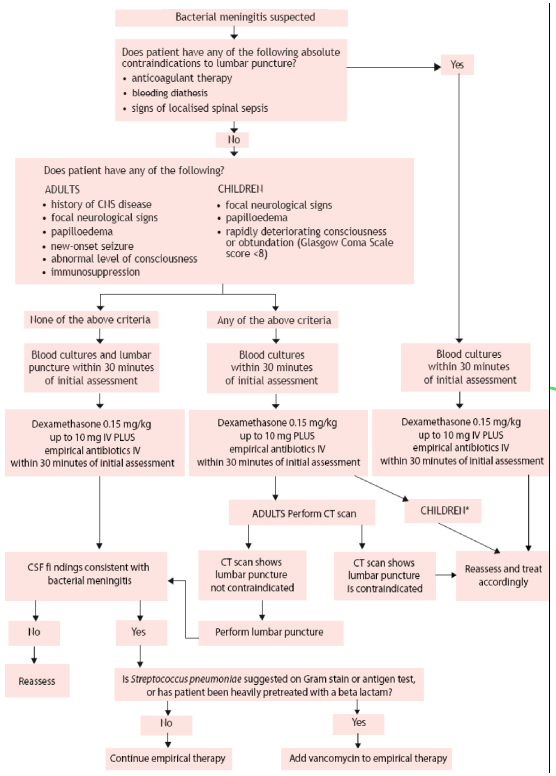
bacterial meningitis [created by Paul Young 27/11/07]



treatment

empirical therapy

1. If the organism or susceptibility is not known, empirical therapy should cover the most common pathogens.
In patients over 3 months of age, use:
(i) 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
(ii) cefotaxime 2 g (child: 50 mg/kg up to 2 g) IV, 6-hourly.
2. Listeria monocytogenes is resistant to cephalosporins. If the patient is immunosuppressed or Listeria infection is suspected, add to the above regimen either:
(i) benzylpenicillin 2.4 g (child: 60 mg/kg up to 2.4 g) IV, 4-hourly
OR
(ii) amoxy/ampicillin 2 g (child: 50 mg/kg up to 2 g) IV, 4-hourly.
3. Add vancomycin if Gram-positive diplococci are seen or a pneumococcal antigen assay in CSF is positive, or if the patient has been heavily pretreated with a beta lactam (eg for recurrent ear infections). 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. Use:
(i) vancomycin 12.5 mg/kg up to 500 mg (child <12 years: 15 mg/kg up to 500 mg) IV,
6-hourly (monitor blood levels and adjust dose accordingly; slow infusion required).
- Cease vancomycin if an organism likely to be susceptible to ceftriaxone/cefotaxime is isolated or if a penicillin-susceptible pneumococcus (MIC <0.125 mg/L) is isolated.

- For neonates and infants under 3 months, the likely organisms are Streptococcus agalactiae, enteric Gram-negative rods or, rarely, Listeria monocytogenes. Treat as for severe sepsis in children under 6 months of age in whom meningitis has not been excluded. Intravenous treatment should continue for a minimum of 2 weeks. Repeat lumbar puncture(s) are usually done to directly assess bacteriological response.

For patients with immediate penicillin or cephalosporin hypersensitivity, use:
(i) vancomycin 12.5 mg/kg up to 500 mg (child <12 years: 15 mg/kg up to 500 mg) IV, 6-hourly
PLUS
(ii) ciprofloxacin 400 mg (child: 10 mg/kg up to 400 mg) IV, 12-hourly
OR
(iii) moxifloxacin 400 mg (child: 10 mg/kg up to 400 mg) IV, daily.

corticosteroids

general
- much of the morbidity of bacterial meningitis is caused by the vigorous host inflammatory response which may be blocked by corticosteroids
- animal studies have shown improvement in outcome when corticosteroids are given as adjuvant therapy with antibiotics

paediatrics:
- children receiving concomitant dexamethasone and antibiotics have decreased morbidity particularly hearing loss; however, in these studies the majority of cases were due to H. influenzae which is a rare cause of meningitis in developed countriessince the introduction of vaccination and questions remain regarding the utility of steroids for other pathogens

adults:
- a randomised controlled trial found a significant reduction in both morbidity and mortality among adults receiving combination therapy with antibiotics and dexamethasoneparticularly among the subgroup with pneumococcal meningitis (in this study most infections were due to penicillin sensitive pneumococci and patients were treated with aminopenicillins)
- evaluation of steroid use for resistant pneumococci has not been performed; however, data that demonstrate reduced vancomycin levels in the CSF when this antibiotic is administered with steroids have raised concern about adjuvant therapy when cephalosporin resistant pneumococci are prevalent
- the dose of dexamethasone is 10mg iv Q6hrly for 4 days in adults

- in the studies in both children and adults, both steroids and antibiotics were given simultaneously and it is unknown whether beneficial effects remain when steroids are delayed

general

- bacterial meningitis is a pyogenic infection of the cerebral ventricles and the subarachnoid space with bacteria usually confined to the nutrient rich cerebrospinal fluid
- brain parenchyma is usually not affected in uncomplicated bacterial meningitis (even when the illness follows a fulminant course)
- exceptions occur in neonates, in whom Citrobacter freundii & H. influenzae may cause focal areas of cerebritis & in adults in whom Listeria monocytogenes may cause encephalitis or brain abscess

routes of infection

- infectious agents can invade the cerebrospinal fluid via three routes:
(i) vascular (via the blood brain barrier)
- most likely pathogens are pneumococci, meningococci, Listeria, E. coli (neonates), group B strep (neonates) & H. influenzae
(ii) transdural
- most likley pathogens are pneumococci, gram negative enteric bacilli, staphlococci (including coagulase negative staph), & H. influenzae
- surgery including VP shunt, trauma especially with cribriform plate fracture & parameningeal infective focus such as sinusitis, mastoiditis, otitis or osteomyelitis may all predispose to infection by this route; congenital defects such as meningocele may also predispose
(iii) transparenchymal
- most likely pathogens are anaerobic bacilli, enteric gram negative bacilli
- occurs when brain abscess ruptures directly into the ventricles or subarachnoid space

