

Pediatric Guidelines

Summary: Meningitis Empirical Treatment in Children:

- There has been an ~80% reduction in the incidence of early-onset (first 3 days of life) group B streptococcus (GBS) meningitis due to maternal screening and intrapartum antimicrobial prophylaxis (IAP). However, GBS¹ remains the predominant bacterial pathogen of both early and late onset neonatal disease, followed by *Escherichia coli*, other gram negative organisms and, more rarely, enterococcal species or *Listeria monocytogenes*.
- In older children, conjugated *Haemophilus influenzae* type B vaccine and conjugated pneumococcal vaccines have reduced the incidence of childhood meningitis by more than half. Even the rate of meningococcal meningitis has receded; the extent to which this can be attributed to vaccine is unknown.
- For children older than 1-2 months, who are vaccinated appropriately for age and who live in the U.S., the predominant bacterial pathogens are pneumococcus and meningococcus.
- Viral etiologies of meningitis are rare, outside of the neonatal period.

Empirical therapy:

(1) Birth to 1-2 months of age: ampicillin, gentamicin & cefotaxime

- GBS is uniformly susceptible to penicillin and ampicillin. However, combination therapy with a penicillin and gentamicin should be employed until clinical improvement, sterility of the bloodstream and/or CSF sterility are achieved. This recommendation is based on in vitro synergy and in vivo efficacy in animal models of infection. Furthermore, accelerated killing of streptococci at low concentrations of antibiotics provides a rationale for the initial use of a combination of penicillin G or ampicillin and gentamicin in the treatment of group B streptococcal meningitis². Therapy can be de-escalated to aqueous penicillin G once clinical aims and lab goals are attained.
- High rates of ampicillin resistance among *E. coli* isolates, in general, as well as a link between maternal IAP with ampicillin and *E. coli* resistance have been reported (the latter only in IUGR infants <1500 g birth weight). Due to its superior CNS penetration versus that of the aminoglycosides, cefotaxime may be added as part of the empirical regimen in the first 2 months of life when gram negative meningitis is being considered. **However, it is imperative to de-escalate therapy once the etiologic organism is identified and MICs are available** to avoid overuse of third generation cephalosporins and associated rapid emergence of cephalosporin resistance. Due to significant morbidity with gram-negative meningitis, repeat lumbar puncture to prove CSF sterility is strongly recommended. Combination therapy is typically undertaken for 7-14 days; specific duration is based on clinical and laboratory criteria.³
- *Listeria* meningitis should be treated with a combination of ampicillin and gentamicin due to improved effectiveness over ampicillin alone in vitro and in vivo in animal models of infection.⁴ Once the patient has clinically improved, has sterile blood and CSF, treatment can be completed with monotherapy with ampicillin.
- Viral etiologies should be strongly considered in the neonate particularly in the first 1 month of life and when CSF parameters suggest aseptic meningitis and in older children who present with meningoencephalitis and/or cerebrospinal fluid parameters are consistent with aseptic meningitis. Herpes simplex, Enterovirus or Parechovirus are etiologies of aseptic meningitis and meningoencephalitis in infants ≤ 1-2 months of age. . CSF PCR is the test of choice to determine viral etiology. The ME panel is recommended (requires 0.25 ml of CSF as a minimum). Viral cultures of CSF are unhelpful. Diagnosis relies on PCR testing with the meningitis/encephalitis (ME) panel. The ME panel detects CMV, Enterovirus, HSV-1, HSV-2, HHV-6, Human parechovirus, VZV, *E.coli* K1 strain, *Haemophilus influenzae*, *Listeria monocytogenes*, *Neisseria meningitides*, *Streptococcus agalactiae* (Grp B Strep), *Streptococcus pneumoniae* and *Cryptococcus neoformans/gattii*.

(2) 2 months to 18 years of age: ceftriaxone & vancomycin

Ceftriaxone-resistant pneumococcal isolates are rare in our region but remain a great enough concern that Vancomycin is added to empirical therapy. Therapy is de-escalated after organism identification and MICs are available.

1. Verani JR, McGee L, Schrag SJ, Division of Bacterial Diseases NCFI, Respiratory Diseases CfDC, Prevention. Prevention of perinatal group B streptococcal disease--revised guidelines from CDC, 2010. *MMWR Recommendations and reports : Morbidity and mortality weekly report Recommendations and reports / Centers for Disease Control* 2010; **59**(RR-10): 1-36.
2. Swingle HM, Bucciarelli RL, Ayoub EM. Synergy between penicillins and low concentrations of gentamicin in the killing of group B streptococci. *The Journal of infectious diseases* 1985; **152**(3): 515-20.
3. Red Book: 2012 Report of the Committee on Infectious Diseases. Elk Grove Village, IL: American Academy of Pediatrics; 2015.
4. Cherubin CE, Appleman MD, Heseltine PN, Khayr W, Stratton CW. Epidemiological spectrum and current treatment of listeriosis. *Reviews of infectious diseases* 1991; **13**(6): 1108-14.

