

Neonatal Fever v5.0: ED Phase (0-28 days old)

[Approval & Citation](#)

[Summary of Version Changes](#)

[Explanation of Evidence Ratings](#)

PHASE I (E.D.)

Inclusion Criteria

- Fever ≥ 38 C (or a reliable history of fever) or [hypothermia](#) < 36 C in children < 28 days of age

Exclusion Criteria

- Patients currently admitted to ICU or admitted > 3 days
- Known immunodeficiency or cancer
- Patients with central venous catheters or VP shunts

Urgent Care Transfer Guidelines (for 0-28 days)

Well appearing neonates with fever transfer via POV to an ED

Ill appearing neonates with fever:

- Initiate transport immediately
- Attempt to obtain labs
- Give antibiotics (IV or IM)

!

Other [differential diagnosis](#) for severely ill neonates

Begin clinical assessment

[Focal Infection](#)
(e.g., omphalitis, pneumonia)

Yes

Off Pathway

No

CSF Normative values

0-1 month: CSF WBC $< 20/mm^3$
 ≥ 1 month: CSF WBC $< 10/mm^3$

!

If CSF pleocytosis consider

[CSF Rapid Viral Qual. PCR](#)

- UA, urine culture
- CBC with diff, Blood culture
- CSF studies
- HSV work up if indicated (see box)
- CXR and respiratory viral panel (if respiratory symptoms)
- Stool PCR (if diarrhea)

HSV work up indications

Perform [complete work up](#) and begin acyclovir for any of the following:

Historical and clinical features

- severe illness
- hypothermia
- lethargy
- seizures
- hepatosplenomegaly
- postnatal HSV contact
- vesicular rash
- conjunctivitis
- interstitial pneumonitis

Laboratory features

- thrombocytopenia
- CSF pleocytosis > 20 WBC/ mm^3 without clear bacterial infection (e.g., + Gram stain)

Inability to obtain CSF in ED

Considerations for Pretreated CSF

- Administer antibiotics (GOAL: within 60 minutes)
- Refer to IR for lumbar puncture as inpatient
- Rapid CSF Bacterial PCR can be sent on pre-treated CSF that demonstrates pleocytosis

Begin empiric treatment

- Ampicillin and cefotaxime (or ceftazidime if cefotaxime unavailable)
- Acyclovir if HSV work up performed
- Admit all patients

Go to Inpatient Phase (0-28d)

!

In well-appearing infants with multiple maternal HSV risk factors, consider [HSV work up](#)

Neonatal Fever v5.0: ED Phase (29-56 days old)

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PHASE I (E.D.)

Inclusion Criteria

- Fever ≥ 38 C (or a reliable history of fever) or [hypothermia](#) < 36 C in children 29-56 days of age

Exclusion Criteria

- Patients currently admitted to ICU or admitted > 3 days
- Known immunodeficiency or cancer
- Patients with central venous catheters or VP shunts

Urgent Care Transfer Guidelines (for 29-56 days)

Ill appearing neonates with fever:

- Initiate transport immediately
- Attempt to obtain labs
- Give antibiotics (IV or IM)

Does not meet low risk criteria:

- Transfer to ED for additional work up and antibiotics

!

If CSF pleocytosis consider

[CSF Rapid Viral Qual. PCR](#)

Focal Infection

(e.g., omphalitis, pneumonia)

Yes

Off Pathway

No

Bronchiolitis?

(increased work of breathing, cough, tachypnea, wheezing)

Yes

CONSIDER [NEONATAL FEVER 29-56 days W/BRONCH ED PHASE](#)

No

- CBC with diff
- Blood culture
- UA, urine culture
- CXR and respiratory viral panel (if respiratory symptoms)
- Stool PCR (if diarrhea)

Inability to obtain CSF in ED

Considerations for Pretreated CSF

- Administer antibiotics (GOAL: within 60 minutes)
- Refer to IR for lumbar puncture as inpatient
- Rapid CSF Bacterial PCR can be sent on pre-treated CSF that demonstrates pleocytosis

Low Risk Criteria

- Well-appearing
- Previously healthy
- Full term (≥ 37 weeks)
- No focal bacterial infection
- [Negative urinalysis](#)
- WBC $> 5,000$ and $< 15,000$ mm^3
- Absolute bands $< 1,500$ mm^3
- No discrete infiltrates on CXR if done

!

Ceftriaxone contraindicated with hyperbilirubinemia

Meets all low risk criteria?

Yes

No

- Obtain CSF studies
- Begin ceftriaxone
- Considerations for [severely ill patients](#) and other clinical scenarios
- Admit

Discharge Criteria (meets all)

- Eating well and well appearing
- No social/family concerns
- Reliable follow-up in 12-24 hours
- Outpatient plan accepted by PMD and family

No

Admit for observation CSF studies and antibiotics if worsens

Go to Inpatient Phase (29-56d)

