

Supplemental Information

Care Process Model

MARCH 2011



INPATIENT MANAGEMENT OF

Febrile Infants 1 to 90 days old

This care process model (CPM) was developed by Intermountain Healthcare's Pediatric Specialties and Intensive Medicine Clinical Programs, in collaboration with the University of Utah Department of Pediatrics. It recommends an evidence-based approach for assessing, monitoring, and treating infants 1 to 90 days old who are being admitted to the hospital with a rectal temperature of 38° C or higher. Note that a separate CPM for febrile infants in the emergency department complements this model and that a separate document defines care for neonatal sepsis (Neonatal Early Onset Sepsis Clinical Pathway for Level I and II Nurseries).

► About this update

This update reaffirms all key points of the original 2008 model while adding clarification and new recommendations regarding viral testing.

KEY POINTS REAFFIRMED

- **Risk classification is crucial.** Our care shouldn't be the same for all infants with fever. Low-risk infants have approximately a 1.4% occurrence of serious bacterial infection (SBI), but high-risk infants have an occurrence of 21%.¹ Modified Rochester criteria for high risk, as determined by studies within Intermountain Healthcare,² are listed on page 3 of this model.
- **Lab tests (CBC and UA) are needed to classify infants as high or low risk for SBI.** CBC and urinalysis (obtained via cath urine specimen) are key in identifying high-risk infants. You cannot assess risk through examination alone. In a study of over 3,000 febrile infants, only 58% of those with bacteremia/bacterial meningitis appeared clinically ill.³ CBC and UA can help staff decide whether to admit or discharge to home — and can help guide treatment and length of stay if the infant is admitted.
- **Viral testing helps to classify infants further, which can decrease hospital stays and unnecessary use of antibiotics.** Testing for respiratory viruses should be performed throughout the year. Although RSV and influenza peak during the winter (November to April), other viruses circulate year-round. Since the incidence of enterovirus (EV) in febrile infants is particularly high in the summer (up to 50% higher in August and October), enterovirus PCR testing is recommended from June through November as well as with any finding of CSF pleocytosis.^{4,5}
- **If SBI test results are negative and viral status is confirmed, antibiotics can be stopped and most infants sent home.** After 24 hours you can use viral and other test results to shorten antibiotic treatment and length-of-stay for admitted infants and those with non-serious viral infection.^{2,6} Minimum recommended discharge criteria are documented on page 3 of this CPM.

NEW IN THIS UPDATE: clarification, new recommendations regarding viral testing

See page 3 of this model for more discussion on the points summarized below:

- **Enterovirus PCR testing.** Note that we recommend testing seasonally (June through November) — and always with a finding of CFS pleocytosis.
- **RSV-positive PCR results.** Treat as low risk any infant age 29 to 90 days old with a positive RSV result and fever less than 38.6° C.
- **Rhinovirus-positive PCR results.** Intermountain data indicate that detection of rhinovirus alone is not significant in predicting a low risk for SBI.⁷ Treat as viral negative.
- **Neonatal HSV signs.** To ensure appropriate testing and treatment for this rare and serious illness, include AST-ALT as part of routine lab testing for infants 42 days or younger.

► Why Focus ON FEVER IN YOUNG INFANTS?

Fever is a very common problem in young infants. While only 8% to 10% of babies will have serious bacterial infection (SBI), the consequences of a missed diagnosis are grave. Yet overtreating the 90% of infants who do not have SBI also poses risks.

What's needed is a consistent approach that effectively evaluates risk, treats infants appropriately, and stops antibiotic treatment as soon as possible. This model outlines such an approach.

