Febrile Infant: 8-21 Days Old

Definition: *Fever ≥ 38.0 C (100.4 F)*

Inclusion Criteria

- 8-21 days old
- Well-appearing
- Rectal temperature> 38 or 100.4
- Gestation ≥ 37 and < 42 weeks
- URI, diarrhea, AOM, or positive viral testing results are not exclusionary

Exclusion Criteria

- Preterm (< 37 weeks)
- Maternal fever, infection, antimicrobials
- Clinical bronchiolitis
- Immunocompromised
- Surgery or infection in neonatal course
- Congenital/chromosomal abnormalities
- Focal bacterial infection/medically fragile

Signs of critically ill infant

- *Listlessness*
- *Fussiness*
- *Lethargy*
- *Mottling*
- *Poor perfusion*

OFF ALGORITHM

Risk Factors for HSV ? ■

- Maternal history of genital HSV lesions and/or fever 48 hours before/after delivery
- Ill appearance
- Vesicular skin lesions
- Seizures
- Hypothermia
- Mucous membrane ulcers
- Lab risk factors (see below)

ABNORMAL IM's ?

- Procalcitonin ≥ 0.5 ng/mL
- ANC ≥ 4000 mm^3
- CRP ≥ 2 mg/dL OR ≥ 20 mg/L

Yes

- Catheterized UA and urine culture
- Blood culture (at least 1 ml of blood)
- Inflammatory markers (IM) and serum studies:
  - CBC with differential
  - Procalcitonin
  - CRP *(only if procalcitonin unavailable)*
  - CMP
- Perform LP and send CSF for:
  - Cell count, glucose, protein
  - Gram stain/culture

- Meningitis/encephalitis CSF PCR ⁑ ***AND*** CSF HSV PCR (*in addition* to above)
- Surface swabs of mouth, nasopharynx, conjunctivae, rectum for HSV PCR
- Blood HSV PCR
- Call Send Out lab to discuss sending CSF for HSV PCR to alternative site (*LAB code 85890*)

Parenteral antibiotics (see table) ***PLUS*** Acyclovir (See table)

Admit

No

- Catheterized UA and urine culture
- Blood culture (at least 1 ml of blood)
- Inflammatory markers (IM) and serum studies:
  - CBC with differential
  - Procalcitonin
  - CRP *(only if procalcitonin unavailable)*
  - CMP
- Perform LP and send CSF for:
  - Cell count, glucose, protein
  - Gram stain/culture
  - Consider meningitis/encephalitis PCR based on clinical judgement (see footnote) ⁑

Laboratory Risk Factors for HSV ?

- Leukopenia
- Thrombocytopenia
- Elevated transaminases (>2x normal)
- CSF Pleocytosis without + gram stain

Yes

No

Parenteral antibiotics (see table)

Admit

Antimicrobial Choice

All medications listed can be given IV or IM

Suspected Source of Infection	Empiric Antimicrobial Therapy: 8-21 days old *(Empiric Duration: 48 hours if cultures remain negative)*
No focus identified	• Ampicillin (*50 mg/kg/dose Q8h*) **AND** • Gentamicin (*5 mg/kg/dose Q24h*) OR Ceftazidime (*50 mg/kg Q8h*)
UTI (UA with > 5 WBC/hpf)	• Ampicillin (*50 mg/kg/dose Q8h*) **AND** • Gentamicin (*5 mg/kg/dose Q24h*) OR Ceftazidime (*50 mg/kg Q8h*)
Bacterial Meningitis (CSF ≥ 15 WBC/mm^3)	• Ampicillin (*75 mg/kg/dose Q6h*) **AND** • Ceftazidime (*50 mg/kg/dose Q8h*)
Risk factors for HSV	• **Add** Acyclovir to one of above regimens *(20mg/kg/dose Q8h)*

■ Some providers factor in age of the neonate to determine which patients are or are not considered to be low risk for invasive HSV infection.[3]

⁑ Use clinical judgement when ordering the meningitis encephalitis panel, with particular consideration when (1) CSF pleocytosis present, (2) patient is ill appearing, (3) LP is traumatic, and/or (4) pre-treatment with antimicrobials prior to LP.