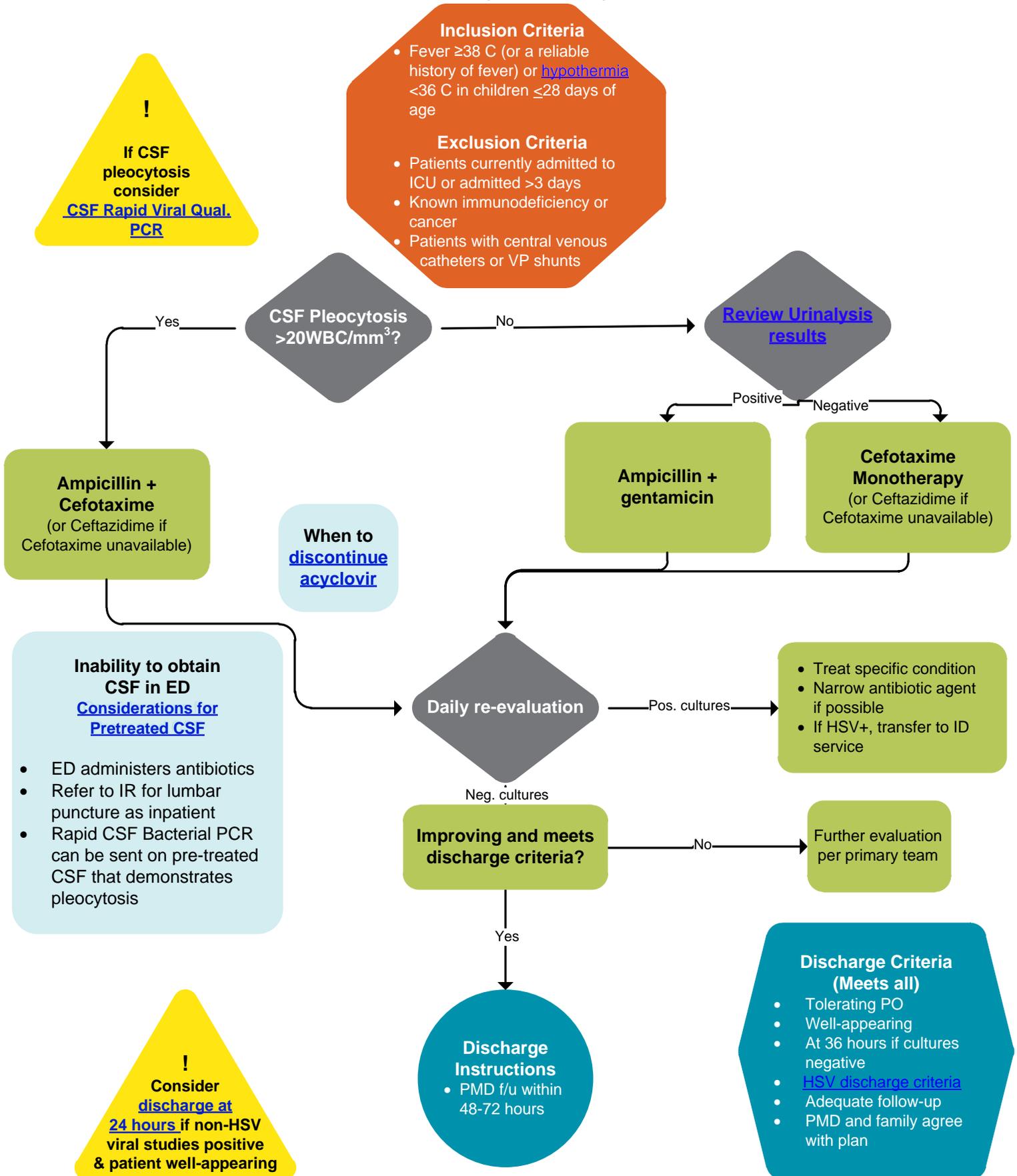
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PHASE II (INPATIENT)



Neonatal Fever v5.0: ED Phase (29-56 days old) with Bronchiolitis

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PHASE I (E.D.)

Inclusion Criteria

- Fever ≥ 38 C (or a reliable history of fever) or [hypothermia](#) < 36 C in children 29-56 days of age **with signs of bronchiolitis**

Exclusion Criteria

- Patients currently admitted to ICU or admitted > 3 days
- Known immunodeficiency or cancer
- Patients with central venous catheters or VP shunts

In patients **PRESENTING** with fever and bronchiolitis, the risk of [bacteremia and meningitis](#) is low.

[UTI](#) should be considered in patients who are persistently symptomatic with fever or vomiting.

!
Onset of **NEW** fever during hospitalization in patients with bronchiolitis can be indicative of a [serious bacterial infection](#).

Symptoms of Bronchiolitis:

(increased work of breathing, cough, tachypnea, wheezing)

Signs of poor perfusion or mental status changes or sepsis score > 3

YES

Continue workup per Neonatal Fever (29-56d) pathway

NO

Consider [UA/Culture](#) in patients who are persistently febrile or vomiting

UA +

Blood CX

Ceftriaxone

Admit to inpatient on [UTI](#) and [Bronchiolitis](#) pathway

[UA -](#)
OR
[UA NOT INDICATED](#)

Off
Pathway

CONSIDER
[BRONCHIOLITIS](#)
[PATHWAY](#)

Neonatal Fever v5.0: Inpatient Phase (29-56 days old)

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PHASE II (INPATIENT)

Inclusion Criteria

- Fever ≥ 38 C (or a reliable history of fever) or [hypothermia](#) < 36 C in children 29-56 days of age

Exclusion Criteria

- Patients currently admitted to ICU or admitted > 3 days
- Known immunodeficiency or cancer
- Patients with central venous catheters or VP shunts

!

If CSF pleocytosis consider

[CSF Rapid Viral Qual. PCR](#)

!

Ceftriaxone contraindicated with Calcium containing fluids or hyperbili

!

