

# Fever in Infants (8 to 21 days old) Pathway

**Pathway Purpose:** Standardize management of febrile infants 8 to 21 days old

## Inclusion Criteria:

- 8-21 days old
- Well-appearing
- Temperature  $\geq 38.0$  C in the past 24 hours (any route)
- Full term infants (Gestational age  $\geq 37$  weeks at birth)
- Presenting from home or clinic

## Exclusion Criteria:

- Ill-appearing
- Preterm infants ( $<37$  weeks gestational age)
- Chronic medical condition
- High suspicion of herpes simplex virus (HSV) (eg, vesicles) [A]
- Focal bacterial infection (eg, cellulitis, omphalitis, septic arthritis, osteomyelitis)
- Clinical bronchiolitis
- Immunization or antibiotic treatment in the past 48 hours

- Obtain urinalysis, blood culture, CBC with differential
  - If urinalysis positive ( $>5$  WBCs/hpf or positive leukocyte esterase), send urine culture by straight catheterization or suprapubic aspiration
- Perform lumbar puncture (LP)\* [B]
- Consider HSV evaluation if HSV risk factors present [A]

\*If unable to obtain CSF after 3 attempts:

- Start parenteral antibiotics
- Consider repeat LP after admission [C]
- Consider use of ultrasound-guided or IR-guided LP [D]

After obtaining above studies, initiate:

- Parenteral antibiotics ([Table 1](#))
- Acyclovir (if HSV work-up performed)

**Admit all patients**

Pathogen or source identified?

Yes

Treat infection

- For UTIs, see [Neonatal and Young Infant UTI Pathway](#)

No

Discontinue antimicrobials and discharge hospitalized patients if all the following are met:

- All bacterial cultures and HSV PCR (if sent) are negative at 24-36 hours, or only positive for contaminants.
- Infant continues to appear clinically well or is improving.
- There are no other indications for hospitalization.

Owner: Guillermo Alberto De Angulo and Marie Wang

Pathway Team: Lisa Bain, Shubhi Goli, Arun Gupta, Katie Fry, Neha Joshi, Julie Kim, Danni Liang, Mia Karamatsu, Preeti Panda, Nita Srinivas, Nichole Wang

Date of 1st approval: 8/2022

Last Updated: 7/2022

Associated Order Set: Fever in Infants  $\leq 60$  days (General Admission [Medical])



# Fever in Infants (22 to 28 days old) Pathway

**Pathway Purpose:** Standardize management of febrile infants 22 to 28 days old

## Inclusion Criteria:

- 22-28 days old
- Well-appearing
- Temperature  $\geq 38.0$  C in the past 24 hours (any route)
- Full term infants (Gestational age  $\geq 37$  weeks at birth)
- Presenting from home or clinic

