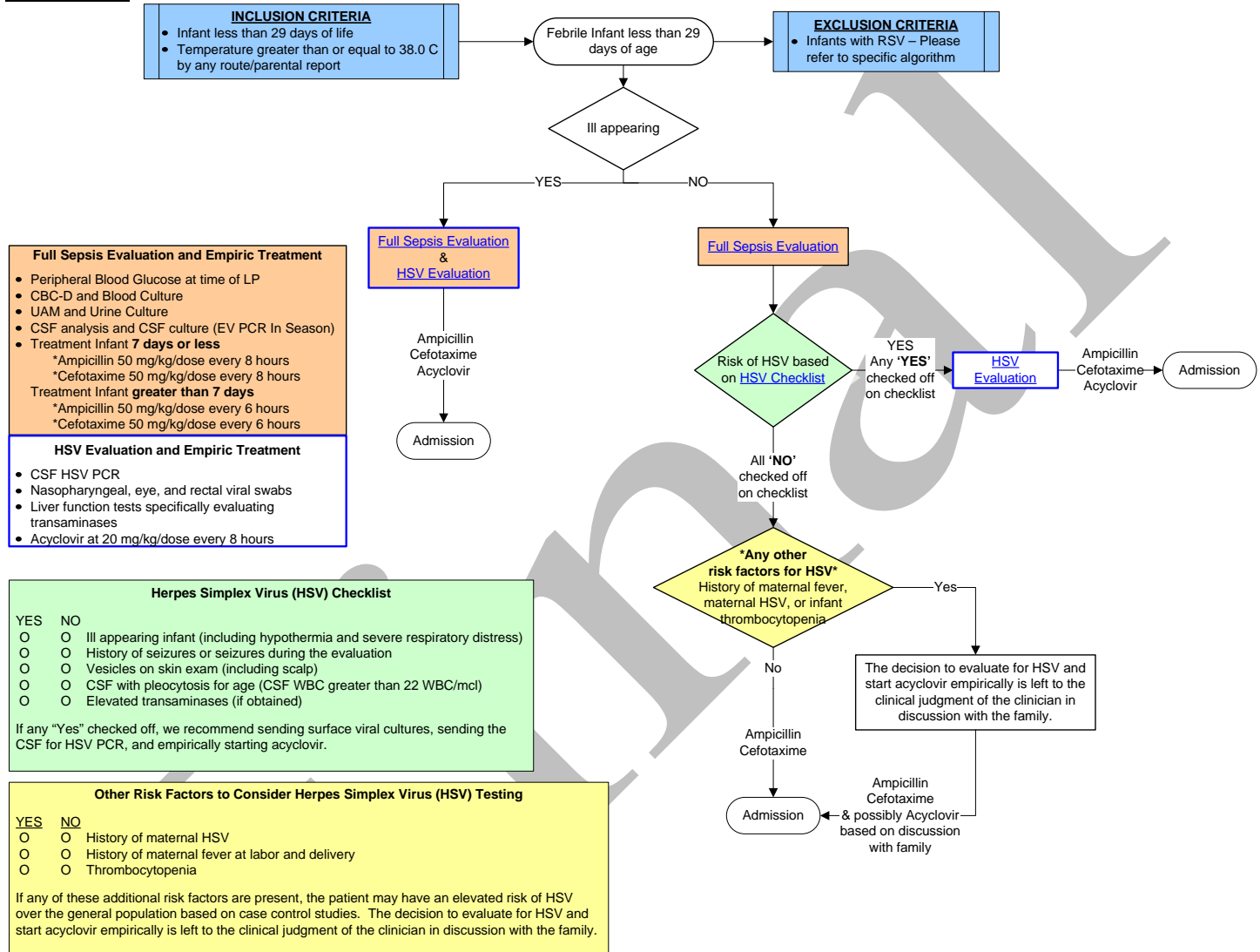


Children's Mercy Hospitals and Clinics Evidence Based Practice Clinical Practice Guideline

Fever in Infants Less Than 29 Days of Age

Algorithm



Objective:

Significant variation exists in the approach to the febrile infant both within Children's Mercy Hospital and throughout the nation. Although most physicians report adhering to guidelines when making decisions for infants presenting with fever, data suggests that true compliance with the recommendations is poor. Despite recommendations to the contrary, many physicians prescribe systemic antibiotics to febrile infants without a lumbar puncture. We don't know the effect of this practice variation or lack of adherence to guidelines on patient outcomes. (Meehan, Fleegler et al.)

The purpose of the Febrile Infant Clinical Practice Guideline is to standardize care around a common clinical problem with the goal of improving patient outcomes (including patient experience). There is currently no

standard of care at Children's Mercy Hospital for the care of febrile infants, which leads to inconsistent care, confusion among the residents, and, most importantly, confusion for patients and families.

