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| MENINGITIS  |

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| 161. What are the most common signs and symptoms of meningitis in infants <2 months old? |  |

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| In general, the findings among neonates and young infants with meningitis are minimal and often subtle. Temperature instability (fever or hypothermia) occurs in approximately 60% of infected infants; increasing irritability is present in about 60%, poor feeding or vomiting in roughly 50%, and seizures in about 40%. Lethargy, respiratory distress, and diarrhea are frequent nonspecific manifestations of meningitis in this patient group. On physical examination, approximately 25% of newborns and young infants have a bulging fontanelle, and only 13% have nuchal rigidity. The diagnosis of meningitis cannot be excluded on the basis of the absence of these physical findings in infants.  |

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| Pong A, Bradley JS: Bacterial meningitis and the newborn infant. Infect Dis Clin North Am 13:711-733, 1999.  |

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| 162. What percentage of neonates with bacterial sepsis and positive blood cultures have meningitis? |  |

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| Up to 25% of infants <28 days old with bacterial sepsis and positive blood cultures will have culture-confirmed meningitis.  |

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| 163. What is the most common cause of aseptic meningitis? |  |

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| Aseptic meningitis is defined as clinical and laboratory evidence of inflammation of the meninges (e.g., CSF pleocytosis and increased protein) without evidence of bacterial infection on Gram stain or culture. More than 80% of cases are caused by *enteroviruses* (i.e., coxsackievirus, enterovirus, echovirus, and, rarely, poliovirus). West Nile virus is an increasingly common cause of aseptic meningitis, especially in the late summer and early fall.  |

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| 164. What is the diagnostic test of choice for enteroviral meningitis? |  |

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| PCR is highly sensitive and specific, and it is more rapid than viral cultures, which typically take 2-5 days to become positive.  |

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| 165. Is intracranial pressure elevated in patients with meningitis? |  |

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| In acute bacterial meningitis, pressure is elevated in up to 95% of cases. Elevation is also common among patients with tuberculous or fungal meningitis. The frequency of elevation in patients with viral meningitis is less well studied.  |

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| 166. Should CT scans be performed before a lumbar puncture (LP) during the evaluation of possible meningitis? |  |

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| CT scans are not routinely indicated before an LP, unless one of the following is present: * Signs of herniation (rapid alteration of consciousness, abnormalities of pupillary size and reaction, absence of oculocephalic response, fixed oculomotor deviation of eyes)
* Papilledema
* Abnormalities in posture or respiration
* Generalized seizures (especially tonic), which are often associated with impending cerebral herniation
* Overwhelming shock or sepsis
* Concern about a condition mimicking bacterial meningitis (e.g., intracranial mass, lead intoxication, tuberculous meningitis, Reye's syndrome)
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| Haslam RH: Role of CT in the early management of bacterial meningitis. J Pediatr 119:157-159, 1991.  |

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| 167. What is the range of values found in CSF of infants and children who do not have meningitis? |  |

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| * **Preterm newborn infants:** WBC count, 0-29/mm3; protein, 65-150 mg/dL; blood glucose, 55-105 mg/dl
* **Term newborn infants:** WBC count, 0-32/mm3; protein, 20-170 mg/dL; glucose, 44-248
* **Infants and children:** WBC count, 0-6/mm3; protein, 15-45 mg/dL; glucose, 60-90
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| McCracken GH: Current management of bacterial meningitis in infants and children. Pediatr Infect Dis J 11:169-174, 1992.  |

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| 168. If bloody CSF is collected during a lumbar puncture, how is CNS hemorrhage distinguished from a traumatic artifact? |  |

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| Most often, the blood is a result of the traumatic rupture of small venous plexes that surround the subarachnoid space, but pathologic bloody fluid can be seen in multiple settings (e.g., subarachnoid hemorrhage, herpes simplex encephalitis). Distinguishing features that suggest pathologic bleeding include the following: * Bleeding that does not lessen during the collection of multiple tubes
* Xanthochromia of the CNS supernatant
* Crenated RBCs noted microscopically
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| 169. How do the CSF findings vary in bacterial, viral, fungal, and tuberculous meningitis in children beyond the neonatal period? |  |