## Exclusion Criteria:

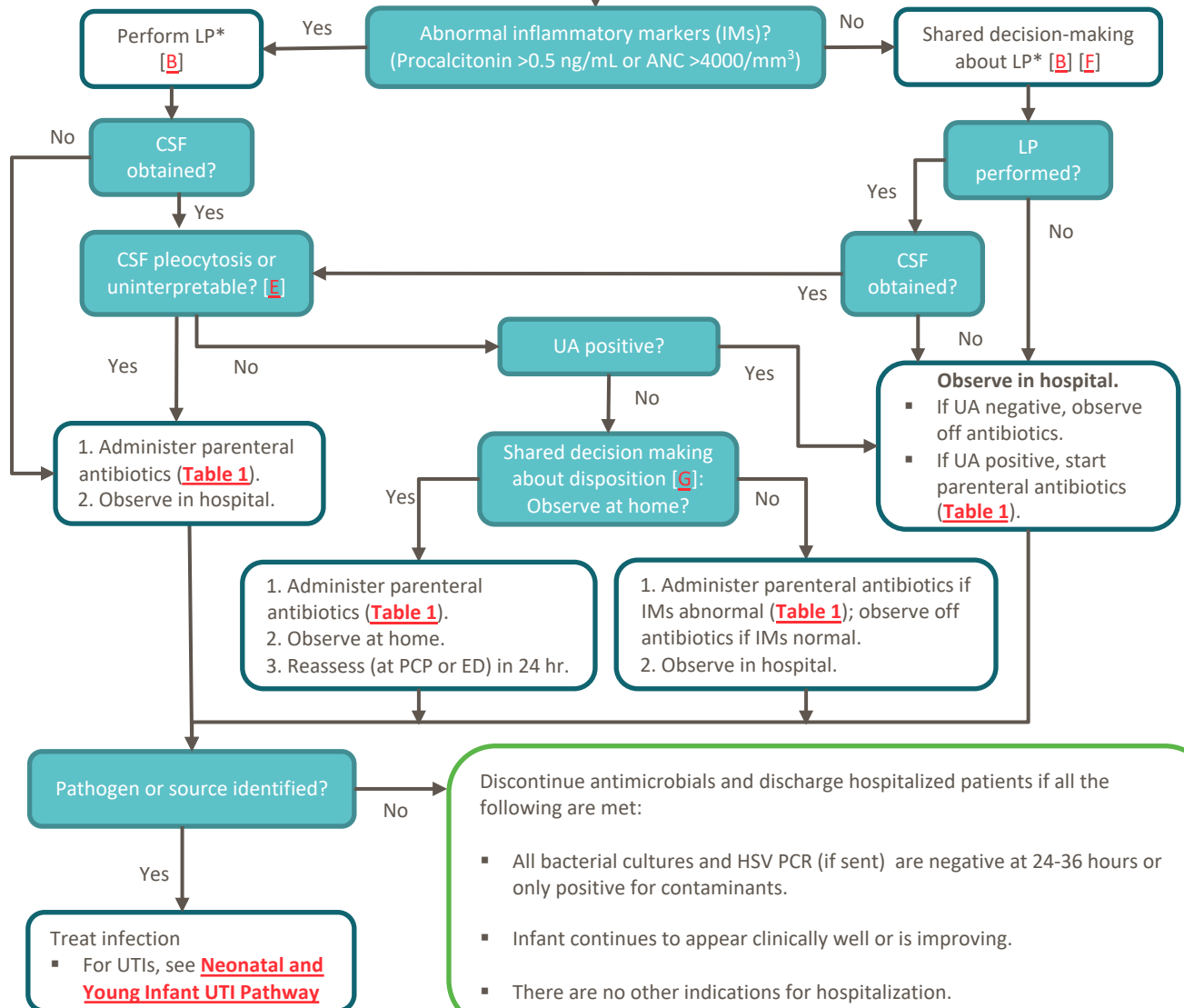
- Ill-appearing
- Preterm infants (<37 weeks gestational age)
- Chronic medical condition
- High suspicion of herpes simplex virus (HSV) (eg, vesicles) [A]
- Focal bacterial infection (eg, cellulitis, omphalitis, septic arthritis, osteomyelitis)
- Clinical bronchiolitis
- Immunization or antibiotic treatment in the past 48 hours

\*If unable to obtain CSF in patients with **elevated IMs** after 3 attempts:

- Start parenteral antibiotics
- Consider repeat LP after admission [C]
- Consider use of ultrasound-guided or IR-guided LP [D]

## In the ED:

- Obtain urinalysis, blood culture, CBC with differential, procalcitonin
- If urinalysis positive (>5 WBCs/hpf or positive leukocyte esterase), send urine culture by straight catheterization or suprapubic aspiration
- Consider HSV evaluation if HSV risk factors present [A]



