

Description

Meningitis is an inflammation of the leptomeninges and underlying subarachnoid CSF.

Classification

Two main syndromes:

- Purulent meningitis
 - Cloudy/polymorph-filled CSF, almost always bacterial
- Aseptic meningitis
 - Meningitis with non-purulent CSF and negative standard bacterial cultures
 - Includes:
 - Viral (most common)
 - Partially treated or early bacterial meningitis
 - Other infective & non-infective causes

NB. Encephalitis - aseptic CSF + severely disturbed LOC

Pathogenesis

In infective meningitis organisms local colonization (e.g. nasopharynx) occurs first, then access to CNS is usually via invasion of the bloodstream (i.e. bacteremia, viremia, fungemia, or parasitemia) and subsequent haematogenous seeding and crossing of BBB. Occasionally access may be by retrograde neuronal (e.g. olfactory and peripheral nerves) pathway or by direct contiguous spread (e.g. sinusitis, otitis media, congenital malformations, trauma, or surgery). In bacterial meningitis, cell wall toxins (e.g. exotoxin of Gram neg, or Gram pos components such as teichoic acid) cause endothelial damage and also incite cytokine production which further damages/opens up the endothelium thus allowing BBB breach and leakage of fluid as well as thrombosis. These lead to increased ICP and cerebral oedema which cause reduced cerebral perfusion and the neuro sequelae.

Epidemiology

- Viral - most common ~11 per 100,000
- Bacterial - 2-3 per 100,000 and falling with ↑vaccination
- Sex: Overall M > F
- Age:
 - 90+% are <5yrs old - in particular infants whose immature immune system poorly recognizes the polysaccharide coated bacteria.
 - Second peak for meningococcus in late teens-young adults
 - Hib rare over 5yrs and with completed immunization.
- More common in Winter

Risk factors:

- CSF shunts or dural defects
- Spinal procedures
- Splenectomy / asplenia / sickle-cell disease
- GBS pos mother for neonate
- Crowding, smoking - college student/young adults
- Other risk factors include bacterial endocarditis, DM, alcoholism and cirrhosis, IVDA, OM/sinus/orbital infections, renal insufficiency, adrenal insufficiency, malignancy (↑risk of Listeria infection), hypoparathyroidism, thalassaemia major and CF

Causes

Purulent (Bacterial) Meningitis

- Birth to ~2 months: Group B streptococcus, *E. Coli* & other G-ve organisms, *Listeria monocytogenes*, *strep. faecalis*, plus those for...
- Infants & young children: *Neisseria meningitides* (A-sub-Saharan Africa, B-most in Aus, C-most virulent, but now vaccine, W-135 & Y-both USA), *Streptococcus pneumoniae* (increasingly resistant to penicillin & cefotaxime), *Haemophilus influenzae* type b
- Adults & older children: As for young children and staphylococci, streptococci and *Listeria monocytogenes*
- Elderly & immunocompromised: Pneumococcus, *Listeria monocytogenes*, TB, Gram -ves.
- Hospital acquired and post-traumatic meningitis (may often be multi-drug-resistant), *Klebsiella pneumoniae*, *E.coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*

Infective aseptic meningitis

- Viral - Many, commonly: Coxsackieviruses, Echoviruses, Polioviruses, Enteroviruses, Arboviruses. Less commonly: Mumps, Herpes viruses (HSV, CMV, EBV, HHV6, HHV7, varicella), HIV (immunocomp), measles, influenza, adenoviruses and others.
- Vaccines: MMR, Polio, Rabies
- Partly treated bacterial meningitis.
- Other possible causative organisms include
 - Nonpyogenic bacteria (atypical mycobacteria, *Leptospira*, syphilis, Lyme disease)
 - Atypical organisms (*Chlamydia*, *Rickettsia*, *Mycoplasma*)
 - Parasites (worms, amoebae, *Toxoplasma*)
 - Fungi (*Candida*, *Cryptococcus neoformans*, *Histoplasma*, immunocompromised)

Non-infective aseptic meningitis

- Kawasaki disease. (no proven infective organism)
- Malignant cells (leukaemia, lymphoma, other tumours)
- Chemical meningitis (intrathecal drugs, contaminants)
- Drugs (NSAIDs, trimethoprim)
- Sarcoidosis
- Systemic lupus erythematosus
- Behcet's disease

Presentation - NB partial treatment by GP antibiotics may mask some features

Neonate/young infant:

Often non-specific. May have fever or hypothermia, bulging fontanelle, irritability, high pitched cry, altered mental state, lethargy, seizures, apnoea, poor feeding, vomiting.