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| Although a large overlap is possible (e.g., bacterial meningitis can be associated with a low WBC count early in the illness, or viral meningitis can often be associated with a predominance of neutrophils early or even persistently in the illness). The usual findings are summarized in Table 11-5.  |

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| 170. How is a traumatic lumbar puncture interpreted? |  |

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| To interpret the number of WBCs in the CSF after a traumatic lumbar puncture, the following correction factor can be applied. It is important to emphasize that the corrected WBC count is an estimate and should be considered in the context of other clinical information.  |

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| Ashwal S, Perkin RM, Thompson JR, et al: Bacterial meningitis in children: Current concepts of neurologic management. Curr Probl Pediatr 24:267-284, 1994.  |

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| Table 11-5. TYPICAL FINDINGS IN BACTERIAL, VIRAL, FUNGAL, AND TUBERCULOUS MENINGITIS |

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| **Cerebrospinal fluid findings** | **Bacterial** | **Viral** | **Fungal/tuberculous** |
| White blood cells per mm3 | >500 | <500 | <500 |
| Polymorphonuclear neutrophils | >80% | <50% | <50% |
| Glucose (mg/dL) | <40 | >40 | <40 |
| Cerebrospinal fluid to blood ratio | <30% | >50% | <30% |
| Protein (mg/dL) | >100 | <100 | >100 |
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| Adapted from Powell KR: Meningitis. In Hoekelman RA, Friedman SB, Nelson NM, et al (eds): Primary Pediatric Care, 3rd ed. St. Louis, Mosby, 1997, p1423.  |

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| 171. When is the best time to obtain a serum glucose level in an infant with suspected meningitis? |  |

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| Because the stress of a lumbar puncture can elevate serum glucose, the serum sample is ideally obtained just before the lumbar puncture. When the blood glucose level is elevated acutely, it can take at least 30 minutes before there is equilibration with the CSF.  |

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| 172. How often does bacterial meningitis appear in younger patients with normal findings on the initial CSF examination? |  |

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| In up to 3% of cases in children between the ages of 3 weeks and 18 months with positive bacterial cultures of the CSF, the initial CSF evaluation (i.e., cell count, protein and glucose concentrations, and Gram stain) can be normal. Of note is that, in almost all of these cases, physical examination reveals evidence of meningitis or suggests serious illness and the need for empiric antibiotics.  |

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| Polk DB, Steele RW: Bacterial meningitis presenting with normal cerebrospinal fluid. Pediatr Infect Dis J 6:1040-1042, 1987.  |

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| 173. Does antibiotic therapy before lumbar puncture affect CSF indices? |  |

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| In most cases, shortly after the initiation of antibiotics, the CSF Gram stain still demonstrates bacteria with typical staining properties, and chemistry values and cell counts are abnormal. Even when children have received appropriate antibiotic therapy for 44-68 hours, chemical and cytologic analysis of the CSF generally still reflects a bacterial process. In earlier studies of patients with *Haemophilus influenzae* meningitis who received oral antibiotic therapy before lumbar puncture, CSF cultures often grew the organism. By contrast, there is a tendency for oral therapy to sterilize the CSF of children with meningococcal disease or with meningitis as a result of sensitive *Streptococcus pneumoniae*.  |

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| 174. What are the most common organisms responsible for bacterial meningitis in the United States? |  |

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| **0-1 month old** * Group B streptococci
* *Escherichia coli*
* *Listeria monocytogenes*
* *Streptococcus pneumoniae*
* Miscellaneous Enterobacteriaceae
* *Haemophilus influenzae* (especially other than type b)
* Coagulase-negative staphylococci (in hospitalized preterm infants)

**1-23 months old** * *Streptococcus pneumoniae*
* *Neisseria meningitidis*
* Group B streptococci

**2-18 years old** * *Neisseria meningitidis*
* *Streptococcus pneumoniae*
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| Schuchat A, Robinson K, Wenger JD, et al: Bacterial meningitis in the United States in 1995. Active Surveillance Team. N Engl J Med 337:970-976, 1997.  |

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| KEY POINTS: MINIMAL DURATION OF THERAPY FOR BACTERIAL MENINGITIS |