# Fever in Infants (29 to 60 days old) Pathway

**Pathway Purpose:** Standardize management of febrile infants 29 to 60 days old

## Inclusion Criteria:

- Age 29-60 days old
- Well-appearing
- Temperature  $\geq 38.0$  C in the past 24 hours (any route)
- Full term infants (Gestational age  $\geq 37$  weeks at birth)
- Presenting from home or clinic

## Exclusion Criteria:

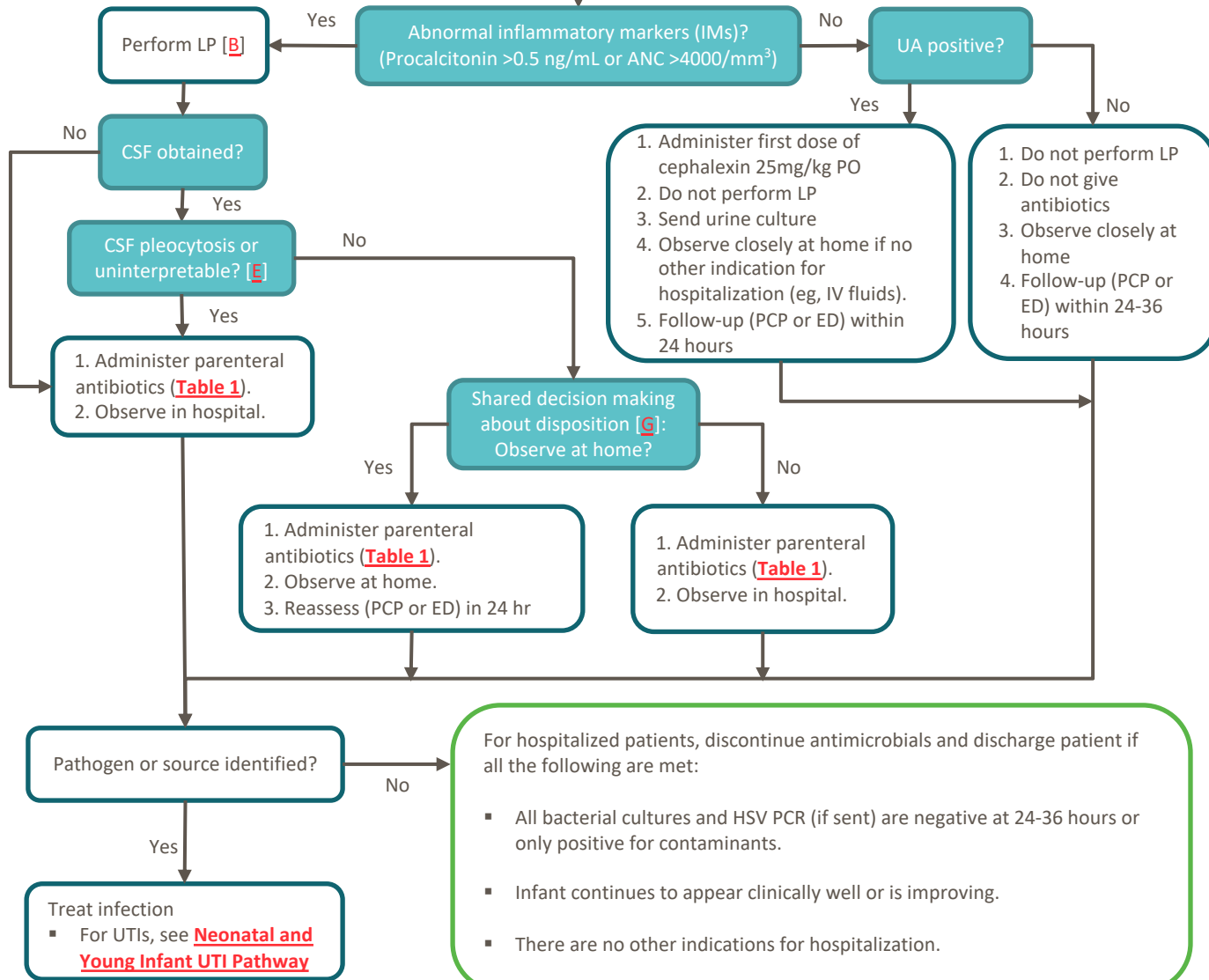
- Ill-appearing
- Preterm infants (<37 weeks gestation)
- Chronic medical condition
- High suspicion of herpes simplex virus (HSV) (eg, vesicles) [A]
- Focal bacterial infection (eg, cellulitis, omphalitis, septic arthritis, osteomyelitis)
- Clinical bronchiolitis
- Immunization or antibiotic treatment in the past 48 hours