Older children/adults:

More likely to have some CNS specific signs (elderly may have fewer signs):

- Meningism:
 - Headache
 - Neck stiffness (60-80%, esp >3yrs)
 - Kernig's (pain/resistance on knee extension) & Brudzinski's (hip flexion on neck flexion) signs - present in 50%
 - Photophobia (80%)

- Raised ICP
 - Headache
 - Irritability, lethargy or altered mental state (highly variable)
 - Nausea and/or vomiting
 - Focal deficits (10-20%) or seizures (30-40% in children, 20-30% in adults)
 - Papilloedema (late) sign (33%)
- Fever (50-80% bacterial, 30-40% viral cases)
- Classic triad of headache/fever/neck stiffness present in 50%.
- Almost all have 2 from headache/fever/neck stiffness/altered LOC.
- 25% bacterial cases present <24h, viral more often sub-acute over 1-7 days.
- Septicaemia
 - Malaise, fever, arthritis
 - Rash - petechial (but often absent or macular esp <12-24hrs)
 - Meningococcal early red flags: limb pain, cold peripheries, abnormal skin colour

Differential diagnosis

- Other sepsis
- Encephalitis
- Cerebral abscess
- SAH, SDH
- Other causes of altered mental state and coma, e.g. HI, NAI, SOL, drug ingestion

Investigations

Vital signs - TPR + BP, BSL, GCS

Urine - culture +/- GBS antigen test

Bloods: FBC, UEC, glucose, CRP, (procalcitonin), Coags (if rash), cultures (before ABx), serology (syphilis, N. meningitidis & viral), PCR

Imaging - CT if HI, DDx, or ?↑ICP

Lumbar puncture (not if fitting, focal neuro, obtunded/GCS<8 or falling rapidly, Cushing reflex, papilloedema) & CSF testing: cytology, biochem, culture & PCR (See separate article)

Consider: CXR (if ?lung abscess, TB), nasal swabs and stool (virology), skin scraping

Management of bacterial meningitis

Steroids

- Shown to reduce hearing complications in children (proven in Hib, maybe in pneumococcus)
- Rationale: steroids reduce cytokine storm initiated by early ABx bactericidal effect
- Reduce morbidity & mortality in adults for pneumococcus, less evidence in children.
- Dose: **dexamethasone** 0.15mg/kg to 10g q6h IV x 4 days at or before the first ABx.
- Avoid/no clear benefit: <2 mo, severe sepsis, presenting late, in developing countries, immunocompromised, meningitis following surgery

Antibiotics for 7-10 (meningococcus, Hib), 10-14 (pneumococcus) or 21+ days (neonatal)

- Prehospital: **Benzylpenicillin** 300mg (<1y), 600mg (≤10y) or 1.2g (>10yrs) IV/IM
- Empirical at hospital:
 - **Cefotaxime** 50mg/kg to 2g q6h (or if >3mo **ceftriaxone** 50mg/kg to 2g bd) IV
 - If <3-6mo, >15yr or immunocomp: **Ampicillin** 50mg/kg to 2g q4-6h or **benzylpenicillin** 60mg/kg to 2.4g q4h IV (for *Listeria*)
 - If pneumococcus (?resist.) or no LP add **vancomycin** 15mg/kg (max 500mg) q6h IV

