Bacterial Meningitis and Brain Abscess
[CNS Symposium]
Dr David Enoch, March 2014

Meningitis

- Viruses are the commonest overall (enteroviruses, HSV, mumps, measles - see later).
- **Clinical symptoms, signs.** Frequently there’s a 2-3 day prodrome of mild upper respiratory tract illness, including sore throat.
  - **Non specific:** headache, fever, photophobia, neck stiffness, Kernig’s sign, Brudzinski’s sign, disturbed conscious level, fits.

- **Petechial or purpuric rash** suggests meningococcal septicaemia --> give immediate IM/IV benzylpenicillin or ceftriaxone.

- A much less acute onset and more chronic course tend to be seen with mycobacteria and *Cryptococcus* meningitis.

- Important distinction between meningism (which is a constellation of symptoms and signs which can accompany focal infections elsewhere (eg childhood UTI), or irritation of the meninges by an adjacent infection (eg brain abscess); and meningitis (which implies an inflammatory process of the meninges with a cellular reaction, but may be clinically unsuspected in neonatal, elderly, and paralysed/ventilated patients where clinical symptoms referable to the meninges may be absent).

Many bacteria occasionally cause meningitis, and there are no hard-and-fast rules, but there are some important age-related associations:

<table>
<thead>
<tr>
<th>Neonate</th>
<th>Infancy - 6y</th>
<th>Young adult - middle aged</th>
<th>Elderly</th>
</tr>
</thead>
</table>
| **Common** | *Streptococcus agalactiae* (Gp B streptococcus).  
*Escherichia coli* (type K1). | *Neisseria meningitidis*. | *Streptococcus pneumoniae*. |
| **Rare** | *Streptococcus pneumoniae*.  
*Listeria monocytogenes*.  
*Salmonella* (3rd World).  
Other coliforms (especially in premature babies on SCBUs). | *Streptococcus pneumoniae*.  
*Neisseria meningitidis*.  
*Haemophilus influenzae* type b. | *Listeria monocytogenes*.  
*Listeria monocytogenes*. |
| **Sources** | Maternal genital tract.  
"Maternal septicaemia.  
Cross-infection on SCBU from other babies via staff hands. | Droplet spread to colonize upper respiratory tract, then haematogenous spread to involve meninges.  
** from food. | |
Other causes & predispositions:

- **Systemic infections** – e.g. leptospirosis, syphilis, Lyme disease, *Staph. aureus* septicaemia etc. in which the meninges are involved as part of a generalised infection.

- **Trauma** - sinus mucosa source (streptococci, anaerobes, haemophilus), skin source (*Staph. aureus*, coagulase-negative staphylococci)

- **Neurosurgery** - as traumatic associations above, plus shunt-associated infection (especially coagulase-negative staphylococci), and pseudomonas acquired from wet sources in theatre or post-operatively on the ward via CSF drains.

- **Immunocompromised patients** - the common possibilities, plus *Cryptococcus neoformans, Listeria monocytogenes*, and mycobacteria. Compliment deficient patients (very rare) get recurrent meningococcal meningitis. Recurrences also seen with CSF leaks and congenital meningeal deficiencies.

- **Immigrants from developing world, homeless, elderly** - think of TB.

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**Cases of meningococcal meningitis & septicaemia:** **Dr Barker** to present.

**Histopathology of bacterial meningitis:** **Dr Dean** to present.

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**General features of management:**

1. **CSF examination.**
   - Perform an LP unless the patient has septicaemic shock (especially with DIC/thrombocytopenia) or there is evidence of a mass lesion in CNS causing raised intracranial pressure and shifting brain substance (-> risk of 'coning').
   - Consider performing an urgent CT scan
   - Send 3 tubes of CSF (>5ml; >10ml if TB suspected), consecutively labelled - a traumatic tap shows as reducing redness, while a subarachnoid haemorrhage gives constant redness. CSF opening pressure is raised in meningitis.

- a **Gram stain of the CSF** enables rapid identification of the specific cause as long as bacteria are seen.

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Acute bacterial</th>
<th>Viral</th>
<th>TB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>Gin clear (xanthochromia after subarachnoid haemorrhage).</td>
<td>Turbid.</td>
<td>Usually clear, occasionally slightly turbid.</td>
<td>Often slightly turbid. Occasionally has a 'spider web' clot.</td>
</tr>
<tr>
<td>Cells</td>
<td>&lt;5 polymorphs or monocytes.</td>
<td>Usually 500 - 10000 polymorphs (+ some monocytes)</td>
<td>Usually 50 - 1000 monocytes.</td>
<td></td>
</tr>
<tr>
<td>Bacteria</td>
<td>None.</td>
<td>Usually readily identifiable on Gram stain, unless partially treated.</td>
<td>None.</td>
<td>Sometimes seen on careful searching of Auramine-stained CSF.</td>
</tr>
<tr>
<td>Protein</td>
<td>&lt;0.4 g/l</td>
<td>Usually raised.</td>
<td>Sometimes raised.</td>
<td>Usually raised.</td>
</tr>
</tbody>
</table>
Glucose | >50% of blood glucose. | Low. | Normal. | Low.