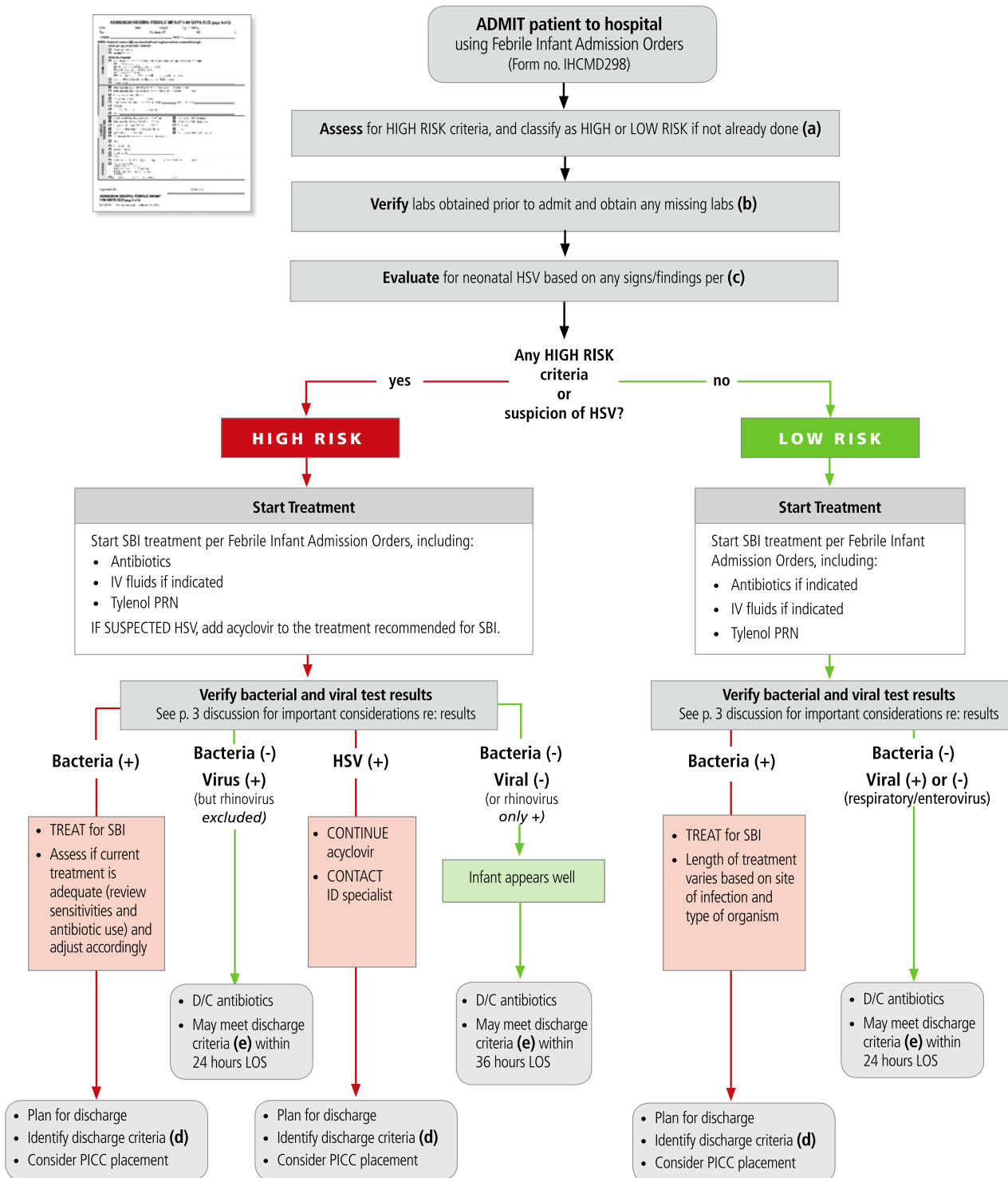
► RESULTS

- **Pilot:** Early discharge based on the recommendations in this CPM was piloted on 100 infants at Primary Children's Medical Center and resulted in savings over \$3,000 per admission and a 98% satisfaction rating from parents.⁸
- **System-wide implementation:** This model has helped ensure that febrile infants 1 to 90 days old consistently receive appropriate, evidence-based care at Intermountain hospitals. In the last 5 years and since system-wide implementation 3 years ago, we have seen these improvements (shown as a % of our cases):
 - Initial lab testing to determine risk status (from 57% to 87%)
 - Appropriate viral tests conducted (from 56% to 74%)
 - Discontinuation of antibiotics within 36 hours for inpatient febrile infants with negative cultures (from 38% to 60%)
 - Length of stay less than 42 hours with negative cultures (from 46% to 84%)