Consider [discharge at 24 hours](#) if non-HSV viral studies positive & patient well-appearing

Discharge Criteria (Meets all)

- Tolerating PO
- Well-appearing
- At 36 hours if cultures negative and antibiotics begun
- At 24 hours if cultures negative and no antibiotics begun
- Adequate follow-up
- PMD and family agree with plan

Daily re-evaluation

Positive cultures

- Treat specific condition
- Consider LP in patients with bacteremia if not done prior
- Begin antibiotics if not begun prior; narrow antibiotic agent if possible

Negative cultures

Improving and meets discharge criteria?

[Considerations for Pretreated CSF](#)

- Rapid CSF Bacterial PCR can be sent on pre-treated CSF that demonstrates pleocytosis

No

Further evaluation per primary team

Yes

Discharge Instructions

- PMD f/u within 48-72 hours

Background

Fever is a common presenting symptom in neonates and young infants:

- 12-28% will have a serious bacterial infection (which include bacteremia/sepsis, bacterial gastroenteritis, cellulitis, osteomyelitis, septic arthritis, meningitis, pneumonia and urinary tract infection)
(Source: Cincinnati Children's Hospital; Fever of Uncertain Source Guideline)
 - UTI is the most common.
 - 0-1.2% of all febrile neonates will have bacterial meningitis
- 0.3% will have HSV (Caviness)

Because the clinical exam alone is unreliable to predict serious illness in this age group, clinicians must rely on a combination of history, physical exam and diagnostics tests to determine a patient's risk of Serious Bacteria infection (SBI) and balance this risk with the cost and morbidity of empiric treatment.



Initial ED phase 0-28d

Initial ED phase 29-56d

Inpatient Phase 0-28d

Inpatient Phase 29-56d

Introduction – Neonatal Fever

This clinical standard work pathway is meant to guide the management of febrile neonates age 0-56 days in the Emergency Department and Inpatient Medical Unit.

Inclusion Criteria	Exclusion Criteria
Fever ≥ 38 C (or a reliable history of fever)	Patients currently admitted to ICU or admitted >3 days
Hypothermia <36 C in children <56 days of age	Known immunodeficiency or cancer
	Patients with central venous catheters or VP shunts

Febrile neonates 0-56 days will enter on this Neonatal Fever pathway and may move to another CSW pathway, such as UTI, pneumonia or bronchiolitis when diagnosis is established.

Initial ED phase 0-28d

Initial ED phase 29-56d

Inpatient Phase 0-28d

Inpatient Phase 29-56d

Risk of Serious Bacterial infections in patients with bronchiolitis and/or RSV (Fever and Bronchiolitis)

Bacteremia and meningitis are uncommon in patients with bronchiolitis and/or RSV

Levine 2004: 1248 patients < 60 days, 269 (22% with RSV)

- Overall rate Levine of SBIs = 11.4%
- Rate of SBI in RSV+ patients = 7% (all were UTIs, no bacteremia or meningitis)
- Rate of SBI in RSV- patients = 12.5%
- **CONCLUSION:** Febrile infants <60d who have RSV infections are at significantly lower risk of SBIs than infants without RSV infection

Purcell 2002: 2396 patients, 285 (11.9%) < 6 weeks

- 12 + blood cultures, all deemed contaminants
- 27 + urine cultures

Oray-Schrom 2003: 191 infants with RSV age 0-90 days; complete sepsis work-up performed on 52.5% of febrile cohort

- 5 with UTI (7.2%)
- 1 with bacteremia (1.2%)
- None with meningitis (0%)



Risk of Serious Bacterial infections in patients with bronchiolitis and/or RSV

Bacteremia and meningitis are uncommon in patients with bronchiolitis and/or RSV

Purcell 2004: 912 patients with bronchiolitis

- 2 of 470 patients tested had positive blood culture (0.43%)
- 0 of 101 patients tested had positive CSF (0%)
- 28 of 234 patients tested had positive urine (12%)

CONCLUSION: Routine sepsis and meningitis work-ups are not necessary in non-toxic appearing infants and young children with RSV lower respiratory tract infections.

Tsolia 2002: 636 infants < 12 months; blood and urine obtained on patients with fever >38 or ill appearing (174 patients)

- 0 positive blood cultures
- 8 positive urine cultures (4.6%)



Hypothermia

Hypothermia

- Septic work-up should not be delayed in neonate with a rectal temperature of less than 36 C
- Neonates should be able to maintain temperature stability when dressed in one layer of clothes more than adults and a hat.
 - If there is concern that low temperature is caused by environmental factors: swaddle, place a hat on the baby and have caregivers hold for 30 minutes. Re-check temperature. Low temperatures due to environmental factors should be resolved by these measures.
- Hypothermic babies are at higher risk for hypoglycemia. Consider checking a glucose

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Initial ED phase 29-56d

Inpatient Phase 0-28d

Inpatient Phase 29-56d

Neonatal Fever (29-56d)
w/Bronchiolitis ED

Other Exclusions: Focal Infection

Patients with clinical evidence of focal infections (e.g., omphalitis, pneumonia, cellulitis) are excluded from the neonatal fever pathway.