- In the very early stages of viral and TB meningitis there can be a predominance of polymorphs. After a few days of treatment of acute bacterial meningitis a monocyte predominance develops.
- CSF cell count is often moderately raised with other causes of meningeal irritation (subarachnoid haemorrhage, encephalitis, brain abscess).
- Latex agglutination tests on CSF for bacterial capsular antigens (meningococci, pneumococci, haemophilii) are now recognized as diagnostically almost useless - Gram-stain is more sensitive + specific.

2. **Blood tests.**
   a) **Blood culture.** *Always* do a blood culture when meningitis is suspected.
   b) **EDTA blood.** For meningococcal and pneumococcal PCR
   c) **Blood glucose.** To compare with CSF level - in most cases of bacterial meningitis the CSF glucose is less than 50% of the simultaneous blood level.
   d) Full blood count + differential, clotting studies (if Disseminated Intravascular Coagulation is suspected), renal function, inflammatory markers.

3. **Other tests.** Done selectively according to likelihood of specific causes - see below.

4. Meningitis is a **notifiable disease.**

**Empirical Treatment of Acute Meningitis:**

- High-dose IV ceftriaxone if cause uncertain.
- Add amoxicillin if *Listeria* is a reasonable possibility (immunosuppressed, age >60).
- See below for specific therapy if cause is known or likely.
- Use chloramphenicol and vancomycin if the patient is known to be cephalosporin-allergic / anaphylaxis to penicillin (rare).

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**Notes on specific causes: (see overleaf for box on meningococcal infection)**

**Pneumococcal meningitis:** Associated sometimes with pneumococcal pneumonia, otitis media or endocarditis; also sometimes with skull fracture. Treat with benzylpenicillin or ceftriaxone (penicillin-resistance currently uncommon (1 - 5%) in UK but increasing). Poor prognosis overall, especially if there are many pneumococci and few polymorphs in CSF. Pneumococcal vaccine is protective (covers commonest 23 capsular types; give to elderly, asplenic, chronic illness, immunocompromised). Consider HIV test

**Haemophilus influenzae capsular type B meningitis:** Pleomorphic Gram-negative rod; non-capsulate strains cause exacerbations of chronic bronchitis in adults. Often produce beta-lactamase (hence often amp/amoxicillin resistant). Treat with ceftriaxone. Grows best on chocolate agar; 'satellite' colonies around *Staph. aureus*. Also causes epiglottitis, cellulitis, sinusitis in children. Commonest in ages 6 months to 6 years; great reduction since introduction of Hib vaccine at 2, 3 and 4 months. Give 4 days rifampicin (alternatives ciprofloxacin, ceftriaxone) prophylaxis to all members of a family when there is a case and the family has other children under the age of 4.

**Meningitis in the immunocompromised:** see Immunocompromised and HIV lectures. Send CSF for India Ink stain and cryptococcal antigen (CrAg) for *Cryptococcus neoformans*. **Think of TB.**

**Suspected viral meningitis:** send i) throat swab and faeces in virus transport medium and ii) serum for acute titres. See virology section of this symposium + tutorial.
Neisseria meningitidis (‘meningococcus’) systemic infection

Neonatal meningitis: see Neonatal Infection lecture.
**Invasive meningococcal disease – *Neisseria meningitidis***

Fastidious Gram negative coccus (usually diplococci seen).  
Remains reliably penicillin sensitive in UK (resistance rising in S. Africa, Spain).  
15% normal people carry non-capsulate strains in nose and throat.  
- commoner in young adults, upon ‘crowding’ (e.g. barracks, universities), and during outbreaks.

Capsulate pathogenic types A, B, C, W135, Y.  
- A rare in UK, but epidemics in Africa etc.  
- B commonest in UK (immunologically unstable capsule).  
- C was rising in UK, but now falling precipitously with vaccine introduction.

Now 2500 cases in England & Wales per annum; rising; local clusters.  
Commonest in winter. See graphs.