\*If unable to obtain CSF in patients with **elevated IMs** after 3 attempts:

- Start parenteral antibiotics
- Consider repeat LP after admission [C]
- Consider use of ultrasound-guided or IR-guided LP [D]

## In the ED:

- Obtain urinalysis, blood culture, CBC with differential, procalcitonin
- If urinalysis positive ( $>5$  WBCs/hpf or positive leukocyte esterase), send urine culture by straight catheterization or suprapubic aspiration
- Consider HSV evaluation if HSV risk factors present [A]



# Fever in Infants (8 to 60 days old) Pathway

## Table 1. Empiric Antibiotics

Suspected source of infection	8-21 days old	22-28 days old	29-60 days old
No focus identified or UTI	Ampicillin 50 mg/kg/dose IV/IM q8hrs  and  Gentamicin 5 mg/kg/dose IV/IM q24 hours	Ceftriaxone 50 mg/kg/dose IV/IM q24 hours*	Ceftriaxone 50 mg/kg IV/IM q24 hours  For UTI, infants may be discharged with cephalexin 25mg/kg/dose PO TID
Bacterial meningitis	Ampicillin 75 mg/kg/dose IV/IM q6hrs  and  Ceftazidime 50 mg/kg/dose IV/IM q 8 hours	Ampicillin 75 mg/kg/dose IV/IM q6hrs  and  Ceftazidime 50 mg/kg IV/IM q 8 hours	Ceftriaxone 50 mg/kg IV/IM q12 hours  and  Vancomycin 10-15 mg/kg IV for the 1 <sup>st</sup> dose (if in the ED) or vancomycin per pharmacy protocol (if inpatient)

\*Do not use ceftriaxone in hyperbilirubinemic neonates, particularly those who are premature since ceftriaxone is reported to displace bilirubin from albumin binding sites; concomitant use with intravenous calcium-containing solutions/products in neonates  $\leq 28$  days of age is contraindicated.

### [A] Indications for HSV Evaluation

Consider evaluation for HSV with any of the following risk factors:

- Ill appearance
- Hypothermia
- Seizures
- Vesicles
- Mucous membrane ulcers
- Hepatosplenomegaly
- Maternal history of genital HSV lesions or concern for primary HSV infection (eg, fevers from 48 hours before to 48 hours after delivery)
- Thrombocytopenia
- CSF pleocytosis without a positive Gram stain
- Elevated ALT (if obtained)

HSV Work-up

- CSF HSV PCR
- Blood HSV PCR
- HSV PCR from separate surface swabs of conjunctivae, nasopharynx, mouth, and anus
- HSV PCR from any suspicious mucocutaneous lesions
- ALT

### [B] CSF Studies

- Cell count and differential
- Protein
- Glucose
- Gram stain and culture
- Meningitis/encephalitis PCR panel
  - Send if pleocytosis present (CSF WBC  $\geq 18/\text{mm}^3$  for age  $\leq 28$  days and CSF WBC  $\geq 10/\text{mm}^3$  for age 29-60 days)

[C] Decisions on repeat LP should take into account factors such as suspected source of infection, blood culture results, and clinical presentation.