- These patients may still need to undergo a “febrile neonate” work-up
- Based on site of infection, empiric antibiotic choice may be different

Initial ED phase 0-28d

Initial ED phase 29-56d

Inpatient Phase 0-28d

Inpatient Phase 29-56d

Infants 0-28 Days: HSV – Complete HSV Work-up

Comprehensive testing for neonatal HSV infection should include:

- Surface swabs from nasopharynx and bi-lateral conjunctivae sent for HSV Rapid PCR and viral culture Herpes group (1 swab)
 - These specimens will be collected by RN
- CSF for CSF Rapid Viral Qual. PCR
- Blood for HSV PCR Quant. blood
- Skin vesicle fluid for HSV Rapid PCR and viral culture Herpes group
 - Provider will unroof vesicle and swab lesion
- CBC with differential, BUN, creatinine, AST and ALT

Complete the work-up for HSV in the Emergency Department.



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Initial ED phase 29-56d

Inpatient Phase 0-28d

Inpatient Phase 29-56d

Infants 0-28 Days: Inpatient Management (Cont'd)

HSV

If positive for HSV, continue acyclovir and transfer to ID service.

If CSF Rapid HSV PCR positive, add on quantitative CSF HSV PCR

Discontinue Acyclovir when:

- If patient is **well-appearing and no evidence of HSV SEM disease**: negative surface and CSF Rapid PCRs (may consider discharge before blood HSV PCR result)
- If patient **has a definitive alternate diagnosis** (even if not well-appearing): negative surface and CSF Rapid PCRs
- If **high ongoing HSV suspicion**: wait for all HSV studies (including surface cultures and surface/blood PCRs) to return negative



Infants 0-28 Days: Inpatient Management (Cont'd)

Discharge Criteria:

- Well-appearing
- Tolerating PO/enteral feeds
- At 36 hours all cultures negative
- Meets HSV discharge criteria, if applicable
- Follow-up available with 48-72 hours
- PMD and family agree with plan



Risk of Serious Bacterial infections in patients with bronchiolitis and/or RSV (Fever and Bronchiolitis)

Bacteremia and meningitis are uncommon in patients with bronchiolitis and/or RSV

Levine 2004: 1248 patients < 60 days, 269 (22% with RSV)

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- 5 with UTI (7.2%)
- 1 with bacteremia (1.2%)
- None with meningitis (0%)



**Neonatal Fever (29-56d)
w/Bronchiolitis ED**

Febrile Infants with bronchiolitis and/or RSV remain at risk for co-infection with UTI

Author	Date	Rate of UTI
Levine	2004	5.4% (14/261)
Purcell	2004	14.9% (14/94)
Purcell	2002	27+ (unknown number collected—2396 in study)
Oray-Schrom	2003	7.2% (5/69)
Tsolia	2002	4.65 (8/174)
Randolph	2004	0.6% (1/121)
Titus	2003	1.3% (2/147)

Risk of UTI in patients with bronchiolitis and/or RSV ranges from 0.6% to 15%

RECOMMENDATIONS:

Febrile Infants **age 0-28 days** of age remain at risk for serious bacterial infections and should have a full sepsis work-up despite the presence or absence of bronchiolitis.

Febrile infants **age 29-56 days** who are non-toxic appearing (no symptoms of poor perfusion, acute mental status changes or significant tachycardia) and have clinical symptoms of bronchiolitis do not require a full sepsis workup. **Blood and CSF cultures are not routinely recommended in this population.**

Urinalysis and culture should be considered in patients age 29-56 days with persistent fever (2 or more occurrences), vomiting or excessive irritability.



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Initial ED phase 29-56d

Inpatient Phase 0-28d

Inpatient Phase 29-56d

Neonatal Fever (29-56d)
w/Bronchiolitis ED

Late Occurrence of Fever in Patients with Bronchiolitis

Patients with bronchiolitis and/or RSV who develop fever during hospitalization are at higher risk for serious bacterial infection and additional work-up should be considered.

Tsolia: 5 of 636 infants admitted with bronchiolitis subsequently acquired bacteremia during their hospitalization for bronchiolitis

Bloomfield demonstrated increased risk of bacteremia in patients with:

- Nosocomial RSV (OR= 23.4)
- PICU admission (OR = 9.4)
- Ventilatory support (OR=7.4)
- Cyanotic heart disease (OR 10.8)



Neonatal Fever (29-56d)
w/Bronchiolitis ED

Introduction – Neonatal Fever

This clinical standard work pathway is meant to guide the management of febrile neonates age 0-56 days in the Emergency Department and Inpatient Medical Unit.

Inclusion Criteria	Exclusion Criteria
Fever ≥ 38 C (or a reliable history of fever)	Patients currently admitted to ICU or admitted >3 days
Hypothermia <36 C in children <56 days of age	Known immunodeficiency or cancer
	Patients with central venous catheters or VP shunts

Febrile neonates 0-56 days will enter on this Neonatal Fever pathway and may move to another CSW pathway, such as UTI, pneumonia or bronchiolitis when diagnosis is established.



Initial ED phase 0-28d

Initial ED phase 29-56d

Inpatient Phase 0-28d

Inpatient Phase 29-56d

Other Exclusions: Focal Infection

Patients with clinical evidence of focal infections (e.g., omphalitis, pneumonia, cellulitis) are excluded from the neonatal fever pathway.