The guideline was made based upon what we believe is the best available evidence. We recognize that some of this evidence is old, but the low risk criteria developed in the late 1980's and early 1990's has not been updated since the pneumococcal vaccine. We hope to change that with this guideline and subsequent research protocol.

The guideline is supposed to apply to 80-90% of the population and will not encompass all scenarios. Clinical decision making by the individual physician at the point is a critical component of any guideline. We hope to learn from those decisions that are made in adherence with the guideline as well as those that are different from the following recommendations.

Definition: Fever in infants less than 29 days is elevation of the rectal temperature to 38° Celsius (C) or higher

Target Users: Clinicians and Nurses in CMH Emergency Department, Urgicare center, PCC, and hospital

Guideline Inclusion Criteria: This guideline is intended to direct care for infants less than 29 days of life who present with a temperature greater than or equal to 38.0° C by any route by healthcare worker or parental report or taken in the ED/UCC/inpatient setting.

Infants with gestational age less than 37 weeks, with congenital medical and/or surgical co-morbidities, and those hospitalized at any time since birth are high risk for SBI and are included in this guideline.

Guideline Exclusion Criteria: Infants greater than 28 days of age, infant without a fever either on exam or by history

Clinical Questions Answered by Guideline:

1. What is the most accurate site (eg axillary, rectal) to measure temperature in infants less than 29 days of age?
2. What is the diagnostic workup of a febrile infant less than 29 days of age with confirmed RSV infection?
3. When should HSV testing be performed and treatment initiated in a febrile infant less than 29 days of age?
4. When should infants less than 29 days of age with confirmed enterovirus infection be discharged?

Differential Diagnosis: The main differential is a serious bacterial infection that can manifest as urinary tract infection, bacteremia, meningitis, pneumonia and/or bacterial gastroenteritis. Viral illness such as enterovirus infection in the summer months can also cause fever in infants.

Practice Recommendations:

Assessing Fever in the Infant

History: Fever in infants less than 29 days of age is not to be ignored. Parent report of fever, regardless of the temperature measurement technique used, is to be believed and the infant evaluated further (Callanan 2003). There is mixed evidence about the ability of parental report to accurately detect fever in the infant population without a thermometer. Whether the clinician accepts the report as sole evidence of fever is an individual decision. (Teng, Ng et al. 2008; Katz-Sidlow, Rowberry et al. 2009)

Physical Assessment:

1. Initial temperature measurement:

- a. Rectal temperature is the only method with sufficient accuracy to detect fever in infants less than 60 days (Asher C 2008)
- b. Axillary, tympanic, and temporal artery temperature measurement cannot be recommended for initial temperature measurement in this age group.

2. Ongoing temperature measurement:

- a. When fever has already been detected and the infant is admitted to the hospital, repeated temperature measurements may be taken via the axillary route in order to facilitate rest.
- b. When the axillary temperature is elevated to 37.5° C or higher, rectal temperature is measured to accurately detect the extent of fever. Consensus opinion of the Febrile Infant CPG working group based upon (Asher C 2008)
- c. When a febrile infant is administered antipyretic medication, the temperature is measured one hour after administration. (Vital Sign Policy. (2010). Patient Care Services Standards Manual, Children's Mercy Hospitals & Clinics).
- d. The frequency of temperature measurement is determined by the hospital practice guideline. (Vital Sign Policy. (2010). Patient Care Services Standards Manual, Children's Mercy Hospitals & Clinics).

Rationale and Evidence Base

Once the febrile infant is admitted, evaluation is complete, and antibiotics have been administered, the absolute accuracy of temperature measurements is less critical in clinical decision making and infant and family comfort may favor axillary temperature measurements.

Management of Febrile Infants Less Than 29 Days

Full Sepsis Evaluation for Febrile Infants

An initial full sepsis evaluation is recommended for all febrile newborns less than 29 days of life unless they have documented Respiratory Syncytial Virus (RSV) infection. Further information on the management of infants with confirmed RSV, confirmed Enterovirus (EV), and suspected/confirmed Herpes Simplex Virus infection is included in subheadings below. (Baker and Bell 1999; Kadish, Loveridge et al. 2000) A full sepsis evaluation includes the following:

1. Blood glucose (point of care test)
2. Complete Blood Cell count with differential (CBCD)
3. Blood culture
4. Urine analysis with microscopy (UAM)
5. Urine gram stain and culture (Catheter/Suprapubic specimen)
6. Cerebral Spinal Fluid (CSF) cell count with differential, protein, and glucose
7. CSF gram stain and culture

Inpatient Management

1. All febrile infants less than 29 days of age are admitted to the hospital
2. Empiric administration of intravenous antibiotics is required.