### [D] Process for IR-guided LPs

- M-F 7a-5p: Place an IR consult order and page the IR consult pager at 18533.
- After hours or urgent: Page the IR attending on call.
- Consider obtaining an ultrasound to evaluate for hematoma (if present, IR will not attempt LP).

[E] Would consider CSF to be uninterpretable with CSF RBC  $\geq 10,000$  cells/ $\text{mm}^3$ . CSF WBCs can be interpreted at face value for CSF RBC  $< 10,000$  cells/ $\text{mm}^3$ .

[\[Back to 8-21 days\]](#)

[\[Back to 22-28 days\]](#)

[\[Back to 29-60 days\]](#)



# Fever in Infants (8 to 60 days old) Pathway

## [F] Sample Shared Decision-Making Scripts for CSF Testing

(can be modified to each patient/provider)

### Step 1: Seek the parent's participation

The results of the urine and blood tests we have now are reassuring. However, there is still a possibility that your baby has bacterial meningitis. There are 2 options for your baby – to have a spinal tap now or to be admitted to the hospital without having a spinal tap.

### Step 2: Help the parent explore and compare options

#### Option 1: Spinal Tap

Potential benefits	Potential Harms
<ul style="list-style-type: none"><li>- If the spinal tap shows possible bacterial meningitis, treatment can be started right away</li><li>- If the spinal tap show that your baby probably doesn't have bacterial meningitis, your baby might be able to go home from the ER and not be admitted to the hospital</li></ul>	<ul style="list-style-type: none"><li>- Discomfort for the baby</li><li>- Unsuccessful spinal tap</li><li>- Rare serious complications like bleeding, infection, or injury to the nerves which happen in 0.1% of babies</li></ul>

#### Option 2: Admission to the hospital without a spinal tap

Potential benefits	Potential Harms
<ul style="list-style-type: none"><li>- Avoiding risks of spinal tap, including discomfort, the possibility that the spinal tap isn't successful, and rare serious complications</li></ul>	<ul style="list-style-type: none"><li>- Later diagnosis of bacterial meningitis that may cause injury to the baby's brain</li><li>- Disruption of your family's routine</li><li>- Your baby getting a different infection in the hospital</li><li>- Costs of the hospital admission</li></ul>

### Step 3: Assess the parent's values and preferences

Now that I have 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 2 options and what is important to you in deciding what to do?

### Step 4: Reach a decision with the parent

Now I'd like to learn which option you prefer. Do you prefer that your baby has a spinal tap or gets admitted to the hospital without having a spinal tap?

[\[Back to 8-21 days\]](#)

[\[Back to 22-28 days\]](#)

[\[Back to 29-60 days\]](#)

# Fever in Infants (8 to 60 days old) Pathway

## [G] Sample Shared Decision-Making Scripts for Disposition

(can be modified to each patient/provider)

### 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 2 options for your baby – to be admitted to the hospital or to be discharged home from the ER after 1 dose of an antibiotic.

### Step 2: Help the parent explore and compare options

#### Option 1: Admission to the Hospital

Potential benefits	Potential Harms
<ul style="list-style-type: none"><li>- Your baby can be monitored by doctors and nurses for signs of infection</li><li>- If your baby shows signs of infection, treatment can be given immediately</li><li>- If your baby is not feeding well or is making fewer wet diapers, fluids can be given through an IV</li></ul>	<ul style="list-style-type: none"><li>- Disruption of your family's routine</li><li>- Your baby getting a different infection in the hospital</li><li>- Costs of the hospital admission</li></ul>

#### Option 2: Discharge home after 1 dose of an antibiotic

Potential benefits	Potential Harms
<ul style="list-style-type: none"><li>- Avoiding the potential harms of being admitted to the hospital</li><li>- Less disruption to your family's routine</li></ul>	<ul style="list-style-type: none"><li>- Small chance of having a bacterial infection</li></ul>

Signs to monitor for at home: persistent fevers, a blue color to the skin, breathing too fast or too slow, vomiting, not feeding well, making fewer wet diapers, or your baby is not acting well or is too sleepy, irritable, or crying a lot and is not able to be consoled. If he/she is getting sicker, you will need to return to the ER.