► GOALS

- Ensure that appropriate labs are collected for infants 1 to 90 days old being admitted to the hospital with a fever.
- Minimize use of antibiotics and length of hospitalization for infants ruled out for SBI.
- Decrease inappropriate HSV testing and treatment.
- Improve treatment — using appropriate antibiotics — for infants with confirmed SBI.

ALGORITHM: INPATIENT CARE OF FEBRILE INFANTS 1-90 DAYS OLD



► DISCUSSION

Several points from the algorithm and notes are discussed below.

Laboratory studies

- **Samples for bacterial studies.** Samples for all planned bacterial studies should be gathered before any antibiotic treatment is begun. Collecting CSF or blood samples after antibiotics have been started may result in false negative results.
- **Viral studies: importance, conditions.** Viral studies can help determine risk for SBI; infants with a virus (other than rhinovirus) are less likely to have SBI. Enterovirus PCR on blood and CSF is recommended from June through November and with all findings of CSF pleocytosis.^{4,5} Testing for respiratory viruses is recommended year-round.^{2,6}
- **RSV-positive PCR results.** Follow these guidelines:
 - If the infant is 28 days or younger, we recommend testing at least blood and urine. The most common cause of SBI in this group is UTI with or without bacteremia.^{9,10,11}
 - If the infant is 29 to 90 days old and the fever is $<38.6^{\circ}\text{C}$, treat the infant as low risk for SBI. (These infants have less than 2% risk of SBI).^{2,12}
 - At any age, if you intend to give antibiotics (for example, for pneumonia), then complete all testing: blood, urine, and CSF.
- **Rhinovirus-positive PCR results.** Although rhinovirus is the most frequently identified virus, Intermountain data indicate that detection of rhinovirus alone is not significant in predicting a low risk for SBI. Infants with only rhinovirus detected have the same risk of SBI as viral negative infants (approximately 12%).⁷ Treat as a viral negative result; use clinical judgment for discharge planning.
- **Neonatal HSV: signs, testing, treatment.** Herpes simplex virus infection is less common than SBI, but it has devastating results. Initial signs of HSV infection can occur any time between birth and approximately 6 weeks of age.¹³ Thus, because transaminase levels are often significantly elevated with neonatal HSV, we recommend liver function testing for febrile infants 42 days or younger. Further, we recommend testing for HSV in certain cases — see note (c) at right — and recommend treatment with acyclovir when testing is indicated.^{14,15} *Note: when obtaining lesion and surface culture samples, use a new swab for each site to eliminate the possibility of spreading infection. (Swabs may be placed in same tube for a single, multi-site analysis.)*

Medication

Data from 1999 to 2005 from Primary Children's Medical Center and across Intermountain show that *E. coli* remains the most common cause of SBI in infants 1 to 90 days old.¹⁶ Antibiotics selected for treating SBI should be active against both Gram-negative and Gram-positive causes of SBI, since ampicillin resistance occurs in at least 50% of cases. Acyclovir is the standard treatment for neonatal HSV; it should be discontinued if test results prove negative for HSV.

Note that in the table below, none of the recommended regimens is appropriate for treatment of *Staphylococcus aureus*; if *S. aureus* is suspected, consider an alternative regimen with guidance from a pediatric infectious disease specialist.

