

Evaluation of Infant 0-21 days

Fever ($\geq 38^{\circ}\text{C}$ measured in ED or at home) in Infant Without a Source 0 to 28 days

Full Sepsis Evaluation:

1. UA w/ microscopy and urine culture
2. CBC w/differential
3. Blood culture
4. LP with CSF panel & culture

Ampicillin & Gentamicin

CSF pleocytosis for age?

Complete HSV Risk Checklist

LOW RISK

HIGH RISK

HSV evaluation

1. AST/ALT
2. Multiple surface swabs (conjunctiva, nasopharyngeal, oropharynx, rectum) HSV PCR
3. Vesicle (if present) HSV PCR
4. HSV PCR - Serum
5. HSV PCR - CSF

Continue Ampicillin & Gentamicin

Add Acyclovir

Admit patient

Discharge Disposition: Length of Stay: 36 hours of negative cultures (HSV work up negative, if applicable)

HSV Risk Checklist

IF presentation includes ill appearing infant, (apnea, hypothermia DIC, sepsis) HSV should be part of the evaluation

1. Maternal history of HSV lesions or fever 48 hours prior or 48 hours post-delivery
2. Infant with history of seizures or seizures during the evaluation
3. Vesicles on skin exam (including scalp) hypothermia, mucous membrane ulcers
4. Leukopenia, thrombocytopenia, or elevated alanine aminotransferase levels.

If any "Yes" proceed to **complete HSV evaluation: HSV PCR surface swab (eye, mouth, rectum), HSV PCR blood, HSV PCR CSF, and HSV PCR vesicle (if present)**

Administer Ceftriaxone (see link for indications) OR Cefazidime if Ceftriaxone is contraindicated

Presumed UTI?

YES

NO

Complete HSV checklist

HIGH RISK

LOW RISK

Continue IV Ceftriaxone (or Cefazidime) & Ampicillin (meningitic dosing)

Administer IV acyclovir, continue Ceftriaxone (or cefazidime) & Ampicillin (meningitic dosing)

Revision Date: 12-17-21

Return to Pathway

Neonatal Drug Guidelines UCSF Benioff Children's Hospital 2019 – 2021

Drug	Dose	Interval	Mode
Antibacterials/Antifungals/Antivirals:			
Acyclovir	20 mg/kg/dose	q 8 hours	IV
Amphotericin	Conventional (Fungizone®) 1 mg/kg/dose	q 24 hours	IV
	Liposomal (Ambisome®) 5 mg/kg/dose	q 24 hours	IV
Ampicillin	Meningitis 100 mg/kg/dose	see Interval A	IV
	Non-meningitis 50 mg/kg/dose	see Interval A	IV
Azithromycin	(pertussis) 10 mg/kg/dose	q 24 hours x 5 days	IV/PO
Cefazolin	25 mg/kg/dose	see Interval B	IV
Cefepime	50 mg/kg/dose	q 12 hours	IV
		Meningitis q 8 hours	IV
Cefotaxime	50 mg/kg/dose	see Interval A	IV
		Meningitis see Interval C	IV
Ceftriaxone	<i>May be considered in neonates ≥ 41 weeks corrected GA and > 14 days PNA without hyperbilirubinemia or any anticipated calcium containing IV solutions within 48 hours of ceftriaxone therapy. Consult pharmacist for verification of criteria and dosing guidance.</i>		
Ceftazidime	50 mg/kg/dose	see Interval B	IV
Clindamycin	see Column E	q 8 hours	IV
Fluconazole	Treatment LOAD 25 mg/kg x1, then 12 mg/kg/dose	q 24 hours	IV/PO
	Prophylaxis 6 mg/kg/dose:		
	≤ 29 wks corr. GA & ≤ 28 d PNA: q 72 hours		IV/PO
	> 29 wks corr. GA or > 28 d PNA: q 48 hours		
Gentamicin and Tobramycin	see chart at bottom for dosing and interval		IV
Meropenem	20 mg/kg/dose (40 mg/kg/dose for meningitis/pseudomonas)		
	< 32 weeks GA & < 14 days PNA	q 12 hours	IV
	> 32 weeks GA or ≥ 14 days PNA	q 8 hours	IV
Metronidazole	≤ 33 weeks corr. GA: 7.5 mg/kg/dose	q 12 hours	
	LOAD 15 mg/kg x1, 34-40 weeks corr. GA: 7.5 mg/kg/dose	q 8 hours	IV
	followed 8-12 hours later by: ≥ 41 weeks corr. GA: 10 mg/kg/dose	q 8 hours	
Nafcillin	50 mg/kg/dose	see Interval A	IV
PenicillinG (aq) congenital syphilis:	50,000 units/kg/dose x 10 days	see Interval A	IV
Piperacillin/tazobactam	Sepsis: 80 mg piperacillin/kg/dose	see Interval C	IV
	Pseudomonas: 100 mg piperacillin/kg/dose		
TMP/SMX (Bactrim/Septa)	<i>Generally avoided ≤44 weeks corrected Gestational Age</i>		
Vancomycin	≤ 29 wks corr. GA: 10 mg/kg/dose	q 12 hours	
	> 29 wks corr. GA: 15 mg/kg/dose	see Interval D	IV