### Step 3: Assess the parent's values and preferences

Now that I have explained the possible harms and benefits of your baby being admitted to the hospital or to be discharged home from the ER after 1 dose of an antibiotic, can you please tell me what you understand about the 2 options and what is important to you in deciding what to do?

### Step 4: Reach a decision with the parent

Now I'd like to learn which option you prefer. Do you prefer that your baby admitted to the hospital or to be discharged home from the ER after 1 dose of an antibiotic?

[\[Back to 8-21 days\]](#)

[\[Back to 22-28 days\]](#)

[\[Back to 29-60 days\]](#)

## REFERENCES:

### AAP Clinical Practice Guideline

Pantell RH, Roberts KB, Adams WG, Dreyer BP, Kuppermann N, O'Leary ST, Okechukwu K, Woods CR Jr; SUBCOMMITTEE ON FEBRILE INFANTS. Evaluation and Management of Well-Appearing Febrile Infants 8 to 60 Days Old. *Pediatrics*. 2021 Aug;148(2):e2021052228. doi: 10.1542/peds.2021-052228. Epub 2021 Jul 19. Erratum in: *Pediatrics*. 2021 Nov;148(5): PMID: 34281996.

### Epidemiology

- Biondi EA, Lee B, Ralston SL, Winikor JM, Lynn JF, Dixon A, McCulloh R. Prevalence of Bacteremia and Bacterial Meningitis in Febrile Neonates and Infants in the Second Month of Life: A Systematic Review and Meta-analysis. *JAMA Netw Open*. 2019 Mar 1;2(3):e190874. doi: 10.1001/jamanetworkopen.2019.0874. PMID: 30901044
- Woll C, Neuman MI, Pruitt CM, Wang ME, Shapiro ED, Shah SS, et al; Febrile Young Infant Research Collaborative. Epidemiology and Etiology of Invasive Bacterial Infection in Infants ≤60 Days Old Treated in Emergency Departments. *J Pediatr*. 2018 Sep;200:210-217.e1. doi: 10.1016/j.jpeds.2018.04.033. Epub 2018 May 18. PMID: 29784512

### Testing

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

- 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. doi: 10.1542/peds.2015-0012. PMID: 26009628.
- 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. doi: 10.1542/peds.2017-3068. Epub 2018 Jan 16. PMID: 29339564

#### Use of inflammatory markers for risk stratification

- 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. doi: 10.1542/peds.2018-3604. Epub 2019 Jun 5. PMID: 31167938
- 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
- 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. doi: 10.1001/jamapediatrics.2018.5501. PMID: 30776077
- 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. doi: 10.1001/jamapediatrics.2018.5501. PMID: 30776077

#### Use of selective lumbar punctures in febrile infants with positive urinalyses

- 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. doi: 10.1001/jamanetworkopen.2021.4544. PMID: 33978724
- 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. doi: 10.1136/archdischild-2020-320468. Epub ahead of print. PMID: 33246922
- 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. doi: 10.1542/peds.2018-3979. Epub 2019 Aug 8. PMID: 31395621.
- 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. doi: 10.1542/hpeds.2017-0254. Epub 2018 Jul 9. PMID: 29987127.

### Disposition

#### Discharge from the hospital within 24-36 hours:

- 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. doi: 10.1542/hpeds.2018-0002. PMID: 29954839
- 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. doi: 10.1001/jamapediatrics.2014.895. PMID: 25048522.

#### Discharge from the emergency department with close follow-up:

- 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. doi: 10.1542/hpeds.2020-0045. PMID: 32868377
- 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. doi: 10.1542/peds.2016-0270. Epub 2016 Nov 1. PMID: 27940667.