pathphysiology

- the anatomy & composition of the CSF combined with the paucity of host immunologic defenses creates a microenvironment that allows persistence and proliferation of microorganisms; once the CSF is innoculated with pathogens the resolution of infection without antibiotics is virtually impossible
- limited local defense mechanisms may explain the importance of using bacteriocidal rather than bacteriostatic antibiotics in bacterial meningitis

clinical course

- most patients with bacterial meningitis exhibit only modest impairment of cognition on presentation. Several days of malaise, fever & headache are typical and meningismus is usually present
- the CSF indices are almost always abnormal and gram stain or culture usually reveals the infecting pathogen unless antibiotics were administered beforehand

- for unclear reasons, pyogenic meningitis follows a more fulminant course in some patients. These patients experience rapid deterioration in signs and symptoms within 48 hours. In addition to having fever, headache and meningismus they exhibit early impariemnt of sensorium ranging from lethargy to coma

Acute meningitis syndrome:
- initial manifestations of the illness may be subtle with low grade fever or headache; however, once meningeal symptoms (vomiting, severe headache and stiff neck) develop, the clinical course is dramatic with patients appearing toxic and higher integrative functions often deteriorating rapidly
- acute meningitis is an infectious disease emergency with a delay in antibiotic therapy being associated with and adverse outcomes
- if a significant dealy in obtaining CSF specimens is anticipated, antibiotics should be given immediately after peripheral blood cultures are obstained. Depending on the pathogen, the yield of CSF fluid declines markedly 15 minutes to 4 hours after antibiotics. nevertheless, the risk of delaying treatment supercedes the need to make a microbiological diagnosis
- common cuases of this syndrome are pyogenic meningitis (pneumococcal, meningococcal, Listeria & others)
- uncommon causes are viral encephalitis (especially herpes simplex), subarachnoid haemorrhage & brain abscess with rupture
- rare causes are viral meningitis, granulomatous meningitis (cryptococcal, mycobacterial), carcinomatous meningitis & brain tumour

Subacute meningitis syndrome:
- febrile illness with a somewhat more gradual progression of signs and symptoms of CNS involvement represents the subacute CNS infection symfrome. Headache can be mild to severe, neck stiffness can be minimum or marked. Patients with this syndrome are typically oriented and clinically stable at the onset of illness with a gradual progression of symptoms over >24-48 hours
- although bacteria can cause this syndrome it is more often caused by other pathogens or non-infectious processes
- common causes are viral meningitis, viral encephalitis, rickettsial infection
- uncommon causes are brain abscess, neurosyphillus, brain tumour, granulomatous meningitis
- rare causes are cerebrovascular accident and carcinomatous meningitis
- the first priority when managing subacute CNS syndrome is rapid diagnosis rather than the rapid therapy approach required for acute meningitis.
- additional diagnostic studies may be indicated for subacute infections. Serological testing for HIV should be performed because the spectrum of infectious agents is musch broafder among HIV infected individuals. Testing for enteroviruses (PCR), crytococcal antigen, neurosyphilis, mycobacterial infection (culture or PCR), tick borne infections (Ehrlichia, Rickettsia, Lyme disease) and arboviral encephalitides should be individualised based on the patient characteristics, severity of illness and knowledge of local pathogens

complications

- systemic complications may dominate the clinical course of acute bacterial meningitis; 40% of patients with pneumococcal meningitis have concomitant sepsis which is usually from an extra-CNS site such as pneumonia. Sepsis may also represent seeding of the blood stream by infected meninges
- many patients with septicaemia in the context of acute bacterial meningitis will meet criteria for activated protein C; however, it is importatnt to realise that limited data on the safety and efficacy of APC in patients with acute meningitis exists and there may be and increased risk of intracranial haemmorrhage in these patients
- general complications include adrenal insufficiency due to infarction (Waterhouse Friderichsen syndrome) and renal failure due to ATN in the setting of hypotension
- neurological complications include deafness, hydrocephalus and cognitive impairment
- complications specific to meningococcal meningitis include purpura fulminans and necrotising vasculitis leading to skin necrosis and digital gangrene

investigation

(i) imaging (NEJM (2005) 354:44-53 recommendations):
cranial imaging should precede lumbar puncture in patients who have:
- new onset seizures
- immunocompromise
- moderate to severe impairment of conscious state (GCS<10) if imaging is not readily available, LP should be given preference to neuroimaging in all patients except those warning signs of a space occupying lesion (eg new seizure, papilloedema, focal neurology)

(ii) lumbar puncture: need to exclude coagulopathy
A. opening pressure:
- 40% of patients have an opening pressure of greater than 40cmH20
B. CSF findings:
- WCC of 100-1000, elevated protein & decreased glucose are usually present; normal or marginally elevated WCC is seen in 5-10% an is associated with poor outcome
- there is usually a predominance of neutrophils (80-85%) but a predominance of lymphocyte
C. Gram stain:
- sensitivity is 60-90% and specificity is at least 97%
D. culture:
- allows further refinement of therapy

(iii) bloods
- FBE, urea, Cr, electrolytes, LFTs, lactate
- blood cultures
- coags

public health considerations

- respiratory isolation is required for 24 hours for patients with known or suspected N. meningitis meningitis; prophylaxis is indicated for close contacts which is defined as those living in the same dwelling or having close social contact or health care workers who perform intubation or ET tube management