Corrected Gestational age (weeks)	Postnatal age (days)	Interval A	Interval B	Interval C	Interval D	Column E
≤ 29	0 – 28	q 12°	q 12°	q 12°	see drug entry	4 mg/kg/dose
	> 28	q 8°	q 8°	q 8°		
30 – 36	0 – 14	q 12°	q 12°	q 8°	q 12°	6 mg/kg/dose
	> 14	q 8°	q 8°	q 6°	q 8°	
37 – 44	0 – 7	q 12°	q 12°	q 8°	q 12°	8 mg/kg/dose
	> 7	q 8°	q 8°	q 6°	q 8°	
≥ 45	All	q 6°	q 8°	q 6°	q 6°	10 mg/kg/dose

Chart below is for dosing of Gentamicin & Tobramycin ONLY

BIRTH to 1 MONTH

Gestational Age (weeks)	Dose	Interval
≤ 28	3.5 mg/kg/dose	q 36 hours
29 – 34	3.5 mg/kg/dose	q 24 hours
≥ 35	5 mg/kg/dose	q 24 hours (q36h for HIE or significant asphyxia)

< 35 week GA: Order Peak/Trough with 4th dose
 ≥ 35 week GA: Order Trough ONLY with 4th dose
 (for HIE or significant asphyxia, P/T with 3rd dose)

> 1 MONTH POSTNATAL

Corrected Gestational Age (weeks)	Dose	Interval
< 35	2.5 mg/kg/dose	q 12 hours
≥ 35		q 8 hours^

^Renal or cardiac dysfunction, use 2.5 mg/kg/dose IV q12 to 24 hours

For most current ICN dosing card guidelines: http://carelinks.ucsfmedctr.org/clinical_guidelines.asp

Approved by ICN Joint Practice 3-2019, BCH Med Committee 3-2019 Approved by P&T 4-2019
 Edition 7: 3/2019

CSF Pleocytosis Reference Ranges

Inability to obtain CSF in ED

- Administer antibiotics within 60 minutes, should not be held for severely ill patients pending LP
- Rapid CSF Bacterial PCR can be sent on pre-treated CSF that demonstrates pleocytosis

CSF Pleocytosis can vary by age, listed values below should be used in conjunction with clinical judgment and patient characteristics

- ≤ 28 days: 15 cells/mm³
- 29-60 days: 9 cells/mm³

Thomson J, Sucharew H, Cruz AT, et al. Cerebrospinal Fluid Reference Values for Young Infants Undergoing Lumbar Puncture. 2018;141(3):11.

Additional reference ranges for healthy newborns

Table 6-12 Hematologic and Chemical Characteristics of Cerebrospinal Fluid in Healthy Newborns: Results of Selected Studies

Study (year)	No. of Patients	Age (days)	White Blood Cells* (mm ³)	Neutrophils* (mm ³)	Glucose* (mg/dL)	Protein* (mg/dL)
Naidoo ⁸¹³ (1968)	135	1	12 (0-42)	7 (0-26)	48 (38-64)	73 (40-148)
	20	7	3 (0-9)	2 (0-5)	55 (48-62)	47 (27-65)
Sarff ⁴⁸⁸ (1976)	87	Most < 7	8.2 ± 7.1, median 5 (0-32)	61	52 (34-119)	90 (20-170)
Bonadio ⁵⁶⁵ (1992)	35	0-4 wk	11.0 ± 10.4, median 8.5	0.4 ± 1.4, median 0.15	46 ± 10.3	84 ± 45.1
	40	4-8 wk	7.1 ± 9.2, median 4.5	0.2 ± 0.4, median 0	46 ± 10.0	59 ± 25.3
Ahmed ⁵⁶⁶ (1996)	108	0-30	7.3 ± 13.9, median 4	0.8 ± 6.2, median 0	51.2 ± 12.9	64.2 ± 24.2

Data from Ahmed A, Hickey S, Ehrett S, et al: Cerebrospinal fluid values in the term neonate, *Pediatr Infect Dis J* 15:298, 1996.

*Expressed as mean with range (number in parentheses) or ± standard deviation unless otherwise specified.

Nizet, V. and Klein, J. ed., 2016. Bacterial Sepsis and Meningitis. In: *Remington and Klein's Infectious Diseases of the Fetus and Newborn Infant*, 8th ed.

TABLE 2 CSF Values in Febrile Infants Without Evidence of UTI, IBI, HSV, Enterovirus, or Traumatic CSF

	Age, d	n	Mean	Median	Range
WBCs per mm ³	1-28	278	6.1	5.0	0-18
	29-60	318	3.1	3.0	0-8.5
Protein mg/dL	1-28	278	75.4	73.0	15.8-131.0
	29-60	318	58.9	54.0	5.5-105.5
Glucose	1-28	278	45.3	46.0	30.0-61.0
	29-60	318	48.0	48.0	20.6-65.5
RBCs per mm ³	1-28	278	95.5	5.5	0-236
RBCs per mm ³	29-60	318	75.5	2.0	0-64.5

Statistical outliers were removed. Other studies reveal slightly different ranges. Local laboratory tests may provide slightly different upper limits of normal. Adapted from Byington CL, Kendrick J, Sheng X. Normative cerebrospinal fluid profiles in febrile infants. *J Pediatr*. 2011;158(1):130-134.