- These patients may still need to undergo a “febrile neonate” work-up
- Based on site of infection, empiric antibiotic choice may be different

Initial ED phase 0-28d

Initial ED phase 29-56d

Infants 0-28 Days: Initial ED Workup

Testing for all patients should include:

- CBC with differential
- Blood culture
- UA, urine culture
- CSF studies (obtain 4 tubes)
 - If patient is clinically unstable, LP can be delayed and antibiotics should be administered
- Respiratory viral panel for respiratory symptoms
- CXR for respiratory symptoms not consistent with bronchiolitis
- Stool PCR if diarrhea present



Initial ED phase 0-28d

Initial ED phase 29-56d

Inpatient Phase 0-28d

Inpatient Phase 29-56d

Infants 0-28 Days: Bronchiolitis

Patients 0-28 days who present with fever = 38 and symptoms of bronchiolitis should still have a full work-up that includes:

- CBC with differential
- Blood culture
- UA, urine culture
- CSF studies (obtain 4 tubes)
- Chest X-ray can be deferred if patient has clear clinical bronchiolitis (Local Consensus)

Initial ED phase 0-28d

Initial ED phase 29-56d

Inpatient Phase 0-28d

Inpatient Phase 29-56d

Infants 0-28 Days: Herpes Simplex Virus (HSV)

In addition to initial work-up, initiate HSV work-up on patients with **ANY** of the following:

Historical and Clinical Features		
Severe Illness	Seizures	Conjunctivitis
Hypothermia	Hepatosplenomegaly	Postnatal HSV contact
Lethargy	Interstitial pneumonitis	Vesicular rash

Laboratory Features	
Thrombocytopenia	
CSF pleocytosis >20 WBC/mm ³ without clear bacterial infection (negative Gram stain)	For well appearing infants with no other HSV risk factors, who have a traumatic tap (>1000 RBC/mm ³), consider deferring HSV workup
Elevated LFTs	We are not recommending routine LFT screening for all neonates, as most patients with disseminated HSV tend to be ill appearing and would meet other criteria for HSV work-up



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Infants 0-28 Days: HSV – Maternal Risk Factors

Infants at greatest risk of neonatal HSV are those born vaginally (especially with use of invasive monitoring or with history of leaking membranes prior to delivery) to mothers with any of the following risk factors for **primary maternal HSV** infection:

- Mother's current or past sex partners have a history of genital or oral HSV
- New sexual partner in pregnancy, especially late in gestation
- Sores in the vagina, or opening of the vagina, during pregnancy, especially bilaterally on the vulva late in gestation
- Urinary retention (sometimes misdiagnosed as an UTI)
- History of frequent yeast infections
- Receipt of oral sex during the last half of pregnancy from partner with history of cold sores

NOTE: These are maternal risk factors for primary HSV infection. Use clinical judgment in determining if HSV work up is indicated in well-appearing infants born to mothers with multiple risk factors.



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Initial ED phase 0-28d

Initial ED phase 29-56d

Inpatient Phase 0-28d

Inpatient Phase 29-56d

Infants 0-28 Days: Inpatient Management (Cont'd)

Discharge Criteria:

- Well-appearing
- Tolerating PO/enteral feeds
- At 36 hours all cultures negative
- Meets HSV discharge criteria, if applicable
- Follow-up available with 48-72 hours
- PMD and family agree with plan

Initial ED phase 0-28d

Initial ED phase 29-56d

Inpatient Phase 0-28d

Inpatient Phase 29-56d

Infants 0-28 Days: ED – Empiric Treatment

All patients should receive a single dose of ampicillin and cefotaxime immediately after appropriate cultures are obtained, without waiting for initial CSF counts:

- Rapid administration of appropriate antibiotics is associated with improved outcomes.
- Goal is for antibiotics to be administered within 60 minutes of presentation
- Antibiotics can be narrowed by the admitting team once cell counts are available.

NOTE: Due to nationwide shortage of Cefotaxime, Ceftazidime should be given if Cefotaxime is unavailable.

NOTE: All patients with suspicion of HSV should receive acyclovir in addition to antibiotics

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Infants 0-28 Days: Inpatient Management

Admission Criteria

Recommend admission of all febrile neonates age 0-28 days for empiric antibiotics.

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Infants 0-28 Days: Inpatient Management (Cont'd)

Antibiotic choice is based on concern for meningitis and risk for enterococcus and listeria:

Concern for Meningitis	Concern for UTI	Antibiotic
High (≥ 20 WBC/mm ³)		Ampicillin and cefotaxime (or ceftazidime)
Low (< 20 WBC/mm ³)	Yes	Ampicillin and Gentamicin
Low (< 20 WBC/mm ³)	No	Cefotaxime (or ceftazidime)

Continue acyclovir for those with an HSV workup pending:

- Recommend 1.5x maintenance fluids to prevent renal tubular injury for patients on acyclovir

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Initial ED phase 29-56d

Inpatient Phase 0-28d

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Infants 0-28 Days: Inpatient Management (Cont'd)

HSV

If positive for HSV, continue acyclovir and transfer to ID service.