Age	Ampicillin	Cefotaxime
Infants 0-7 days	50 mg/kg/dose, every 8 hours	50 mg/kg/dose, every 8 hours
Infants 8-28 days	50 mg/kg/dose, every 6 hours	50 mg/kg/dose, every 6 hours

3. Antipyretic administration: Acetaminophen may be administered (10-15 mg/kg/dose every 4 – 6 hours, based on the electronic dose calculation) orally or rectally to infants with fever when they are assessed to be uncomfortable. The total of all doses administered must be less than 75 mg/kg/day.
4. Treatment of the infant with a positive blood, urine, or CSF culture is based upon the infection site and the bacteria identified.
5. Infectious disease consultation is recommended for infants with confirmed bacterial meningitis.
6. Hospital discharge is planned when urine, blood, and CSF cultures are negative for at least 48 hours and when the patient appears well. (Kaplan, Harper et al. 2000)
7. Persistent fever may necessitate further evaluation and/or observation in the hospital.

Rationale and Evidence Base

Fever in young infants often accompanies bacterial disease. Approximately 10% of febrile infants younger than 2 months will have associated bacteriuria, bacteremia, or meningitis. In addition, clinical appearance does not reliably rule out the presence of bacterial disease in this population. Accordingly, the presence of fever in infants younger than 1 months demands immediate and comprehensive management. (Baker 2008)

Two studies have looked closely at using low risk criteria on children less than 1 month of age. In a retrospective study conducted in Salt Lake City, 45 of 372 febrile infants less than one month of age had a serious bacterial illness. Of those, approximately 13% by Philadelphia criteria and 18% by Boston criteria would have been identified as low risk for bacterial disease. In a similar prospective study of 254 febrile infants less than one month of age in Philadelphia, 5 (15.6%) of 32 who had serious bacterial illnesses would have been identified as low risk for bacterial disease according to the Philadelphia criteria. (Baker and Bell 1999; Kadish, Loveridge et al. 2000)

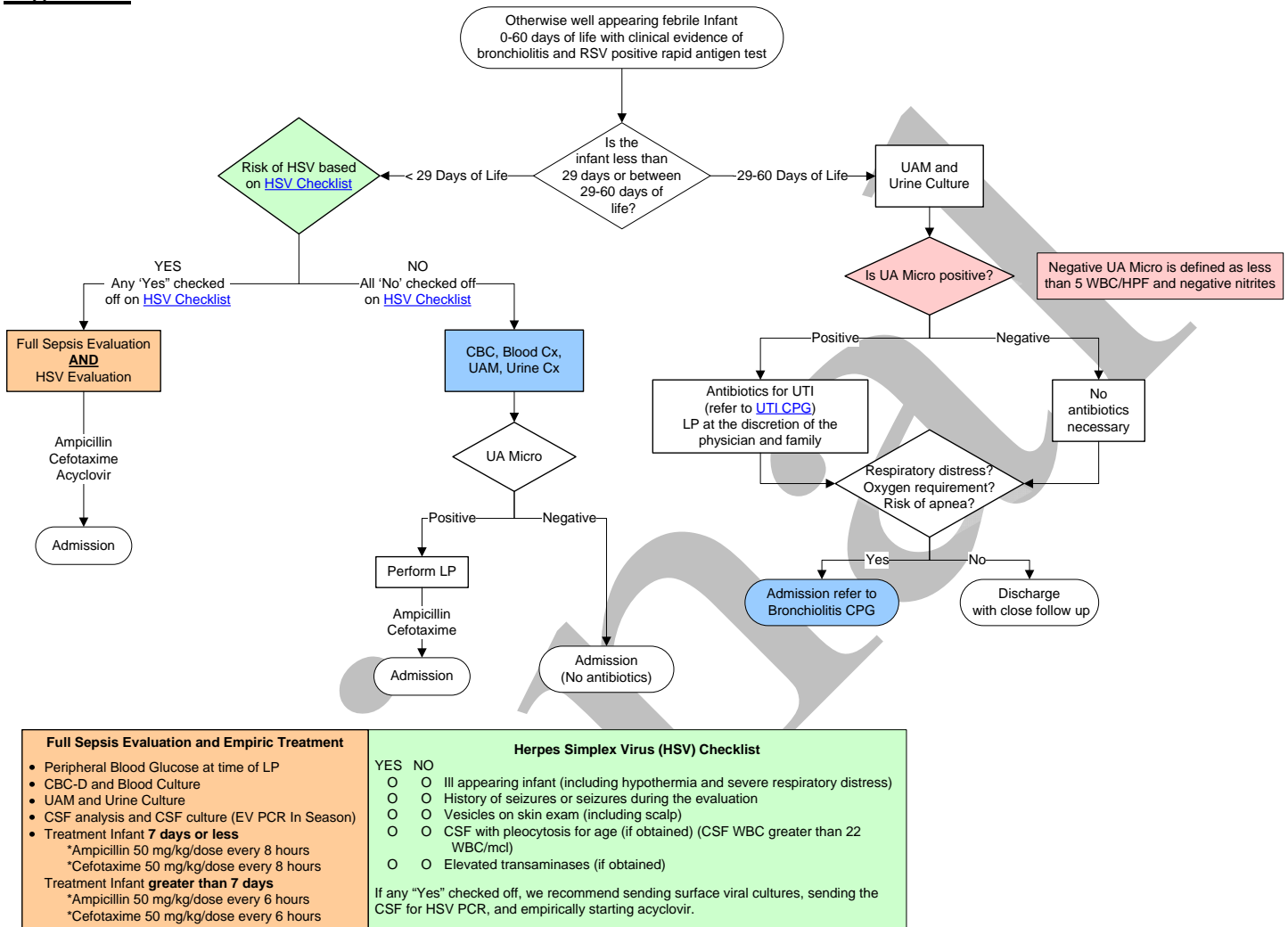
GRADE:

The data for doing a full sepsis evaluation and starting empiric antibiotics for infants comes from descriptive studies and retrospective cohort studies. Given the higher likelihood of infection, consequence of missing a serious bacterial infection, and the absence of low risk criteria for this age group, this is a ***STRONG RECOMMENDATION despite the overall low quality of evidence.***

It is important to note that infants less than 37 weeks gestational age, infants with medical/surgical co-morbidities, and infants hospitalized since birth are at high risk for serious bacterial infection and fall within the scope of this recommendation.

Management of Febrile Infants Less Than 29 Days During Respiratory Syncytial Virus (RSV) Season

Algorithm



RSV Risk Factors, Diagnostic Workup, and Medical Decision Making

- The microbiology laboratory determines when rapid antigen testing for RSV is performed based on when disease prevalence is high enough for this to be a useful test.
- Rapid antigen test for RSV is performed when signs of respiratory illness, tachypnea, wheezing, apnea, rhinorrhea, cough, are reported or accompany fever.
- If the patient is ill appearing, a full sepsis workup is performed regardless of RSV status.
- If the infant is RSV positive, but does not appear ill, the following is performed:
 - Complete Blood Count with differential (CBCD)
 - Blood Culture
 - Urinalysis with microscopy (UAM)
 - Urine Culture (Catheter/Suprapubic specimen)
- If the infant is RSV negative, a full diagnostic workup is performed, regardless of the infant's clinical appearance
- If 5 or more WBC/hpf are detected by UAM in an RSV positive infant, a lumbar puncture is performed for CSF cell count with differential, protein, glucose, and culture.

Inpatient Management

1. Febrile infants who are RSV negative and are ill appearing are admitted to the hospital and managed as described in the section titled “**Management of Febrile Infants Less Than 29 Days.**”
2. All RSV positive infants less than 29 days of life are admitted for observation due to risk of apnea and the need for supportive care. (Reference: Bronchiolitis CPG)
 - a. Intravenous antibiotics are not administered.
 - b. If 5 or more WBC/hpf are detected by UAM, lumbar puncture is performed to complete the sepsis evaluation and intravenous ampicillin and cefotaxime are administered (see dosing guideline above).

Rationale and Evidence Base

Several retrospective and prospective cohort studies have assessed the rates of urinary tract infections, bacteremia, and meningitis in febrile infants with RSV. (Oray-Schrom, Phoenix et al. 2003; Titus and Wright 2003; Levine, Platt et al. 2004) None specifically evaluated patients less than 29 days of life. Levine et al. performed a subanalysis comparing SBI rates stratified by age. Infants who were less than 29 days of age had an overall rate of SBI of 13.3% (95% CI: 10.1%–17.2%), regardless of RSV status. Among the 82 RSV positive infants who were less than 29 days, 10.1% (95% CI: 4.5%–19.0%) had SBIs, including 5 of 82 (6.1%; 95% CI: 2.0%–13.7%) with UTIs and 3 of 82 (3.7%; 95% CI: 0.8%–10.3%) with bacteremia. There were no cases of meningitis in the RSV positive group less than 29 days of life, but only a total of 8 patients with bacterial meningitis in the cohort of patients without RSV. The other studies have similar overall rates of UTIs and bacteremia and no noted cases of meningitis.

In summary, there appears to be a statistically similar and clinically meaningful rate of UTIs and bacteremia in RSV positive infants less than 29 days of life compared to RSV negative febrile infants. While the rates of meningitis are not statistically different in any individual study, no cases of meningitis in RSV positive infants in these studies were reported. As stated, the data is from prospective and retrospective cohort studies.

GRADE:

We **RECOMMEND** admitting all infants less than 29 days of age with RSV. This recommendation is based on the weighing benefit versus harm in the face of overall low quality evidence.