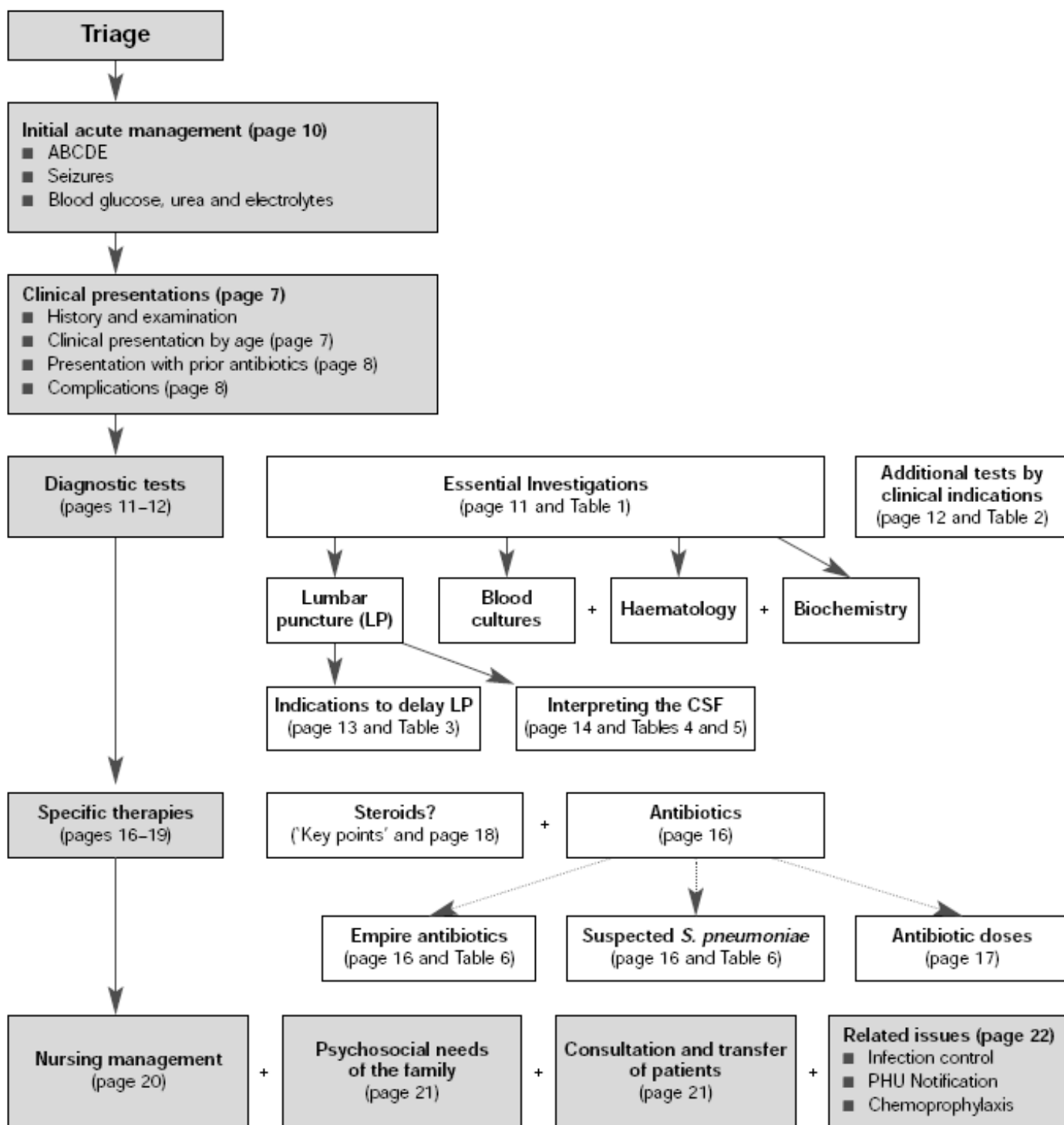
Other microbials as indicated: e.g. **amphotericin B ± flucytosine** (Cryptococcus)

Supportive - Antipyretic/analgesic for comfort, Fluids - if septicaemic may require large volumes, otherwise take care not to exacerbate any SIADH or cerebral oedema

Specific for immediate complications:

- Correct electrolyte imbalances, SIADH (30%)
- Fits (30%) - standard management
- Rising ICP, falling LOC - intubate & ventilate
- Shock (10%) - volume expansion, inotropes
- Coagulopathy, DIC - FFP, cryoprecipitate

Management Flowchart



Complications

- Haemolytic anaemia (Hib).
- Subdural effusions: reported in 40% of children <18mo with bacterial meningitis. Risk factors include young age, rapid onset of illness, low blood WCC and high CSF protein.
- Other: decreased hearing or deafness, other cranial nerve dysfunction, multiple seizures, focal paralysis, hydrocephalus, intellectual deficits, ataxia, blindness, Waterhouse-Friedrichsen syndrome, and peripheral gangrene.

Prognosis

- Excellent with aseptic/viral meningitis - full recovery is the norm.
- Treated bacterial meningitis still has mortality of 10-30%. Worst with pneumococcus
- 30% survivors have long term effects
- Meningococcal disease has a better prognosis if meningitis accompanies septicaemia due probably to the fact that they have survived long enough to develop the meningitis which is secondary to the bacteraemia.

Prevention

Vaccination: Vaccines based on polysaccharide capsule component. Conjugate vaccines boost immunogenicity & memory of vaccine by linking the polysaccharide to an immunogenic protein carrier e.g. tetanospasmin (also called tetanus toxoid), mutant diphtheria protein, and meningococcal group B outer membrane protein. Available vaccines:

- Haemophilus type b - only conjugate vaccines available now
- Pneumococcus - polysaccharide: 23-valent, conjugate: 7, 10, 13-valent,
- *N. meningitides* - polysaccharide: A, C, W135, Y, conjugate: C.
 - No vaccine for B whose polysaccharide capsule resembles brain glycoproteins.

Public health notification

Close contact treatment:

- Meningococcus chemoprophylaxis (include patient if only had penicillin):
 - **Rifampicin** 600mg (child 10 mg/kg, infants 5 mg/kg) PO bd x 2 days.
 - **Ciprofloxacin** 500 mg (child 5-12 years 250 mg) PO stat.
 - **Ceftriaxone** (preferred for pregnant women) 250mg (child 125 mg) IM/IV stat.
- Hib chemoprophylaxis (include patient):
 - If <4y **Rifampicin** 600mg (child ≤3mo: 10 mg/kg, >3mo: 20 mg/kg) PO od x 4 days.
 - **Ceftriaxone** (preferred for pregnant women) 250mg (child 125 mg) IM/IV stat