If CSF Rapid HSV PCR positive, add on quantitative CSF HSV PCR

Discontinue Acyclovir when:

- If patient is **well-appearing and no evidence of HSV SEM disease**: negative surface and CSF Rapid PCRs (may consider discharge before blood HSV PCR result)
- If patient **has a definitive alternate diagnosis** (even if not well-appearing): negative surface and CSF Rapid PCRs
- If **high ongoing HSV suspicion**: wait for all HSV studies (including surface cultures and surface/blood PCRs) to return negative

Infants 0-28 Days: Inpatient Management (Cont'd)

Discharge Criteria:

- Well-appearing
- Tolerating PO/enteral feeds
- At 36 hours all cultures negative
- Meets HSV discharge criteria, if applicable
- Follow-up available with 48-72 hours
- PMD and family agree with plan

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Inpatient Phase 0-28d

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Evidence: All Age Groups

Inpatient discharge at 36 hours:

Evidence
Approximately 90% of bacterial pathogens are identified within the first 24 hours of incubation. (Cincinnati)
In blood cultures of infants age 0-6 months: <ul style="list-style-type: none">• Mean time to positivity for true pathogens is approximately 17.5 hours.• Median time to positivity for urine and CSF cultures are 16 and 18 hours, respectively. (Cincinnati; Byington)

Seattle Children's 2012 Data
Total of 41 patients <61 days of age with a positive blood culture (including NICU).
Of the 41, 7 patients, or 14%, had their first culture turn positive after 36 hours.
Of the 7, only one qualified for the fever pathway and that child was identified with a UTI and treated appropriately



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Evidence: All Age Groups (Cont'd)

Inpatient discharge at 36 hours: (Cont'd)

Evidence
2190 patients with all 3 cultures (Blood/CSF/Urine): <ul style="list-style-type: none">• 28 positive blood culture: median time to positivity 16 hours (6-50)• 8 positive CSF cultures: median time to positivity 18 hours (3-24)• 165 positive urine cultures: median time to positivity 16 hours (1-34)
In low risk patients, 6/6 blood cultures, 14/17 urine cultures were positive within 24 hours (no low risk patients had positive CSF).
Source: Kaplan RL

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Infants 29-56 Days of Age



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Infants 29-56 Days: ED Management

Rationale for avoiding Lumbar Puncture:

Evidence
Rates of bacterial meningitis in the reviewed studies ranged from 0-1.2%, with the majority (12/15) demonstrating rates less than 0.5%.
Source: Bachur, Baker, Bonsu, Brik, Paquette, Garcia, Rudinsky, Garra, Pantell, Gomez, Levine, Martinez, Mintegi, Morley, Olaciregui
Patients stratified as low risk using a variety of decision rules demonstrate lower rates of bacterial meningitis.
Source: Bachur, Baker, Baraff, Brik, Paquette



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Infants Age 29-56 Days: Initial ED Work-up

Testing for all patients will include:

TESTS
Blood culture
CBC with diff
CXR (for respiratory symptoms not consistent with bronchiolitis)
Stool PCR (if diarrhea present)
UA and urine culture

Further management will depend on whether patient is stratified as high or low risk for serious bacterial infection.

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Infants 29-56 Days: ED Management Fever and Bronchiolitis

Bronchiolitis:

- Can defer CBC and blood culture in patients 29-56d with clinical bronchiolitis and a single fever up to 38.5, if otherwise well appearing.
- Perform CBC, urine culture, and blood culture in patients 29-56d with bronchiolitis with persistent fever (=2 episodes of documented fever = 38).
- Patients with classic features of bronchiolitis who are otherwise well-appearing can be considered “well-appearing” when determining if patient meets low risk criteria.
- Chest X-ray can be deferred if patient has clinical findings consistent with bronchiolitis.

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Inpatient Phase 0-28d

Inpatient Phase 29-56d

Infants 29-56 Days: ED Management

Low Risk Criteria:

- Well-appearing
- Previously healthy
- Full term (≥ 37 weeks)
- No focal bacterial infection
- Negative urinalysis
- WBC $>5,000$ and $<15,000$ mm³
- Absolute bands $<1,500$ mm³
- No discrete infiltrates on CXR if done
- Stool PCR negative for bacterial pathogens if done

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Infants 29-56 Days: ED Management

ED Discharge: Low Risk Criteria

Discharge low risk patients if they meet all of the following criteria:

- Feeding well and well appearing
- No social/family concerns
- **Reliable follow-up in 12-24 hours**
- Outpatient plan accepted by PMD and family

A subgroup of low risk patients will not meet discharge criteria. These patients will be admitted without antibiotics for observation.

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Infants 29-56 Days: ED Management

High Risk of Serious Bacterial Infection:

Patients who do not meet low risk criteria are at higher risk for serious bacterial infection, including meningitis, therefore:

1. Obtain CSF studies (4 tubes)
2. Administer empiric ceftriaxone
3. Admit for empiric antibiotics

NOTE: All patients started on empiric antibiotics should receive an LP prior to antibiotic administration, unless they are clinically unstable.

Initial ED phase 29-56d

Inpatient Phase 29-56d

Infants 29-56 Days: Inpatient Management

Admission Criteria:

Low risk patients who do not meet ED discharge criteria will be admitted for observation without antibiotic administration

Patients with the following will be admitted with empiric antibiotics:

- Ill appearing
- Pre-term (< 37 weeks)
- Positive urinalysis
- WBC count < 5,000/mm³ or > 15,000/mm³
- Band count > 1,500/mm³
- Infiltrate on chest x-ray
- Stool positive for bacterial pathogens

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Inpatient Phase 29-56d

Infants 29-56 Days: Inpatient Management

Empiric Antibiotics:

- Recommend continuing empiric ceftriaxone pending culture results for all patients not meeting low risk criteria (Cincinnati; Gomez B; Morley EJ)
- Ceftriaxone is contraindicated in the following patients:
 - Those with hyperbilirubinemia
 - Those receiving calcium containing IV fluids