We **STRONGLY RECOMMEND** evidence doing a full sepsis evaluation and starting empiric antibiotics in all ill appearing febrile infants less than 29 days of age regardless of RSV status. Given the higher likelihood of infection and consequence of missing a serious bacterial infection in ill appearing infants less than 29 days of life, this is a **STRONG RECOMMENDATION despite the overall low quality of evidence.**

We **RECOMMEND based on low quality of evidence** doing urine and blood cultures on febrile infants with RSV who appear well and NOT starting empiric antibiotics unless the UA is positive (greater than 5 WBC/hpf and nitrites present), urine gram stain is positive, or blood culture is positive.

We **RECOMMEND** doing a lumbar puncture and CSF culture in infants with RSV who appear well **ONLY WHEN** the initial UA is positive or the subsequent urine and/or blood cultures become positive. In these cases we **RECOMMEND** starting empiric antibiotics once the cultures are obtained. Both recommendations are based on very low quality evidence and the presumed increased risk of meningitis in infants less than 29 days of life with bacteremia and/or urosepsis. It is also important to remember that, while there is no published cases of meningitis in febrile infants with documented RSV infection, the low rates of meningitis in general make it impossible for any study to show a statistical difference in meningitis between RSV and non-RSV infants.

Management of Febrile Infants Less Than 29 Days With Suspicion of Herpes Simplex Virus (HSV) Infection

Epidemiology

1. The incidence of HSV among infants less than 29 days is low: ranging from 0.2 – 0.6% of infants tested (Caviness, Demmler et al. 2008; Caviness, Demmler et al. 2008) or 5.1 – 5.9 cases per 100,000 live births. (Kropp, Wong et al. 2006; Mahnert, Roberts et al. 2007)
2. Mortality (15-20%) and morbidity (25% with neurologic sequelae) for untreated neonatal HSV disease is high.
3. HSV is manifest clinically as: (Kropp, Wong et al. 2006; Mahnert, Roberts et al. 2007; Caviness, Demmler et al. 2008)
 - a. Skin, eye, and mouth infection (25-60% of cases)
 - b. Meningoencephalitis (25 - 37.5% of cases)
 - c. Disseminated infection (18 - 37.5% of cases)

HSV Risk Factors, Diagnostic Workup, and Medical Decision Making

1. Infants less than 29 days of life are recommended for HSV testing when they present with any of the following:
 - a. An ill or septic appearance including hypothermia (rectal temperature less than 36 degrees Celsius) and severe respiratory distress
 - b. Seizures (or the history of seizure)
 - c. Obvious herpetic lesions/vesicles on physical exam
 - d. CSF pleocytosis for age (white blood cell count greater than 20 per microliter)
 - e. Elevated AST and/or ALT of previous labs obtained
2. Additional risk factors as identified by Kropp et al in a prevalence study and Caviness et al in a case control study include the following. Each may increase the risk of HSV over the general population, but should be taken in the context of the entire clinical scenario. We recommend that clinicians speak with families about this risk and determine, along with the input from the family, whether or not to pursue further testing and empiric treatment with acyclovir.
 - a. Known maternal HSV (we recognize that primary infection places the infant at much higher risk than recurrent infection, however there appears to be a 1-2% risk of transmission with recurrent infection and this places the infant at a higher risk than the general population) (Kropp, Wong et al. 2006; Mahnert, Roberts et al. 2007; Caviness, Demmler et al. 2008)
 - b. Thrombocytopenia (exclusively associated with disseminated HSV)
 - c. Maternal fever at labor and delivery (OR: 5.8, 95% CI: 2.3–14.5) (Caviness, Demmler et al. 2008)
3. Required testing, in addition to the full diagnostic workup for febrile infants above, includes:
 - a. Cerebral Spinal Fluid HSV polymerase chain reaction (PCR)
 - b. Nasopharyngeal, eye, and rectal viral cultures
 - c. Liver function tests, specifically evaluating AST and ALT

Inpatient Management

1. Empiric administration of intravenous ampicillin and cefotaxime (see dosing guidelines above) is required.
2. Empiric treatment of suspected HSV is required: acyclovir 20 mg/kg/dose intravenously every 8 hours.
3. Treatment of confirmed HSV is acyclovir 20 mg/kg/dose intravenously every 8 hours for the general duration indicated by the clinical manifestation. (Kimberlin 2001 Pediatrics. 2001 Aug;108(2):230-8.)

- a. Patients with disseminated disease or skin, eye, and mouth disease without central nervous system involvement are generally treated intravenously for 21 days.
- b. Patients with meningoencephalitis are treated intravenously for 21 days
- c. Infants with confirmed HSV disease require Infectious Diseases consultation specific recommendation of therapy duration and for follow-up.