[Return To Pathway](#)

Return to Pathway

Validity of using the UA as a screening tool before sending a urine culture

1. Schroeder AR, Chang PW, Shen MW, Biondi EA, Greenhow TL. Diagnostic accuracy of the urinalysis for urinary tract infection in infants <3 months of age.*Pediatrics*. 2015;135(6):965-971
2. Tzimenatos L, Mahajan P, Dayan PS, et al. Accuracy of the urinalysis for urinary tract infections in febrile infants 60 days and younger.*Pediatrics*. 2018;141(2):e20173068

Use of inflammatory markers for risk stratification

1. Aronson PL, Shabanova V, Shapiro ED, et al. A prediction model to identify febrile infants ≤60 days at low risk of invasive bacterial infection.*Pediatrics*. 2019;144(1):e20183604
2. Gomez B, Mintegi S, Bressan S, et al. Validation of the "Step-by-Step" approach in the management of young febrile infants.*Pediatrics*. 2016;138(2):e20154381. doi: 10.1542/peds.2015-4381. Epub 2016 Jul 5
3. Kuppermann N, Dayan PS, Levine DA, et al. A clinical prediction rule to identify febrile infants 60 days and younger at low risk for serious bacterial infections.*JAMA Pediatr*. 2019;173(4):342-35160
4. Milcent K, Faesch S, Gras-Le Guen C, et al. Use of procalcitonin assays to predict serious bacterial infection in young febrile infants.*JAMA Pediatr*. 2016;170(1):62-69

Use of selective lumbar punctures in febrile infants with positive UAs

1. Burstein B, Sabhaney V, Bone JN, Doan Q, Mansouri FF, Meckler GD. Prevalence of bacterial meningitis among febrile infants aged 29-60 days with positive urinalysis results: a systematic review and meta-analysis.*JAMA Netw Open*. 2021 May 3;4(5):e214544
2. Velasco R, Lejarzegi A, Gomez B, et al. Febrile young infants with abnormal urine dipstick at low risk of invasive bacterial infection.*Arch Dis Child*. 2020 Nov 27:archdischild-2020-320468
3. Wang ME, Biondi EA, McCulloh RJ, et al. Testing for meningitis in febrile well-appearing young infants with a positive urinalysis.*Pediatrics*. 2019;144(3):e20183979
4. Young BR, Nguyen THP, Alabaster A, Greenhow TL. The prevalence of bacterial meningitis in febrile infants 29-60 days with positive urinalysis.*Hosp Pediatr*. 2018;8(8):450-457
5. Use of Oral Antibiotics in Febrile Infants 29-60 days with positive UAs
6. Hoberman A, Wald ER, Hickey RW, et al. Oral versus initial intravenous therapy for urinary tract infections in young febrile children.*Pediatrics*. 1999;104(1 Pt 1):79-86

CSF Values

1. Thomson J, Sucharew H, Cruz AT, et al. Cerebrospinal Fluid Reference Values for Young Infants Undergoing Lumbar Puncture.*Pediatrics*. 2018;141(3). doi:[10.1542/peds.2017-3405](https://doi.org/10.1542/peds.2017-3405)

Disposition

Discharge from the hospital within 24-36 hours:

1. Aronson PL, Wang ME, Nigrovic LE, et al. Time to pathogen detection for non-ill versus ill-appearing infants ≤60 days old with bacteremia and meningitis.*Hosp Pediatr*. 2018;8(7):379-384
2. Biondi EA, Mischler M, Jerardi KE, et al. Blood culture time to positivity in febrile infants with bacteremia.*JAMA Pediatr*. 2014;168(9):844-849

Discharge from the emergency department with close follow-up:

1. Alpern ER, Kuppermann N, Blumberg S et al. Time to positive blood and cerebrospinal fluid cultures in febrile infants ≤60 days of age.*Hosp Pediatr*. 2020 Sep;10(9):719-727
2. Greenhow TL, Hung YY, Pantell RH. Management and outcomes of previously healthy, full-term, febrile infants ages 7 to 90 days.*Pediatrics*. 2016;138(6):e20160270
3. Mintegi S, Gomez B, Martinez-Virumbrales L, Morientes O, Benito J. Outpatient management of selected young febrile infants without antibiotics.*Arch Dis Child*. 2017 Mar;102(3):244-249
4. Pantell RH, Newman TB, Bernzweig J, et al. Management and outcomes of care of fever in early infancy.*JAMA*. 2004;291(10):1203-1212

Parent Engagement

1. Aronson PL, Politi MC, Schaeffer P, et al. Development of an app to facilitate communication and shared decision-making with parents of febrile infants ≤60 days old.*Acad Emerg Med*. 2021;28(1):46-59