**Spectrum of illness:**
**Most cases**

<table>
<thead>
<tr>
<th>Meningitis</th>
<th>Septicaemia</th>
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<tbody>
<tr>
<td>fever, headache,</td>
<td>Mixtures are necrotizing rash, common.</td>
</tr>
<tr>
<td>photophobia,</td>
<td>hypotension, collapse,</td>
</tr>
<tr>
<td>few spots, low mortality.</td>
<td>ARDS, peripheral gangrene: high mortality</td>
</tr>
</tbody>
</table>

Can be very rapid progression in some septicaemic cases - one of the few microbiological emergencies. Overall 5-10% mortality.

Early im benzyl-penicillin by the GP improves survival (but reduces culture-positivity).

Mechanism of pathogenesis = endotoxin --> lymphokines --> destroy capillary barriers ( --> cerebral oedema, hypovolaemic shock, rash etc.).

“Waterhouse-Friedrichsen Syndrome” is just one manifestation of this microvascular damage - the patients have HIGH steroid levels, and die rapidly because of leaky capillaries; they don’t die from the adrenal damage.

**Improve diagnostic rate:**  
- Nose + throat swabs for meningococci.  
  - Scrape skin lesions --> Gram stain, culture.  
  - PCR for meningococcal DNA on CSF, blood (EDTA sample).  
  - Serology for type-specific antibody.

**Further management:**  
- high-dose iv benzylpenicillin for ≥5 days.  
  - support circulation, multi-organ failure.  
  - 2 days rifampicin to case to clear carriage from nasopharynx.  
  - sequelae: deafness, learning difficulties, peripheral gangrene.

**Public health measures:** - notification to local Consultant in Communicable Disease Control (CCDC), who liaises with GPs about prophylaxis and vaccination of contacts.

- 2 days rifampicin prophylaxis to household and kissing contacts (only to medical contacts if they’ve had mucosal contamination). Alternatives are ciprofloxacin or ceftriaxone.  
- consider vaccination of contacts if not type B.  
- late 1999 introduction of conjugated group C vaccine in UK first to toddlers and pre-university students; now to all 14 months to 14 years.
Some further reading on meningitis:
Cartwright & Kroll. Optimising the investigation of meningococcal disease. *BMJ 1997; 315*: 757-8; and also in the same issue pages 774-9.

### Brain abscess.

Up to 80% cases have a predisposing cause or source identifiable, and knowing the bacteria involved may suggest the source if you know the body's normal flora:

<table>
<thead>
<tr>
<th>Recent neurosurgery</th>
<th>Just like a surgical wound infection (may involve staphylococci, or throat/sinus flora).</th>
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</thead>
<tbody>
<tr>
<td>Local parameningeal infection</td>
<td>Sinusitis, otitis, mastoiditis, dental abscess - abscesses occur in adjacent areas of brain (involve mucosal anaerobes, oral streptococci, coliforms).</td>
</tr>
<tr>
<td>Distant infection with haematogenous spread</td>
<td>Lung abscess, empyema, neglected appendicitis, endocarditis (involve anaerobes, streptococci).</td>
</tr>
<tr>
<td>Cranial trauma</td>
<td>Skin or mucosal flora, plus external inoculation from environment.</td>
</tr>
</tbody>
</table>

- 50% cases involve mixtures of bacteria.
- Risk is greatly increased by congenital heart disease with right --> left shunts.

**Presentation:** intracranial mass effects + raised intracranial pressure.

**Differential diagnosis:** tuberculosis or cryptococcoma; toxoplasmosis or PML in AIDS; and various others including Aspergillus, Nocardia, hydatid disease and neurocysticercosis (i.e. pork tapeworm).

**Investigations:**
- CT scan, with enhancement.
- CSF unhelpful and lumbar puncture can lead to 'coning'.
- Blood culture.
- Culture other possible sources.

**Principles of management:**
- Consider aspiration (ask a neurosurgeon’s opinion); Gram-stain and culture of aspirate.
- Ceftriaxone + metronidazole IV empirically, then be guided by culture results.
- Consider meropenem in immunosuppressed
- Control cerebral oedema.

**Further reading on brain abscess:**
Computer-based learning resources on CNS infection

http://www2.provlab.ab.ca/bugs/webbug/virbug/ent1.htm

http://www2.provlab.ab.ca/bugs/webbug/moleculr/entpcr.htm

are good for enterovirus diagnosis in meningitis.

See the up-to-date UK epidemiology of meningitis and meningococcal disease and current clinical advice at the HPA site:

http://www.hpa.org.uk/infections/topics_az/meningo/menu.htm

Some up-to-date epidemiological information on meningococcal meningitis, and detailed background on the new Group C vaccine strategy:

http://www.aldesurg.enta.net/Meningitis/MenC.htm

[All web links checked 11/03/04]