Rationale and Evidence Base

Infants less than 29 days of life are at risk of neonatal HSV. In the second week of life, the risk of neonatal HSV approaches that of bacterial meningitis. However, there is no consensus recommendation for the empiric treatment of HSV with acyclovir in infants less than 29 days of life. While some experts recommend acyclovir routinely in all febrile infants less than 29 days of life, others risk stratify based on known risk factors. This lack of consistency may lead to the lack of recognition and delayed treatment of neonatal HSV. (Caviness, Demmler et al. 2008)

We have adopted a conservative approach, including known risk factors in a check list to help clinicians identify the infant at risk for neonatal HSV disease. The data that support our recommendation come from descriptive and case control studies on the epidemiology and risk factors of neonatal HSV disease. (Kropp, Wong et al. 2006; Mahnert, Roberts et al. 2007; Caviness, Demmler et al. 2008) It is also important to recognize that red blood cells in the CSF are not a risk factor of HSV meningitis.

GRADE:

We **RECOMMEND** based on *low quality evidence* that empiric treatment with acyclovir and a thorough HSV evaluation (see # 1 above) be completed if any item of the HSV checklist is present (Figure 1 – Algorithm).

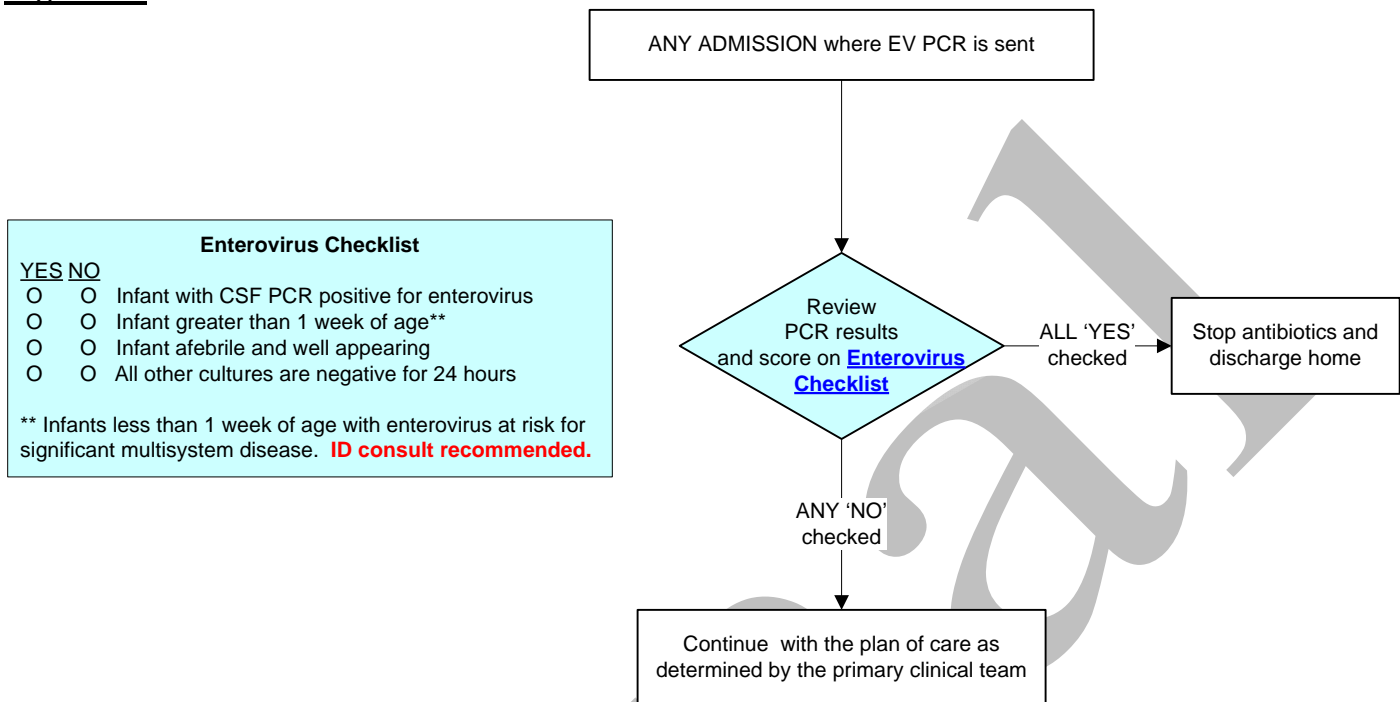
Additional risk factors as identified by Kropp et al in a prevalence study and Caviness et al in a case control study are listed in # 2 above. Each may increase the risk of HSV over the general population, but should be taken in the context of the entire clinical scenario. We **RECOMMEND** based on *low quality evidence* that clinicians speak with families about this risk and determine, along with the input from the family, whether or not to pursue further testing and empiric treatment with acyclovir.