Initial ED phase 0-28d

Initial ED phase 29-56d

Inpatient Phase 0-28d

Inpatient Phase 29-56d

Infants 29-56 Days: Inpatient Management

Daily Re-evaluation, if positive culture:

- Treat specific condition (if identified) and transfer to appropriate CSW pathway (UTI, Pneumonia) if applicable
- If LP was not performed at admission, obtain LP prior to starting antibiotics if patient has bacteremia
 - For patients with UTI and negative blood cultures, LP can be deferred
- Narrow antibiotics as appropriate per culture results

Initial ED phase 0-28d

Initial ED phase 29-56d

Inpatient Phase 0-28d

Inpatient Phase 29-56d

Infants 29-56 Days: Inpatient Management

Discharge criteria:

Meet all of the following criteria:

- Well appearing
- Tolerating PO
- **At 36 hours:** if cultures negative and high risk patient (i.e. antibiotics begun)
- **At 24 hours:** if cultures negative and low risk patient (i.e. admitted for observation without antibiotics)
- Adequate follow-up
- PMD and family agree with plan



Initial ED phase 0-28d

Initial ED phase 29-56d

Inpatient Phase 0-28d

Inpatient Phase 29-56d



Information for All Age Groups



Initial ED phase 0-28d

Initial ED phase 29-56d

Inpatient Phase 0-28d

Inpatient Phase 29-56d

Cautions

Interpreting CSF:

CSF Normative Values

< 1 month: CSF WBC <20/mm³

≥ 1 month: CSF WBC <10/mm³

Seattle Children's 2012 Data

50-60 CSF samples were obtained that met criteria for pleocytosis as defined above

Initial ED phase 0-28d

Initial ED phase 29-56d

Inpatient Phase 0-28d

Inpatient Phase 29-56d

Cautions (Cont'd)

Interpreting CSF (Cont'd):

Evidence
Three studies attempted to define normative CSF values in infants, and found that CSF WBC >16, regardless of whether it was a traumatic tap or not, was a statistical outlier and represented pleocytosis. (Dubos,F)
Other factors associated with bacterial meningitis were: <ul style="list-style-type: none">• high protein (>120mg/dL)• low glucose(<40mg/dL)• neutrophil predominance (>75%)
An absence of neutrophils makes bacterial meningitis unlikely. Source: Bonsu,B.K

Initial ED phase 0-28d

Initial ED phase 29-56d

Inpatient Phase 0-28d

Inpatient Phase 29-56d

Considerations for severely ill patients:

Antibiotics should not be withheld in severely ill patients pending LP.

Goal is for antibiotics to be administered within 60 minutes of presentation.

Inability to obtain CSF

Consider administration of antibiotics and referral to IR for lumbar puncture (LP) for any patient where LP is unsuccessful in the ED.

- Goal is to complete LP and administer antibiotics within 60 minutes of arrival to ED.

Pre-treated CSF:

Consider adding Rapid CSF Bacterial PCR Qual Panel – detects E.coli, Listeria Monocytogenes, Neisseria meningitides, streptococcus agalactiae (Strep B), Streptococcus pneumonia and Haemophilus Influenzae in pre-treated patients with pleocytosis and a concern for bacterial meningitis.

Initial ED phase 0-28d

Initial ED phase 29-56d

Inpatient Phase 0-28d

Inpatient Phase 29-56d

Additional Clinical Considerations

Differential Diagnosis for Severely Ill Febrile Neonate:

- Serious bacterial infection
- HSV
- Varicella zoster virus
- *Chlamydia*
- Enterovirus
- Adenovirus

Additional Clinical Considerations (Cont'd)

Enterovirus Testing of CSF

Consider CSF Rapid Viral Qual. PCR on all patients with CSF pleocytosis:

Evidence

Examined the CSF of 361 infants age 56 days or younger and determined that when adjusted for other variables, length of stay is DECREASED by 26% in patients with positive CSF PCRs.

Source: [Dewan.M](#)

*NOTE: CSF Rapid Viral Qual. PCR Panel will detect HSV 1 & 2, Enterovirus, Human Parechovirus, VZV, CMV, HHV-6.
Turn around time is approximately 2 hours and the test is run 24/7.*

Initial ED phase 0-28d

Initial ED phase 29-56d

Inpatient Phase 0-28d

Inpatient Phase 29-56d

Additional Clinical Considerations (Cont'd)

Low Risk Criteria – Negative Urinalysis

Definition is consistent with published stratification studies and the CSW UTI pathway:

- <5 WBC/hpf, negative Leukocyte esterase, and negative nitrites
- No bacteria on Gram Stain

Seattle Children's Lab: Situations for Performing Microscopies

Any positive result on the reagent strip, with the exception of positive ketones or urobilinogen

If the dipstick is positive for bilirubin

Specific request is ordered - e.g. look for cystine crystals

Unusual color or the drug Mesna in the urine that could interfere with a reagent strip result

The reagent strip is negative but the urine has an abnormal odor



Initial ED phase 0-28d

Initial ED phase 29-56d

Inpatient Phase 0-28d

Inpatient Phase 29-56d

Additional Clinical Considerations (Cont'd)

Discharge at 24 hours if Viral Testing Positive:

Evidence
Studies have shown that patients with bronchiolitis or other viral infections are at lower risk of serious bacterial infections
Approximately 90% of bacterial pathogens are identified in the first 24 hours of incubation
Source: Cincinnati
Consider discharge at 24 hours for all patients who are well-appearing and have a positive (non-HSV) viral study
Source: Byington CL

Inpatient Phase 0-28d

Inpatient Phase 29-56d

Medical Disclaimer

Medicine is an ever-changing science. As new research and clinical experience broaden our knowledge, changes in treatment and drug therapy are required.