Febrile Infant: 22-28 Days Old

Definition: *Fever ≥ 38.0 C (100.4 F)*

Inclusion Criteria

- 22-28 days old
- Well-appearing
- Rectal temperature> 38 or 100.4
- Gestation ≥ 37 and < 42 weeks
- URI, diarrhea, AOM, or positive viral testing results are not exclusionary

Exclusion Criteria

- Preterm (< 37 weeks)
- Clinical bronchiolitis
- Immunocompromised
- Surgery or infection in neonatal course
- Congenital/chromosomal abnormalities
- Focal bacterial infection/medically fragile

Signs of critically ill infant

- *Listlessness*
- *Fussiness*
- *Lethargy*
- *Mottling*
- *Poor perfusion*

OFF ALGORITHM

- Catheterized UA and urine culture
- Blood culture (at least 1 ml of blood)
- Inflammatory markers (IM) and serum studies:
  - CBC with differential
  - Procalcitonin
  - CRP *(only if procalcitonin unavailable)*
  - CMP

ABNORMAL IM's ? ◆

- Procalcitonin ≥ 0.5 ng/mL
- Absolute neutrophil count (ANC) ≥ 4000 mm³
- *(If obtained)* CRP ≥ 2 mg/dL OR ≥ 20 mg/L

No

CONSIDER LP

CSF TESTING ?

- Pleocytosis (>18 WBC/mm³)
- Results uninterpretable
- LP done, CSF not obtained

Yes

- Parenteral antimicrobials
- Can consider observing **without** antimicrobials if:
  - *IM's negative, LP not performed*
  - *IM's positive, LP negative*
  - *IM's negative, LP negative*

Admit

Yes

Perform LP; Send CSF for:

- Cell count, glucose, protein
- Gram stain/culture
- Consider meningitis/encephalitis PCR based on clinical judgement (see footnote) ¥

CSF TESTING ?

- Pleocytosis (>18 WBC/mm³)
- Results uninterpretable
- LP done, CSF not obtained

Yes

Parenteral antimicrobials (see table)

Admit

No

SAFE FOR HOME OBSERVATION?

- Reliable phone/transportation
- Parent able to observe and communicate changes in condition
- Able to arrange reevaluation within 24 hours

No

Parenteral antimicrobials (see table)

Admit

Yes

Parenteral antimicrobials (see table)

Discharge
Reassess in 24 hours

Antimicrobial Choice

All medications listed can be given IV or IM

Suspected Source of Infection	Empiric Antimicrobial Therapy: 22-28 days old *(Empiric Duration: 48 hours if cultures remain negative)*
No focus identified **OR** UTI (UA with > 5 WBC/hpf)	• Ceftriaxone *(50 mg/kg/dose Q24h)*
Bacterial Meningitis (CSF ≥ 15 WBC/mm³)	• Ampicillin (*75 mg/kg/dose Q6h*) **AND** • Ceftazidime (*50 mg/kg/dose Q8h*)
Risk Factors for HSV Δ	• Consider Acyclovir *(20 mg/kg/dose Q8h)*

HSV Risk Factors ? Δ

- Vesicular rash on exam
- Seizures
- Ill appearance
- Hypothermia
- Mucous membrane ulcers
- Leukopenia
- Thrombocytopenia
- Elevated transaminases (>2x normal)
- CSF pleocytosis and gram stain neg

IF HSV Risk Factors:

- CSF HSV PCR
- Meningitis/ encephalitis panel
- Obtain surface swabs of mouth, nares, conjunctivae, and rectum
- Blood HSV PCR

◆ If procalcitonin is < 0.5 ng/dL, IM's are still considered ABNORMAL if ANC >4,000 mm³ OR CRP (if obtained) ≥ 2 mg/dL; (see PECARN/step-by-step rules in references) [7]

¥ Use clinical judgement when ordering the meningitis encephalitis panel, with particular consideration when (1) CSF pleocytosis present, (2) patient is ill appearing, (3) LP is traumatic, and/or (4) pre-treatment with antimicrobials prior to LP.

Δ HSV can occur in this age group; consider testing/treatment based on the risk factors above.