We **STRONGLY RECOMMEND** based on low-quality of evidence to use the dose of 20mg/kg every 8 hours of acyclovir when treating possible neonatal HSV disease. The strong recommendation is based on weighing the benefits versus risk of side effects of the suggested dose compared with the risks of using a smaller dose when treating a potentially fatal disease.

There are no randomized controlled trials regarding the treatment of HSV infection in neonates. Data on dosing of acyclovir and length of treatment is taken from Lexi-Comp and the American Academy of Pediatrics Red Book and is based on a prospective, open label cohort study. (Kimberlin, Lin et al. 2001)

Management of Febrile Infants Less Than 29 Days During Enterovirus (EV) Season

Algorithm



Enterovirus Risk Factors, Diagnostic Workup, and Medical Decision Making

1. The microbiology laboratory determines when CSF enterovirus PCR testing is performed based on seasonal variation in the prevalence of disease.
2. EV testing is performed in **all** febrile infants less than 29 days during EV season, regardless of CSF cell count, in addition to the full diagnostic workup described in the initial section “Full Sepsis Evaluation of Febrile Infants.”.

Inpatient Management

1. Empiric administration of intravenous ampicillin and cefotaxime (see dosing guidelines above) is required.
2. If the EV CSF PCR is positive and the infant meets all of the following criteria on the EV Checklist, antibiotics can be stopped and the infant can be discharged home.
 - a. Infant is greater than 1 week of age
 - b. Infant is well-appearing and afebrile
 - c. All other cultures are negative for 24 hours
3. If the EV CSF PCR is negative, hospital discharge is planned when urine, blood, and CSF cultures are negative for at least 48 hours and when the patient appears well

Rationale and Evidence Base

Non-polio EV infections commonly cause fever in infants less than 29 days of age. The use of PCR to identify febrile infants with non-polio EV infections may decrease length of hospital stay, unnecessary antibiotic administration, and charges. The studies supporting the use of EV PCR screening and early discharge are retrospective and prospective cohort studies. (Byington, Taggart et al. 1999; Nigrovic and Chiang 2000; Spicher, Berclaz et al. 2000; Rittichier, Bryan et al. 2005)

Infants less than 1 week of life with non-polio EV infections are at a high risk of developing a sepsis-like condition, including meningoencephalitis, myocarditis, and hepatitis. Differentiating neonatal EV from disseminated HSV and bacterial sepsis can be extremely difficult. Presenting symptoms include poor feeding, lethargy, fever, irritability, hypoperfusion, and jaundice. The mothers of these infants often report having a fever and abdominal pain (different from labor pain) the day of delivery. The severity of the illness presumably results from overwhelming viremia in the absence of passive antibody protection in the infant. (Abzug, 1993)

GRADE:

Infectious Disease Consult is **RECOMMENDED based on very low quality of evidence** for infants less than 1 week of age that are EV positive. The recommendation is based on the relatively low incidence and potential severity of neonatal enterovirus infections.

We **STRONGLY RECOMMEND based on low quality of evidence for** EV testing with an EV CSF PCR in all febrile infants less than 29 days.

We **RECOMMEND** based on low quality of evidence for stopping antibiotics and discharging patients home if the EV PCR is positive and the patient is greater than 1 week, well appearing, afebrile, and all cultures are negative after 24 hours. (Abzug, Levin et al. 1993; Kaplan, Harper et al. 2000)

Guideline/Outcome Measures:

- Diagnostic workup variability in infants with confirmed RSV infection.
- Percentage of infants requiring an HSV workup
- Percentage of infants with HSV disease
- Length of stay for infants with enterovirus infection.
- Percentage of infants with an SBI

Potential Cost Implications:

- Decrease in length of hospital stay in infants with EV infection
- Increase in cost associated with possible increase in HSV testing versus increase in cost associated with missing a case of HSV in a neonate.

Supporting tools (i.e. power plans, policies and procedures, care cards, etc.)

Currently under development.

How guideline was piloted: The guideline was implemented hospital wide on February 1st, 2011.

Guideline Preparation: This guideline was prepared by The Office of Evidence Based Practice (EBP) in collaboration with content experts at Children's Mercy Hospitals and Clinics. Development of this guideline supports the Department of Clinical Effectiveness's initiative to promote care standardization that builds a culture of quality and safety that is evidenced by measured outcomes. If a conflict of interest is identified the conflict will be disclosed next to the team members name.