Diagnosis	1 to 28 days old	29 to 90 days old
Suspected UTI (WBC/hpf over 10) OR no focus identified	Ampicillin (50 mg/kg/dose IV every 6 hours) AND Cefotaxime (50 mg/kg/dose IV every 6 hours)	Ceftriaxone (100 mg/kg/dose IV every 24 hours)
Suspected bacterial meningitis* OR Abnormal CSF	Ampicillin (75 mg/kg/dose IV every 6 hours), Gentamicin (5 mg/kg/dose IV every 24 hours, trough less than 1) AND Cefotaxime (75 mg/kg/dose IV every 6 hours)	
Suspected neonatal HSV*	Acyclovir (20 mg/kg/dose IV every 8 hours)	

* Consult with pediatric infectious disease specialist

(a) HIGH RISK for SBI Criteria:

Any ONE of the following:

- Age ≤ 28 days
- WBC $<5,000$ or $>15,000$
- Absolute band count $\geq 1,500$
- UA >10 WBC/hpf
- Prematurity (<37 weeks) AND an underlying medical condition

(b) LABS

- UA with micro: catheterized specimen
- Urine culture: catheterized specimen
- Complete blood count with manual differential
- Blood culture
- AST-ALT for all infants ≤ 42 days; older infants as indicated
- Respiratory virus testing (DFA or RVPCR). *Note: If RSV is positive and the infant is ≤ 28 days, test at least blood and urine. At any age, if you plan to give antibiotics, complete all testing: blood, urine, and CSF.*
- Enterovirus PCR (blood and CSF, sterile body fluids only): order June–November and with any finding of CSF pleocytosis.^{4,5}

(c) Neonatal HSV EVALUATION

INITIAL EVALUATION is based on signs:

- **Age 42 days or younger:**
 - **TEST AND TREAT** if infant exhibits **vesicular skin lesions, abnormal CSF, or seizures.**
 - Testing and treating may be indicated if infant exhibits **septic appearance** or **elevated transaminases.**
- **Older infants:** primary neonatal HSV is rare in infants older than 42 days. Infectious disease team consult may be indicated.

TESTING for HSV:

- Order blood PCR, CSF PCR, culture/PCR of skin lesions, culture/PCR of surface sites (mouth and throat, eyes, umbilicus, perirectal).
- With HSV testing, consider infant "High Risk" — begin treatment per Admission Orders.

(d) Minimum DISCHARGE CRITERIA

For **UTI** and **BACTEREMIA**:

- Able to eat
- Afebrile
- Home antibiotics arranged
- Follow-up arranged
- For bacteremia only: follow-up blood culture is negative

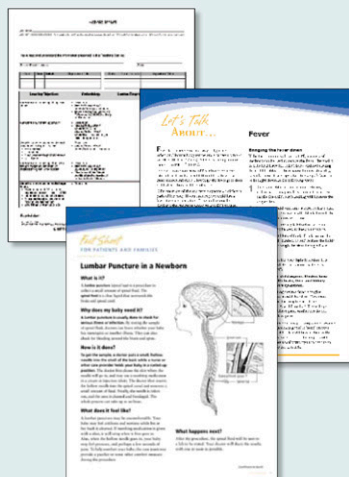
For **BACTERIAL MENINGITIS** and **HSV**:

- Consult with infectious disease specialist

(e) Minimum DISCHARGE CRITERIA^{17,18}

For **SBI RULED OUT**:

- Able to eat
- Follow-up arranged



RESOURCES

Patient and provider tools relating to care of the febrile infant are available on the Clinical Programs website at: intermountain.net/clinicalprograms. Select the “Febrile Infant” topic page to access the following tools:

- This CPM
- A related CPM for Emergency Department assessment
- Febrile Infant Admission Orders
- Febrile Infant e-learning Care Process Update (CPU)
- Patient education
- Links to other resources and references



► CAREGIVER EDUCATION

Caregiver education is a critical part of discharge planning. Education for caregivers of febrile infants should include the following topics:

- How to give prescribed medication
- How to take their baby’s temperature
- Signs of dehydration
- Steps to take to reduce fever and prevent the spread of infection
- The importance of returning for follow-up appointments

The following tools are available to guide this education. These tools are available on intermountain.net/clinicalprograms on the “Febrile Infant” topic page.

