coexists with viral meningitis) → the distinction can be made by the presence of a distinct neurologic abnormalitiy in encephalitis, whereas meningeal symptoms and signs occur in meningitis

- Common causative viruses → HSV-1, HZV, EBV, CMV (rabies and arbovirus in America)

PATHOPHYSIOLOGY:

- Entry portals are highly specific for the causative viruses → impaired immune status plays a role in HZV and CMV
- Most viruses reach the CNS by haematogenous spread, but HSV, VZV have novel modes of entry via retrograde spread from the spinal cord
- Grey matter is predominantly effected → results in cognitive and psychiatric signs as well as lethargy and seizures

CLINICAL FEATURES:

- Encephalitis should be considered in patients presenting with the following features (either alone or in combination):
  - New psychiatric symptoms
  - Cognitive deficits (aphasia, amnestic syndrome, acute confusional state)
  - Seizures
  - Movement disorders
  - Features of meningeal involvement (fever, meningism) are usually (but not always) present → should seek signs of meningeal irritation and ↑d ICP
- HSV involves limbic structures (frontotemporal predilection) → prominent psychiatric features, memory disturbance, aphasia)

DIAGNOSIS:

- Rests on imaging studies using MRI or CT, as well as EEG and LP
- Neuroimaging excludes abscess, but also may display findings highly suggestive of HSV encephalitis such as involvement of temporal and inferior frontal grey matter (THIS IS CRUCIAL AS HSV IS A TREATABLE CONDITION)
- Findings of viral meningitis on LP are typical → it is possible to have encephalitis without meningitis, but it is quite rare

TREATMENT:

- In HSVVZV → see algorithm below:

For adults and children in suspected or proven cases, use:

aciclovir 10 mg/kg IV, 8-hourly for at least 14 days (adjust dose for renal function, see Table 2.31).

- For those with CMV encephalitis → ganciclovir 5mg/kg q12h
- Prognosis depends on the host and the causative virus
  - Patients who are already in a coma do VERY POORLY → a timely diagnosis is crucial in HSV

<u>BRAIN ABSCESS:</u>

PATHOPHYSIOLOGY:

- A brain abscess is a focal pyogenic infection
- Organisms reach the brain by ONE OF THREE ROUTES:

- Contiguous infection of the middle ear, sinus or teeth (1/3)
    - Gram-negatives (Bacteroides) play a large role in otogenic brain abscesses
    - Anaerobic and microaerophilic streptococci are most common in sinogenic and odontogenic abscesses (frontal lobe predominance)
- Direct implantation by trauma or neurosurgery (10%) → STAPH
- Haematogenous spread (33%)
    - Often multiple and polymicrobial
- Cause unknown in 20%

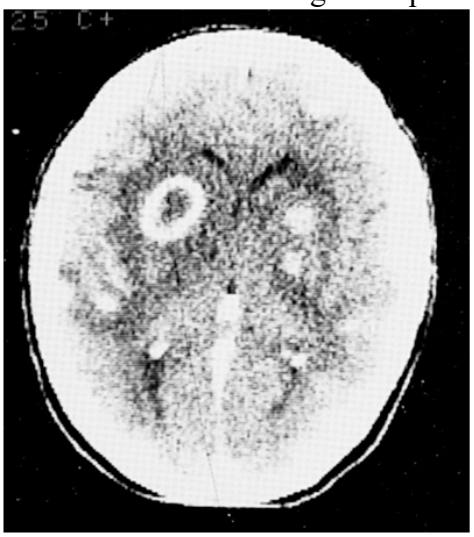
- Circumstances that reduce brain oxygenation are important → anaerobic bacteria play a prominent role

CLINICAL FEATURES:

- Nonspecific
- CLASSIC TRIAD (headache, fever and focal neurology) → present in less than 33%
- Rarely appear acutely ill
- Symptoms reflect the infectious neurological aspects of the disease
- Headache present in almost ALL CASES
- Fever in less than 50%
- Focal neurological symptoms → HEMIPARESIS, SEIZURES → ≤1/3
    - Focal neuro signs reflecting site of abscess → 60% cases
- Symptoms of ↑ICP → obtundation, confusion, vomiting in 50% cases
- Presentation may be dominated by origin of infection
- Meningism seen in <50%

DIAGNOSIS:

- Diagnosed by imaging studies → CT with contrast classiclally demonstrates smoothly contoured rings of enhancement surrounding a low-density centre and surrounding white matter oedema
- LP avoided when focal neuro signs are present



Ring-enhancing lesion of a brain abscess

TREATMENT:

metronidazole 500 mg (child: 12.5 mg/kg up to 500 mg) IV, 8-hourly

PLUS EITHER

1 **ceftriaxone 4 g (child: 100 mg/kg up to 4 g) IV, daily**
or ceftriaxone 2 g (child: 50 mg/kg up to 2 g) IV, 12-hourly

OR

2 **cefotaxime 2 g (child: 50 mg/kg up to 2 g) IV, 6-hourly.**

- **URGENT NEUROSURGICAL REFERRAL → ASPIRATION TO GUIDE CLINICAL MICROBIOLOGY IS ESSENTIALY. ANTIBIOTICS REMAIN CORNERSTONE OF TREATMENT**

For postneurosurgical brain abscess, use:

vancomycin 1.5 g (child less than 12 years: 30 mg/kg up to 1.5 g) IV, 12-hourly (adjust initial dosage for renal function and monitor blood concentrations, see Dosing and monitoring of vancomycin; slow infusion required)

PLUS EITHER

1 **ceftazidime 2 g (child: 50 mg/kg up to 2 g) IV, 8-hourly**

OR

1 **meropenem 2 g (child: 40 mg/kg up to 2 g) IV, 8-hourly.**