Evaluation of Infant 22-28 days

Ill appearing infant:
Full Sepsis Evaluation &
Complete HSV checklist
Work up includes but not limited to Blood culture, UA/urine culture, procalcitonin & CSF studies. HSV work up as indicated
Ceftriaxone & Vancomycin (follow sepsis pathway)
Add Acyclovir if HIGH risk HSV

Fever (≥38°C measured in ED or at home) in Well Appearing Infant Without a Source 22 to 28 days

1. UA w/ microscopy and urine culture
2. CBC w/ differential
3. Procalcitonin (PCT)
4. Blood culture

PCT ≥0.5 ng/mL
OR
ANC ≥ 4000 mm^3

YES

Obtain LP

CSF pleocytosis or uninterpretable

YES

Admit with Ceftriaxone and Vancomycin (meningitic dosing), Consider need for HSV eval/treatment

NO

Admit with Ceftriaxone

NO

LP may be preformed (see shared decision making)

LP preformed?

YES

CSF pleocytosis or uninterpretable

YES

Admit: start Ceftriaxone and Vancomycin (meningitic dosing)

NO

Ceftriaxone

UA positive?

YES

Discharge home on Cephalexin

NO

Home observation (discharge criteria)

NO

UA positive?

YES

Ceftriaxone

NO

No antibiotics

Admit to hospital

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. Consider in cases with 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)**

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	*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.*				
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/Septra)	*Generally avoided ≤44 weeks corrected Gestational Age*				
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

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

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 conjunctiion with cilnical judement and patient characterstics

- $\leq$ 28 days: 15 cells/mm^3
- 29-60 days: 9 cells/mm^3

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
Glucose	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.

HSV should be considered when there is:

- Maternal history of genital HSV lesions or fever from 48 hours before to 48 hours after delivery
- Infants with vesicles, seizures, hypothermia, mucous membrane ulcers
- CSF pleocytosis in the absence of a positive Gram stain result
- Leukopenia, thrombocytopenia, or elevated alanine aminotransferase levels.

Return to Pathway

Discharge Checklist

- Are the parents comfortable with monitoring the child at home
- Do parents have reliable means of receiving communication from hospital
- Can culture results be followed daily by hospital staff
- Can patient follow up with PCP within 24 hours
- Can patient tolerate oral antibiotics, if indicated

If NO to ANY: Admit

Return to Pathway

Parent Engagement – CSF
Metric:
75% of infants 22-28 days of age with normal inflammatory markers and negative UA have documented physician-parent discussion about the harms/benefits of having CSF obtained.
Epic Smartphrase: .***

I did shared decision-making with the parents/guardians regarding performing a lumbar puncture. I discussed the harms/benefits of performing a lumbar puncture, including the risks of bacterial meningitis vs. the risks of a serious complication from lumbar puncture. I elicited the parents'/guardians' values and preferences about the decision. After consideration of the harms/benefits, the parents and I jointly decided [to obtain/not obtain a lumbar puncture].

Shared decision-making script template (mapped to each Step):

Step 1: Seek the parent's participation
The results of the urine and blood tests mean that your baby probably doesn't have a bacterial infection. However, there is still a possibility that your baby has bacterial meningitis. There are two options for your baby – to have a spinal tap now or to be admitted to the hospital without having a spinal tap. It is important for me to know how you feel about a spinal tap for your baby.

Step 2: Help the parent explore and compare options
The **first option i**s for your baby is to have a spinal tap. The potential benefits of the spinal tap are that you will know for sure if your baby has bacterial meningitis. If the spinal tap shows that your baby might have bacterial meningitis, treatment can be started right away. If the results of the spinal tap show that your baby probably doesn't have bacterial meningitis, your baby might be able to go home from the emergency room and not be admitted to the hospital. The potential harms of the spinal tap are discomfort for your baby, the possibility that the spinal tap isn't successful, and rare serious complications like bleeding, infection, or injury to the nerves which happen in an estimated 1 out of 1,000 (or 0.1%) babies.