- Febrile Infant Teaching Outline
- Fact sheet and “Let’s Talk About...” handouts, in English and Spanish:
 - Lumbar Puncture in a Newborn
 - Fever
 - Urinary tract infection
 - Sepsis in babies
 - How to take your child’s temperature
 - How to give medicine
 - Placing an IV

► REFERENCES

1. Baraff LJ, Oslund SA, Schriger DL, Stephen ML. Probability of bacterial infections in febrile infants less than three months of age: a meta-analysis. *Pediatr Infect Dis J*. 1992;11(4):257-64.
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EMERGENCY MANAGEMENT OF THE

Well-appearing Febrile Infant 1 to 90 days of age 2012 UPDATE

This **evidence-based care process model (CPM)** was developed by Intermountain Healthcare's **Pediatric Specialties Clinical Program** in collaboration with the **Intensive Medicine Clinical Program**. It recommends a protocol for assessing, evaluating, and treating well-appearing infants 1 to 90 days of age who present to the emergency department with a rectal temperature of 38° C or higher or with a reliable history of fever. Note that a separate document defines care for neonatal sepsis (Neonatal Early Onset Sepsis Clinical Pathway for Level I and Level II Nurseries) and that the Inpatient Management of Febrile Infants CPM complements this model.

This update reaffirms key points of the original 2008 model while adding clarification and new recommendations regarding testing.

KEY POINTS REAFFIRMED

- **Risk classification is crucial.** Testing and care shouldn't be the same for all infants with fever. Low-risk infants have approximately a 1.4% occurrence of serious bacterial infection (SBI), but some high-risk infants have an occurrence of up to 21%.^{1,2} Note that urinary tract infection (UTI) is the most common serious bacterial infection among febrile infants.
- **Lab tests (CBC and UA) are important for classifying infants as high or low risk for SBI.** Risk for SBI cannot be determined through physical examination alone. In a study of over 3,000 febrile infants, only 58% of those with bacteremia/bacterial meningitis appeared clinically ill.³ Along with consideration of the infant's age, CBC and UA results can help providers decide whether to admit or discharge to home.
- **Viral testing helps to classify infants further.** Testing for respiratory viruses should be performed throughout the year. Although RSV and influenza peak during the winter (November to April), other viruses circulate year-round. Since the incidence of enterovirus (EV) in febrile infants is particularly high in the summer (up to 50% higher in August and October), enterovirus PCR testing is recommended from June through November as well as with any finding of CSF pleocytosis.^{4,5,6}

NEW IN THIS UPDATE: clarification, new recommendations regarding testing

See pages 2 and 3 of this model for more detail on the points summarized below:

- **Urinalysis and urine culture.** A dipstick urinalysis should be performed for all febrile infants to determine the presence of leukocyte esterase (LE).^{*} If the LE result is positive, a urine culture with Gram stain should be performed from a catheterized urine specimen. In an Intermountain study of over 5000 febrile infants, LE was the single best test for identification of UTI in febrile infants. An LE result of trace or greater predicted UTI with a sensitivity of 87%. In addition, 98% of febrile infants with negative LE results had no UTI detected.
- **Enterovirus PCR testing.** Note that we recommend testing seasonally (June through November) — and always with a finding of CFS pleocytosis (>18 WBC for infants 1 to 28 days of age; >9 WBC for infants 29 to 90 days).⁵
- **RSV-positive results.** Treat as low risk any infant 29 to 90 days of age with a positive RSV result and temperature \leq 38.5° C.
- **Rhinovirus-positive PCR results.** Intermountain data indicate that detection of rhinovirus alone is not significant in predicting a low risk for SBI.⁷ Treat as viral negative.
- **HSV signs.** To ensure appropriate testing and treatment for this rare and serious illness, include AST-ALT as part of routine lab testing for infants 42 days or younger.

**See the algorithm for exception in infants 29 to 90 days with confirmed RSV infection.*

► Why Focus ON FEVER IN YOUNG INFANTS?