Febrile Infant: 29-60 Days Old

Definition: *Fever ≥ 38.0 C (100.4 F)*

Inclusion Criteria

- 29-60 days old
- **Well-appearing**
- Rectal temperature> 38 or 100.4
- Gestation >37 and < 42 weeks
- +/- URI, diarrhea, dx of AOM, positive viral testing results

Exclusion Criteria

- Preterm (<37 weeks)
- Clinical bronchiolitis
- Immunocompromised
- Surgery or infection in neonatal course
- Congenital/chromosomal abnormalities
- Focal bacterial infection/medically fragile

Signs of critically ill infant

- *Listlessness*
- *Fussiness*
- *Lethargy*
- *Mottling*
- *Poor perfusion*

→ **OFF ALGORITHM**

- Catheterized UA and urine culture
- Blood culture (at least 1 ml of blood)
- Inflammatory markers (IM) and serum studies:
  - CBC with differential
  - Procalcitonin
  - CRP *(only if procalcitonin unavailable)*
  - Consider CMP

ABNORMAL IM's ? ◆

- Procalcitonin ≥ 0.5 ng/mL
- Absolute neutrophil count (ANC) ≥ 4000 mm^3
- *(If obtained)* CRP ≥ 2 mg/dL OR ≥ 20 mg/L

No → **POSITIVE UA ?** > 5 WBC/hpf

- **Yes** → Oral antimicrobials (see table) → **Discharge*** Follow up in 12-24 hrs
- **No** → **Discharge*** Follow up in 12-24 hrs

Yes → Consider LP ^ *(see footnote)* and, if performed, send CSF for:

- Cell count, glucose, protein
- Gram stain/culture
- Consider meningitis/encephalitis PCR based on clinical judgement (see footnote) ¤

- **CSF POSITIVE** (CSF >9 WBC/mm^3) → Parenteral antimicrobials (see table) → **Admit**
- **CSF NOT OBTAINED or UNINTERPRETABLE** → Parenteral antimicrobials (see table)
- **CSF NEGATIVE** → **POSITIVE UA ?** > 5 WBC/hpf
  - **Yes** → Oral/IV antimicrobials (see table)
  - **No** → Ceftriaxone (see table)

→ **Discharge* vs Admit**

***Discharge Requirements:** (1) Reliable phone and transportation, (2) parent able to observe & discuss changes in condition, and (3) concrete plan for reevaluation

Antimicrobial Choice

Parenteral medications listed can be given IV or IM

Suspected Source of Infection	Empiric Antimicrobial Therapy: 29-60 days old *(Empiric Duration: 48 hours if cultures remain negative)*
UTI (UA with >5 WBC/hpf)	• Oral: Cephalexin *(25 mg/kg/dose Q8h)* **OR** • Ceftriaxone (*50 mg/kg/dose Q24h*) if NPO/pyelonephritis
No focus identified	• Ceftriaxone *(50 mg/kg/dose Q24h)*
Bacterial Meningitis (CSF ≥ 9 WBC/mm^3)	• Ceftriaxone (*50 mg/kg/dose Q12h*) **AND** • Vancomycin *(15 mg/kg/dose Q6h)*
Risk factors for HSV△	• Consider Acyclovir *(20mg/kg/dose Q8h)*

HSV Risk Factors ? △

- Vesicular rash on exam
- Seizures
- Ill appearance
- Hypothermia
- Mucous membrane ulcers
- Leukopenia
- Thrombocytopenia
- Elevated transaminases (>2x normal)
- CSF pleocytosis and gram stain neg

IF HSV Risk Factors:

- CSF HSV PCR
- Meningitis/encephalitis panel
- Obtain surface swabs of mouth, nares, conjunctivae, and rectum
- Blood HSV PCR

◆ If procalcitonin is < 0.5 ng/dL, IM's are still considered abnormal if ANC >4,000 mm^3 or CRP (if obtained) ≥ 2 mg/dL; (see Pecarn/Step-by-Step rules in references) [7]

^IM's that are exceedingly high or low, or several abnormal IM's increase risk of meningitis.[1]

¤Use clinical judgement when ordering the meningitis encephalitis panel, with particular consideration when (1) CSF pleocytosis present, (2) patient is ill appearing, (3) LP is traumatic, and/or (4) pre-treatment with antimicrobials prior to LP.