Pediatric Meningitis: Empiric Therapy

Excludes premies < 37 wks GA, recently hospitalized, and pts w/ significant co-morbidities

UCDMC Children's Hospital

Neonates and Infants, ages 0-2 months old with evidence of meningitis

Ampicillin + Gentamicin. Cefotaxime may be added at the discretion of team as discussed above.

De-escalate antibiotic therapy upon return of organism ID and MICs

- Suggest ME panel for CSF, hepatic function panel and consider PCR of blood (sent out lab). Add Acyclovir 20 mg/kg q8h to the above regimen if any of the following are present on history/exam or lab findings:
 - Seizures or other neurologic signs
 - Vesicles/rash
 - Sepsis-like picture (transaminitis, fever, hypothermia, lethargy, respiratory distress, apnea, abdominal distension, hepatomegaly, thrombocytopenia)
 - CSF: lymphocyte predominance, normal/minimally-low glucose, normal/minimally-elevated protein
 - *OR* any other concerns for HSV

Note: Mother may have no history of symptomatic HSV. Perinatally acquired HSV infection usually presents at 5-21 days of age so addition of acyclovir for newborns at <72 hours of age in the absence of the above should not be routine

Dosing- Neonates 0-28 days old, per Red Book guidelines 2015; Body Weight > 2kg:

Ampicillin

<= 7 days old: 100mg/kg q8h (300mg/kg/day)

8-28 days old: 75 mg/kg q6h (300mg/kg/day)

Gentamicin

<= 7 days old: 4 mg/kg q24h

8-28 days old: 4 mg/kg q12-24h

Cefotaxime

<= 7 days old: 50 mg/kg q12h

8-28 days old: 50 mg/kg q8h

Dosing- Infants 1-2 mo old:

Ampicillin: 50-100 mg/kg q6h

Gentamicin: 1- 2.5 mg/kg q8h

Cefotaxime: 50 -75 mg/kg q6h

Acyclovir: 20 mg/kg q8h

Infants, children & adolescents age >2 months- 18 years old:

Ceftriaxone + Vancomycin

- Strongly consider sending HSV-PCR and add Acyclovir (*dosing below*) to the above regimen if any of the following are present:
 - Signs of meningoencephalitis (altered mental status, headache, etc), *OR*
 - Seizures or focal neurologic signs
 - AND
 - CSF parameters suggestive of viral process: lymphocyte predominance, normal/minimally-low glucose, normal/minimally-elevated protein

Dosing >2 mo to 18 yrs old:

- Ceftriaxone 50 mg/kg q12h (max 2gm q12h)
- Vancomycin 15-20 mg/kg q8h
- Acyclovir 20 mg/kg q8h for 2 -3 mo old
- 10-15 mg/kg q8h for >=3 mo-12 yo
- 10 mg/kg q8h for >= 12 yo

Duration of therapy once organism identified:

- *S. pneumoniae* – 10 to 14 days
- *N. meningitidis* –5-7 days
- *H. influenzae* type b – 10 days
- GBS- 14-21 days
- *L. monocytogenes* –14-21 days
- Gram-negative bacilli – 21 days minimum
- HSV- 21 days minimum AND a negative PCR

Special considerations for Peds ID consult:

- Encephalitis
 - Recent neurosurgery
 - VP shunt
 - CSF leak
 - Penetrating head trauma
 - Allergy to beta-lactam
 - Allergy to Vancomycin
-

Labs for all age groups	When to order?	Special comments for order (if any)
CSF cell count, glucose, protein and bacterial culture with gram stain	All CSF samples	
HSV 1 and 2 DNA-PCR	See above considerations	ME panel
Enterovirus PCR	All neonates < 28 days old, OR > 28 days old + CSF parameters c/w viral process	CSF for ME panel Blood for PCR
Viral stool culture	All neonates < 28 days old, OR > 28 days old + CSF parameters c/w viral process	Select specimen: stool OR rectal swab. “Test for Enterovirus”
Viral ENT culture	All neonates < 28 days old, OR > 28 days old + CSF parameters c/w viral process	Select specimen: nasal OR oral sample. “Culture for Enterovirus.”
Parechovirus	All neonates < 28 days old AND CSF parameters c/w viral process	ME panel
Miscellaneous lab	If want other studies, e.g. EBV, West Nile, autoimmune studies, Neurologic Surveillance Testing via Public Health	“extra CSF for additional studies”

Indications for CT head prior to LP:

- Signs of increased ICP
- History of:
 - hydrocephalus
 - VP shunt
 - head trauma
 - focal neurologic signs