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| 1. Five days of therapy for meningococcal meningitis
2. Between 7 and 10 days for Haemophilus influenzae meningitis
3. Ten days for pneumococcal meningitis
4. Between 14 and 21 days for group B streptococcal or Listeria monocytogenes meningitis
5. Twenty-one days or more for gram-negative enteric bacilli (after the cerebrospinal fluid has become sterile)
6. Among patients with complications (e.g., brain abscess, subdural empyema, delayed cerebrospinal fluid sterilization, persistence of meningeal signs, prolonged fever), the duration of therapy should be individualized and may need to be extended
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| 175. Why are *Haemophilus influenzae* type B strains more virulent than nontypeable *Haemophilus* strains? |  |

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| *H. influenzae* type b expresses the type b polysaccharide capsule, which is a polymer of ribose and ribitol-5 phosphate. In the absence of type-specific antibody, the type b capsule promotes intravascular survival by preventing phagocytosis and complement-mediated bactericidal activity. It is likely that other factors also contribute to the unique virulence of *H. influenzae* type b.  |

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| 176. What are the drugs of choice for the empirical treatment of bacterial meningitis in children >1 month old? |  |

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| In cases of suspected bacterial meningitis, both vancomycin and a third-generation cephalosporin are recommended for empirical therapy because resistance to penicillin and cephalosporins is present in 10-30% of *Streptococcus pneumoniae* isolates. The exception is when the Gram stain suggests another etiology (e.g., gram-negative diplococci). Treatment failures have been reported when the dosage of vancomycin is <60 mg/kg/day. Vancomycin should not be used alone to treat *S. pneumoniae* meningitis because data from animal models indicate that bactericidal levels may be difficult to maintain. The combination of vancomycin plus cefotaxime or ceftriaxone has been shown to produce a synergistic effect in vitro, in animal models, and in the CSF of children with meningitis.  |

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| Ahmed A: A critical evaluation of vancomycin for treatment of bacterial meningitis. Pediatr Infect Dis J 16: 895-903, 1997.  |

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| American Academy of Pediatrics, Committee on Infectious Diseases: Therapy for children with invasive pneumococcal infections. Pediatrics 99:289-299, 1997.  |

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| 177. How quickly is the CSF sterilized in children with meningitis? |  |

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| In successful therapy, the CSF is usually sterile *within 36-48 hours* of the initiation of antibiotics. In patients with meningococcal meningitis, CSF is typically completely sterile in no longer than 2 hours after starting treatment. With other organisms, the time until sterilization is generally at least 4 hours.  |

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| Kanegaye JT, Soliemanzadeh P, Bradley JS: Lumbar puncture in pediatric bacterial meningitis: Defining the time interval for recovery of cerebrospinal fluid pathogens after parenteral antibiotic pretreatment. Pediatrics 108:1169-1174, 2001 |
| 178. How long after treatment has been initiated must individuals with meningitis remain in respiratory isolation? |  |

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| *24 hours*. Respiratory isolation is recommended for patients with suspected *Haemophilus influenzae* type b or meningococcal meningitis, but it can be discontinued after 24 hours of therapy.  |

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| 179. What is the accepted duration of treatment for bacterial meningitis? |  |

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| The duration of antibiotic treatment is based on the causative agent and clinical course. In general, a minimum of 5 days of therapy is required for meningococcal meningitis, 7-10 days for *Haemophilus influenzae* meningitis, and 10 days for pneumococcal meningitis. Disease as a result of group B streptococci or *Listeria monocytogenes* should be treated for 14-21 days, and meningitis caused by gram-negative enteric bacilli should be treated for a minimum of 21 days after the CSF has become sterile. Among patients with complications such as brain abscess, subdural empyema, delayed CSF sterilization, persistence of meningeal signs, or prolonged fever, the duration of therapy may need to be extended and should be individualized.  |

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| 180. What is the role of corticosteroids in the treatment of bacterial meningitis? |  |