Nearly 20% of emergency room visits for this age group are for evaluation of fever. While only 8% to 10% of babies will have serious bacterial infection (SBI), the consequences of a missed diagnosis are significant. Yet overtreating the 90% of infants who do not have SBI also poses risks.

What's needed is a consistent approach that effectively evaluates risk and treats infants appropriately. This model — and the companion CPM, Inpatient Management of Febrile Infants — outlines such an approach.

► RESULTS

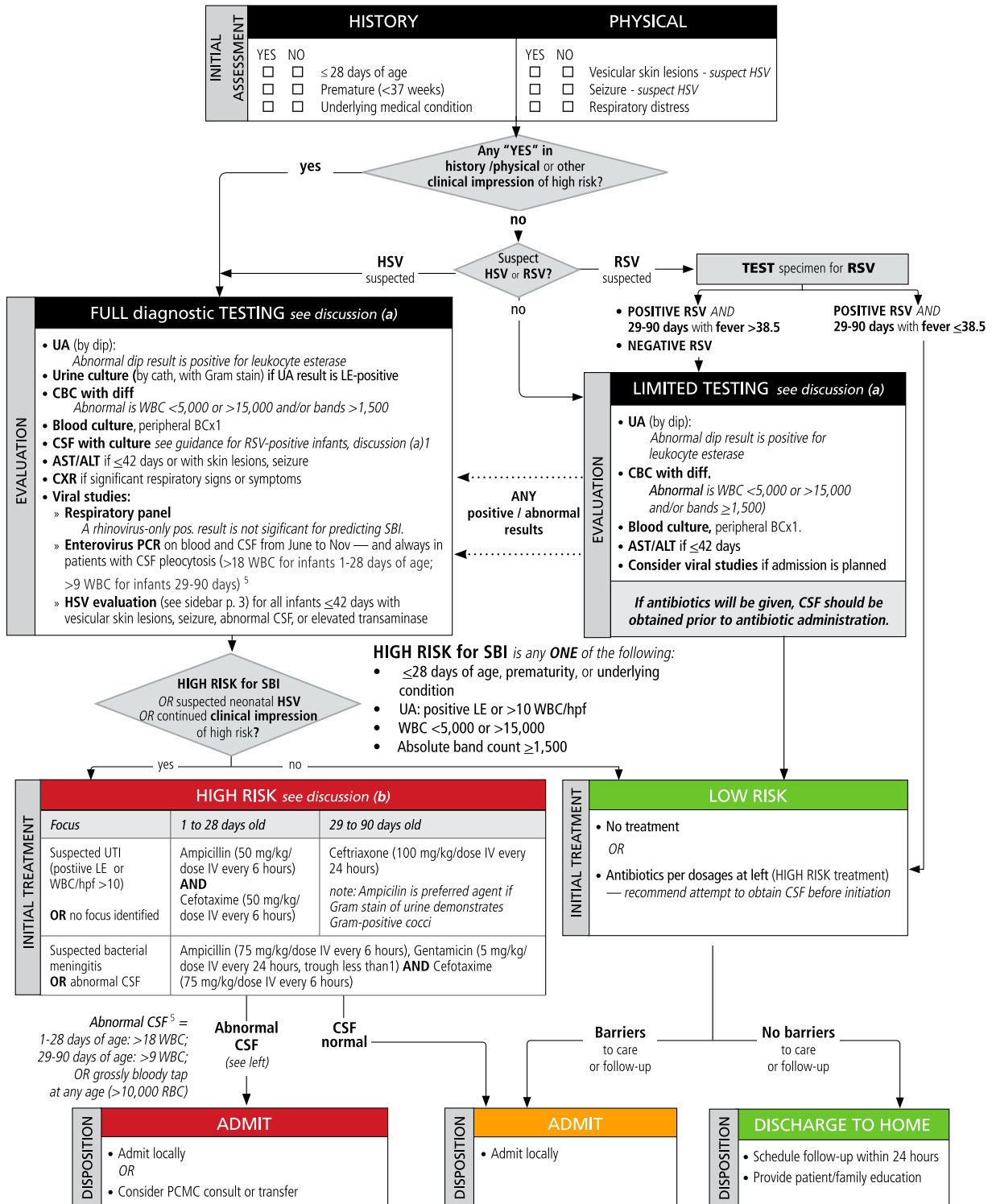
- **Pilot:** Early discharge based on the recommendations in this CPM was piloted on 100 infants at Primary Children's Medical Center and resulted in savings over \$3,000 per admission and a 98% satisfaction rating from parents.⁸
- **System-wide implementation:** This model has helped ensure that febrile infants 1 to 90 days of age consistently receive appropriate, evidence-based care at Intermountain hospitals. Since system-wide implementation in 2008, we have seen these improvements (shown as a % of our cases):
 - Initial lab testing to determine risk status (from 57% to 87%)
 - Appropriate viral tests conducted (from 56% to 74%)