The **second option** is for your baby to be admitted to the hospital without having a spinal tap. The benefits of your baby not having a spinal tap are to avoid the risks of spinal tap, including discomfort, the possibility that the spinal tap isn't successful, and rare serious complications. The potential harms of not having a spinal tap are that your baby has an estimated 1 out of 1,000 (0.1%) chance of having bacterial meningitis that will be diagnosed later may cause injury to your baby's brain. The potential harms of being admitted to the hospital are disruption of your family's routine, your baby getting a different infection in the hospital, and the costs of the admission.

Step 3: Assess the parent's values and preferences
Now that I've explained the possible harms and benefits of your baby having or not having a spinal tap, can you please tell me what you understand about the two options and what is important to you in deciding what to do?
Now I'd like to learn which option you prefer. Do you prefer that your baby has a spinal tap or gets admitted without having a spinal tap, or do you not have a preference?

Step 4: Reach a decision with the parent
We have decided that your baby [will have a spinal tap/will be admitted without having a spinal tap].

Step 5: Evaluate the parent's decision
This step involves following up to assess the outcome of the decision. For example, if the baby did not have a lumbar puncture, was the baby subsequently diagnosed with bacterial meningitis? Or if the baby had a lumbar puncture, was the spinal tap successful?

Return to Pathway

Parent Engagement – Disposition
Metric:
75% of infants 22-28 days with normal inflammatory markers, negative UA, and normal CSF have documented physician-parent discussion about the harms/benefits of hospitalization vs. discharge from the ED after one dose of parenteral antibiotic therapy.
Smartphrase:
.EDREVISESDMDispofebrileinfants

I did shared decision-making with the parents/guardians about hospitalization vs. discharge home from the ED after one dose of ceftriaxone. I discussed the harms/benefits of hospitalization vs. discharge home, including the risks of subsequent hospitalization and the risks of a delayed diagnosis of bacteremia or bacterial meningitis. I elicited the parents'/guardians' values and preferences about the decision. After consideration of the harms/benefits, the parents and I jointly decided on [hospitalization/discharge home from the ED with 24-hour follow-up].
Shared decision-making script template (mapped to each Step):

Step 1: Seek the parent's participation
The results of the spinal tap mean that your baby probably doesn't have bacterial meningitis. However, there is still a possibility that your baby has a bacterial infection. There are two options for your baby – to be admitted to the hospital or to be discharged home from the emergency room after one dose of an antibiotic. It is important for me to know how you feel about this decision.

Step 2: Help the parent explore and compare options
The **first option** is for your baby to be admitted to the hospital. The potential benefits of admission are that your baby can be monitored by doctors and nurses for signs of infection. If your baby shows signs of infection, treatment can be given immediately. If your baby is not feeding well or is making fewer wet diapers, fluids can be given through an IV. The potential harms of being admitted to the hospital are disruption of your family's routine, your baby getting a different infection in the hospital, and the costs of the admission.
The **second option i**s for your baby to be discharged home from the emergency room after one dose of an antibiotic. The benefits of your baby going home from the emergency room include avoiding the potential harms of being admitted to the hospital. You may also have less disruption to your family's routine. The potential harms of going home from the emergency room are that your baby still has a small chance of having a bacterial infection. You will need to closely monitor your baby at home for any signs that he/she is getting sicker. If he/she is getting sicker, you will need to return to the emergency room.

Step 3: Assess the parent's values and preferences
Now that I've explained the possible harms and benefits of your baby being admitted to the hospital or discharged home from the emergency room after one dose of an antibiotic, can you please tell me what you understand about the two options and what is important to you in deciding what to do?
Now I'd like to learn what you prefer. Do you prefer that your baby be admitted to the hospital or discharged home after one dose of an antibiotic?

Step 4: Reach a decision with the parent
We have decided that your baby [will be admitted to the hospital/will be discharged from the emergency room after one dose of an antibiotic].

Step 5: Evaluate the parent's decision
This step involves following up to assess the outcome of the decision. For example, if the baby was discharged home, did the baby return to the emergency department? Or if the baby was admitted to the hospital, did the baby have any complications?

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

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