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| The inflammatory response plays a critical role in producing the CNS pathology and resultant sequelae of bacterial meningitis. Several studies have demonstrated that treatment with dexamethasone reduces the incidence of hearing loss and other neurologic sequelae in infants and children with *Haemophilus influenzae* meningitis. For cases of meningitis caused by pathogens other than *H. influenzae*, the current recommendations by the American Academy of Pediatrics are to *consider* the use of dexamethasone. The role of steroids in meningitis caused by other bacterial pathogens (particularly *Streptococcus pneumoniae)* remains controversial.  |

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| Arditi M, Mason EO, Jr., Bradley JS, et al: Three-year multicenter surveillance of pneumococcal meningitis in children: Clinical characteristics, and outcome related to penicillin susceptibility and dexamethasone use. Pediatrics 102:1087-1097, 1998.  |

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| Feigin RD: Use of corticosteroids in bacterial meningitis. Pediatr Infect Dis J 23:355-357, 2004.  |

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| McIntyre PB, Berkey CS, King SM, et al: Dexamethasone as adjunctive therapy in bacterial meningitis. A meta-analysis of randomized clinical trials since 1988. JAMA 278:925-931, 1997.  |

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**Tuberculous meningitis**

Generally occurs within 6-8 weeks of primary pulmonary infection or during miliary

tuberculosis **(TB).** Commonest in age range 6 months to 3 years.

Leads to basal arteritis, which may cause hydrocephalus and cranial neuropathies. Symptoms

otherwise are often non-specific, lethargy, fever, headache.

CSF - high white cell count, predominantly lymphocytes, raised protein often > 2 dl, low

glucose, tuberculous cultures may be positive.

**Treatment**

Antituberculous chemotherapy

Optimal treatment not determined

Usually triple therapy (rifampicin, isoniazid, pyrazinamide) for at least 6 months but

many authorities suggest a fourth drug for the first 2 months

The place of corticosteriods in treatment is unclear but these are often used in the first

few months to reduce inflammation

Mortality and morbidity remain high despite treatment.

**10.2 Encephalitis**

Numerous viruses may lead to inflammation of the brain: herpes viruses, adenoviruses, arboviruses and enteroviruses for example.

 The underlying causative agent in undiagnosed encephalitis may remain obscure. It is therefore usual practice to treat with cefotaxime/ ceftriaxone, aciclovir and erythromycin/azithromycin until results are available.

Clinical features - confusion, coma, seizures, motor abnormalities

Infection usually starts to resolve 7-1 **4** days after the onset. However, recovery may be

delayed for several months

**Herpes simplex encephalitis**

Common

Often focal brain inflammation, located in temporal lobes

High mortality, high morbidity (50%)

Specific treatment: aciclovir

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**Investigations for encephalitis**

CSF examination/cultures

Electroencephalogram

Brain imaging

Occasionally, brain biopsy

**Treatment**

Supportive (fluid management/ventilation if necessary)

Aciclovir

**10.3 Immune-mediated and other infectious disorders**

**Sydenham's chorea**

Main neurological feature of rheumatic fever

Chorea results from immune reaction triggered by Croup A streptococcal infection

May be associated with emotional lability

Probably overlaps with PANDAS (psychiatric and neurological diseases associated with

streptococcal infection)

In about **75%** of cases the chorea resolves within 6 months

**Subacute sclerosing panencephalitis**

A slow viral infection, caused by an atypical response to measles infection. Exposure to measles virus is usually in the first 2 years. Risk is higher after contracting'natural measles, compared with that after measles immunization. Median interval .between measles and subacute sclerosing panencephalitis is 8 years.Subtle deficits initially

Increasing memory difficulties

Worsening disabilities - seizures, motor difficulties, learning disability

**Mycoplasma encephalitis**

*Mycoplasma pneumoniae* is the commonest cause of community-acquired pneumonia in adults and commonly leads to infection in the paediatric age range. It may cause encephalitis, predominantly through immune-mediated mechanisms which may respond to steroid administration. The evidence base is small.

**Acquired immune deficiency syndrome**

Caused by human immunodeficiency virus, an RNA retrovirus which eventually leads to the death of its host cell CD4-positive T lymphocyte.

Neurological features include:

Neurological features of opportunistic infection such as meningitis or encephalitis

I Dementia

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