Following implementation in our EDs, there have been 0 missed cases of meningitis.

► GOALS

- Ensure that appropriate labs are collected for infants 1 to 90 days of age.
- Improve decision-making regarding the inpatient or outpatient management of the well-appearing febrile infant.

ALGORITHM: EMERGENCY CARE OF THE WELL-APPEARING FEBRILE INFANT 1-90 DAYS OF AGE
 Fever of $\geq 38^{\circ}\text{C}$ on a single rectal temperature (or a reliable history of fever)



DISCUSSION

(a) Laboratory studies

1. RSV-positive results.

- At any age, if you intend to give antibiotics, complete full diagnostic testing, including blood, urine, and CSF cultures.
- For infants 28 days or younger with confirmed RSV, the physician may elect to test blood and urine and to observe inpatient without antibiotics. The most common cause of SBI in this group is UTI with or without bacteremia.^{9,10,11} Bacterial meningitis is very rare in infants with confirmed RSV.⁹
- If the infant is 29 to 90 days of age and the temperature is $\leq 38.5^{\circ}\text{C}$, treat the infant as low risk for SBI. (These infants have less than 2% risk of any SBI.)^{2,12}

2. Urinalysis results.

A dipstick urinalysis, obtained by bag or catheterized specimen, should be performed for all febrile infants to determine the presence of leukocyte esterase (LE). The only exception is in infants 29 to 90 days of age with confirmed RSV infection and a temperature $\leq 38.5^{\circ}\text{C}$, who may be considered low risk for SBI without UA testing. In infants with an LE result of trace or greater, a urine culture with Gram stain should be performed from a catheterized urine specimen. In an Intermountain study of over 5000 febrile infants, LE was the single best test for identification of UTI in febrile infants. A LE result of trace or greater predicted UTI with a sensitivity of 87%. In addition, 98% of febrile infants with negative LE results had no UTI predicted.

3. Collecting samples for bacterial studies.

Samples for all planned bacterial studies should be gathered before any antibiotic treatment is begun. Collecting CSF or blood samples after antibiotics have been started may result in false negative results.

4. Viral studies.

Viral studies can help determine risk for SBI; infants with a virus (other than rhinovirus) are less likely to have SBI.

- **Testing for respiratory viruses is recommended year-round.**^{2,6} Note that although rhinovirus is the most frequently identified virus, Intermountain data indicate that **detection of rhinovirus alone is not significant in predicting a low risk for SBI.** Infants with only rhinovirus detected have the same risk of SBI as viral negative infants (approximately 12%).⁷ Treat as a viral negative result; use clinical judgment for discharge planning.
- **Enterovirus PCR on blood and CSF is recommended from June through November and with all findings of CSF pleocytosis.**^{4,5}

5. HSV: signs, testing, treatment.

HSV infection is less common than SBI, but often results in significant morbidity and mortality in this age group. Initial signs of HSV infection can occur any time between birth and approximately 6 weeks of age.¹³ Thus, because transaminase levels are often significantly elevated with HSV, we recommend liver function testing for febrile infants 42 days or younger. Further, we recommend additional testing for HSV when infants fulfill the criteria noted in the box at right. Infants who are evaluated for HSV should receive IV acyclovir therapy pending the results of diagnostic testing.^{14, 15, 16} *Note: when obtaining lesion and surface culture samples, use a new swab for each site to eliminate the possibility of spreading infection. (Swabs may be placed in same tube for a single, multisite analysis.)*