△HSV can occur in this age group; consider testing/treatment based on the risk factors above.

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7. Inflammatory Marker (IM) Interpretation

- If **procalcitonin** and **ANC** available, follow PECARN and/or Step-By-Step
- If **procalcitonin** and **CRP** available, follow Step-by-Step

Step-By-Step[4]

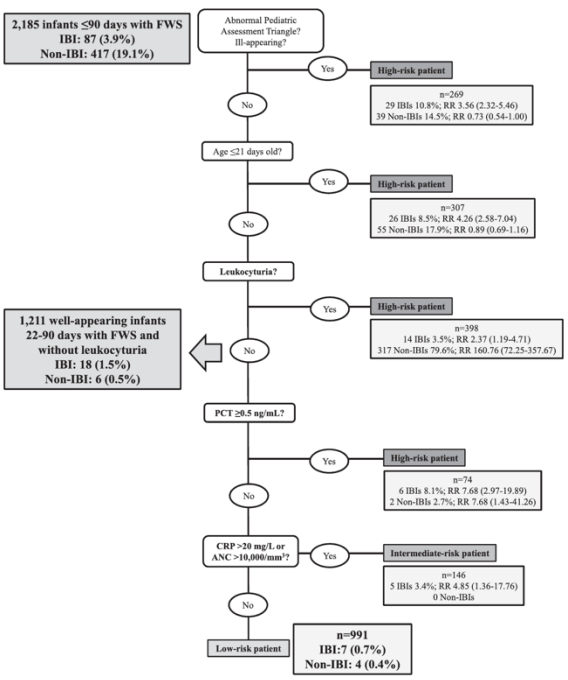
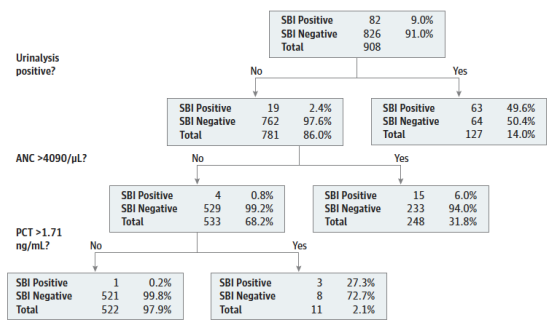


FIGURE 3
Prevalence of invasive and non-IBI in the different risk subgroups and OR for those infants presenting each risk factor.

PECARN[5]

Figure 2. Recursive Partitioning Analysis



	Derivation, No.			Validation, No.		
	SBI	No SBI	Total	SBI	No SBI	Total
SBI per rule	81	305	386	86	330	416
No SBI per rule	1	521	522	2	495	497
Total	82	826	908	88	825	913

	Derivation, No.	Validation, No.
Prediction rule sensitivity (95% CI), %	98.8 (92.5-99.9)	97.7 (91.3-99.6)
Prediction rule specificity (95% CI), %	63.1 (59.7-66.4)	60.0 (56.6-63.3)
Negative predictive value (95% CI), %	99.8 (98.8-100.0)	99.6 (98.4-99.9)
Positive predictive value (95% CI), %	21.0 (17.1-25.5)	20.7 (16.9-25.0)
Negative likelihood ratio (95% CI)	0.02 (0.003-0.14)	0.04 (0.01-0.15)
Positive likelihood ratio (95% CI)	2.68 (2.44 - 2.93)	2.44 (2.23-2.67)

Meningitis-Encephalitis Panel Pathogens: E. coli (K1 serotype), H. influenzae, Listeria, Neisseria meningitidis (encapsulated strains only), Group B Strep, S. pneumoniae, CMV, Enterovirus, HSV-1, HSV-2, HHV-6, Human parechovirus, Varicella, Cryptococcus neoformans/gattii

(*Do NOT rely solely on the ME Panel if there is strong clinical concern for HSV infection.*)

Ochsner Children's Clinical Pathways Committee
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