The authors have checked with sources believed to be reliable in their efforts to provide information that is complete and generally in accord with the standards accepted at the time of publication.

However, in view of the possibility of human error or changes in medical sciences, neither the authors nor Seattle Children's Healthcare System nor any other party who has been involved in the preparation or publication of this work warrants that the information contained herein is in every respect accurate or complete, and they are not responsible for any errors or omissions or for the results obtained from the use of such information.

Readers should confirm the information contained herein with other sources and are encouraged to consult with their health care provider before making any health care decision.

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Evidence Ratings

We used the GRADE method of rating evidence quality. Evidence is first assessed as to whether it is from randomized trial, or observational studies. The rating is then adjusted in the following manner:

Quality ratings are *downgraded* if studies:

- Have serious limitations
- Have inconsistent results
- If evidence does not directly address clinical questions
- If estimates are imprecise OR
- If it is felt that there is substantial publication bias

Quality ratings can be *upgraded* if it is felt that:

- The effect size is large
- If studies are designed in a way that confounding would likely underreport the magnitude of the effect OR
- If a dose-response gradient is evident

Quality of Evidence:

- ★★★★ High quality
- ★★★○ Moderate quality
- ★★○○ Low quality
- ★○○○ Very low quality
- Expert Opinion (E)

Reference: Guyatt G et al. J Clin Epi 2011: 383-394

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Literature Search

Literature searches were conducted in two phases: May and August of 2018. The initial search targeted synthesized literature on neonatal fever. The second search targeted primary or synthesized literature in two ways: (1) fever or meningococcal infections combined with bronchiolitis, influenza, respiratory syncytial virus, or respiratory syncytial virus; or (2) spinal taps. All literature was limited to neonates. The initial search was limited to January 2012 to date, and the second search was limited to January 2015 to date. Searches were run using controlled subject headings where available, and text words in the following databases: Ovid MEDLINE, Cochrane Database of Systematic Reviews, EMBASE, National Guidelines Clearinghouse, and Transforming Research into Practice (TRIP).

Identification

Records identified through database searching (n=366)

Additional records identified through other sources (n=2)

Screening

Records after duplicates removed (n=319)

Records screened (n=319)

Records excluded (n=272)

Eligibility

Records assessed for eligibility (n=47)

Articles excluded (n=44)

Did not answer clinical question (n=44)

Did not meet quality threshold (n=0)

Outdated relative to other included study (n=0)

Included

Studies included in pathway (n=8)

Flow diagram adapted from Moher D et al. BMJ 2009;339:bmj.b2535

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Bibliography

- England J.T., Del VM, Aronoff S.C. Use of serum procalcitonin in evaluation of febrile infants: A meta-analysis of 2317 patients. *J Emerg Med.* 2014;47(6):682-688.
- Leazer R., Perkins A.M., Shomaker K., Fine B. A meta-analysis of the rates of listeria monocytogenes and enterococcus in febrile infants. *Hosp Pediatr.* 2016;6(4):187-195.
- Vachani J.G., McNeal-Trice K., Wallace S.S. Current evidence on the evaluation and management of fever without a source in infants aged 0-90 days: A review. *Rev Recent Clin Trials.* 2017;12(4):240-245.

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[Approval & Citation](#)

Summary of Version Changes

- **Version 1.0 (8/13/2013):** Go live
- **Version 1.1 (9/5/2013):** Clarified maternal risk factors for HSV and decision to test for neonatal HSV
- **Version 2.0 (2/26/2016):** Addition of the Neonatal Fever (31-60 days) with Bronchiolitis ED Phase
- **Version 3.0 (2/21/2017):** Modification of HSV management (0-30 days)
- **Version 4.0 (9/11/2017):** Modification- Guidance on inability to obtain CSF and fever at home
- **Version 5.0: (1/7/2019):** Periodic update that included the modification change of the inclusion criteria to 0-28 days and 29-56 days. Updated antibiotic choices for the inpatient phase of 0-28 days

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Neonatal Fever Approval & Citation

Approved by the CSW Neonatal Fever for January 8, 2019

CSW Neonatal Fever Team:

Pathway Owner, Hospital Medicine:	Julianne Bishop, MD
Pathway Owner, Emergency:	Heath Stanford Ackley, MD
Clinical Nurse Specialist, Medical Unit:	Ellie McMahon, RN
Clinical Nurse Specialist, Emergency:	Sara Fenstermacher, MN, RN

Clinical Effectiveness Team:

Consultant:	Sara Vora, MD MPH
Project Manager:	Asa Herrman
CE Analyst:	James Johnson
CIS Informatician:	Carlos Villavicencio, MD, MMI
CIS Analyst:	Maria Jerome
	Julia Hayes
Librarian:	Peggy Cruse
Program Coordinator:	Kristyn Simmons

Executive Approval:

Sr. VP, Chief Medical Officer	Mark Del Beccaro, MD
Sr. VP, Chief Nursing Officer	Madlyn Murrey, RN, MN
Surgeon-in-Chief	Bob Sawin, MD

Retrieval Website: <http://www.seattlechildrens.org/pdf/neonatal-fever-pathway.pdf>

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