(b) Medication

Data from 1999 to 2011 from Primary Children's Medical Center and across Intermountain show that *E. coli* remains the most common cause of SBI in infants 1 to 90 days of age.¹⁸ Antibiotics selected for treating SBI should be active against both Gram-negative and Gram-positive causes of SBI. Because ampicillin resistance occurs in over 50% of SBI pathogens, addition of a third-generation cephalosporin is recommended in all cases of suspected bacterial meningitis or abnormal CSF. Acyclovir is the treatment for suspected HSV.

Obtain guidance from a pediatric infectious disease specialist in these cases:

- **If *S. aureus* is suspected.** None of the recommended regimens presented in the algorithm is appropriate for treatment of *Staphylococcus aureus*; consult a specialist to determine an alternate regimen.
- **If bacterial meningitis or HSV infection is suspected or confirmed.**

Urinary tract infection (UTI) is the most common serious bacterial infection among febrile infants.

Data from over 8000 febrile infants seen at Primary Children's Medical Center show that approximately 10% of all febrile infants have an SBI. Of these, UTI accounts for 80%.

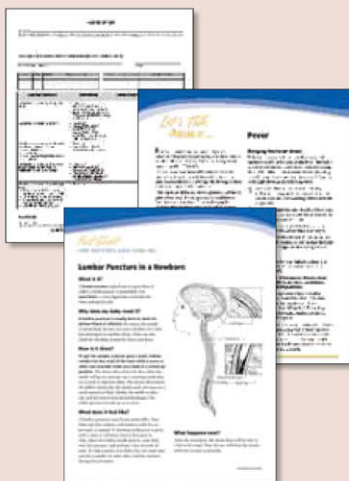
HSV EVALUATION

INITIAL EVALUATION is based on signs:

- **42 days or younger:**
 - **TEST AND TREAT** if infant exhibits **vesicular skin lesions, abnormal CSF, or seizures.**
 - Testing and treating may be indicated if infant exhibits **septic appearance or elevated transaminases.**
- **Older infants:** primary HSV is rare in infants older than 42 days. Infectious disease team consult may be indicated.

TESTING for HSV:

- Order blood PCR, CSF PCR, culture/PCR of skin lesions, culture/PCR of surface sites (mouth and throat, eyes, umbilicus, perirectal).
- With HSV testing, consider infant "High Risk"—begin treatment per the algorithm.



RESOURCES

Patient and provider tools relating to care of the febrile infant are available on the Clinical Programs website at: intermountain.net/clinicalprograms. Select the "Febrile Infant" topic page to access the following tools:

- This CPM
- A related CPM for Inpatient Management of the Febrile Infant
- Febrile Infant Admission Orders
- Patient education
- Links to other resources and references



► CAREGIVER EDUCATION

Caregiver education is a critical part of discharge planning. Education for caregivers of febrile infants should include the following topics:

- How to give prescribed medication
- How to take their baby's temperature
- Signs of dehydration
- Steps to take to reduce fever and prevent the spread of infection
- The importance of returning for follow-up appointments

Several fact sheet and "Let's Talk About..." handouts are available to guide caregiver education. These are available on intermountain.net/clinicalprograms on the "Febrile Infant" topic page.

- Lumbar Puncture in a Newborn
- Fever
- Urinary tract infection
- Sepsis in babies
- How to take your child's temperature
- How to give medicine
- Placing an IV

► REFERENCES

1. Baraff, LJ, Oslund, SA, Schriger, DL, Stephen, ML. Probability of bacterial infections in febrile infants less than three months of age: a meta-analysis. *Pediatr Infect Dis J*. 1992;11(4):257-64.
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