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Guideline development funded by: N/A

Development Process:

The review summary documents the following steps:

1. Review of existing internal and external guidelines and standards
 - a. Internal guidelines: None
 - b. External guidelines: Cincinnati Children's Febrile Infant Guideline
2. Review preparation
 - a. PICOT questions established
 - b. Team leaders confirmed search terms used.
3. Databases searched
 - a. AHRQ National Guideline Clearinghouse
 - b. Medline
 - c. Cochrane
 - d. CINAHL
4. Critically analyze the evidence
 - a. Guidelines
 - i. AGREE criteria were used to analyze published clinical guidelines
 - b. Literature
 - i. CASP tools were used to analyze the literature (e.g. study limitations, consistency of results, directness of evidence, precision and reporting bias)
 - ii. GRADE criteria evaluated the literature based on:
 1. The balance between desirable and undesirable effects
 2. Patient values and preferences
 3. Resource utilization

The table below defines how the quality of the evidence is rated and how the recommendation is established based on the type of evidence:

Quality	Type of Evidence
High	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies.
Moderate	Evidence from RCTs with important limitations (inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies.
Low	Evidence for at least 1 critical outcome from observational studies, from RCTs with serious flaws or indirect evidence.
Very Low	Evidence for at least 1 of the critical outcomes from unsystematic clinical observations or very indirect evidence.
Recommendation	Type of Evidence
Strongly Recommend	Desirable effects clearly outweigh undesirable effects or vice versa
Recommend	Desirable effects closely balanced with undesirable effects

5. Recommendations for the guideline were developed by a consensus process incorporating the three principles of EBP (current literature, content experts, and patient and family preference [when possible])

Approval Process: Guidelines are reviewed and approved by internal (Lisa Schroeder, MD and Angela Myers, MD, MPH) and external (Chris D. Maloney, MD, PhD) reviewers. Content Expert Team, the Office of EBP, and other appropriate hospital committees as deemed suitable for the guidelines intended use. Guidelines are reviewed and updated as necessary every 3 years within the Office of EBP at CMH&C. Content expert teams will be involved with reviews and updates.

Disclaimer:

The content experts and the Office of EBP are aware of the controversies surrounding the care of infants less than 29 days of age. When evidence is lacking or inconclusive, options in care are provided in the guideline and the power plans that accompany the guideline.

These guidelines do not establish a standard of care to be followed in every case. It is recognized that each case is different and those individuals involved in providing health care are expected to use their judgment in determining what is in the best interests of the patient based on the circumstances existing at the time.

It is impossible to anticipate all possible situations that may exist and to prepare guidelines for each. Accordingly these guidelines should guide care with the understanding that departures from them may be required at times.

References

- Abzug, M. J., M. J. Levin, et al. (1993). "Profile of enterovirus disease in the first two weeks of life." Pediatr Infect Dis J **12**(10): 820-4.
- Asher C, N., LK (2008). Position Statement for Measurement of Temperature/Fever in Children, Society of Pediatric Nurses.
- Baker, M. D. (2008). "The Febrile Infant: What's New?" Clinical Pediatric Emergency Medicine **9**: 231-220.
- Baker, M. D. and L. M. Bell (1999). "Unpredictability of serious bacterial illness in febrile infants from birth to 1 month of age." Arch Pediatr Adolesc Med **153**(5): 508-11.
- Byington, C. L., E. W. Taggart, et al. (1999). "A polymerase chain reaction-based epidemiologic investigation of the incidence of nonpolio enteroviral infections in febrile and afebrile infants 90 days and younger." Pediatrics **103**(3): E27.
- Callanan, D. (2003). "Detecting fever in young infants: reliability of perceived, pacifier, and temporal artery temperatures in infants younger than 3 months of age." Pediatr Emerg Care **19**(4): 240-3.
- Caviness, A. C., G. J. Demmler, et al. (2008). "Clinical and laboratory features of neonatal herpes simplex virus infection: a case-control study." Pediatr Infect Dis J **27**(5): 425-30.
- Caviness, A. C., G. J. Demmler, et al. (2008). "Cost-effectiveness analysis of herpes simplex virus testing and treatment strategies in febrile neonates." Arch Pediatr Adolesc Med **162**(7): 665-74.
- Kadish, H. A., B. Loveridge, et al. (2000). "Applying outpatient protocols in febrile infants 1-28 days of age: can the threshold be lowered?" Clin Pediatr (Phila) **39**(2): 81-8.
- Kaplan, R. L., M. B. Harper, et al. (2000). "Time to detection of positive cultures in 28- to 90-day-old febrile infants." Pediatrics **106**(6): E74.
- Katz-Sidlow, R. J., J. P. Rowberry, et al. (2009). "Fever determination in young infants: prevalence and accuracy of parental palpation." Pediatr Emerg Care **25**(1): 12-4.
- Kimberlin, D. W., C. Y. Lin, et al. (2001). "Safety and efficacy of high-dose intravenous acyclovir in the management of neonatal herpes simplex virus infections." Pediatrics **108**(2): 230-8.
- Kropp, R. Y., T. Wong, et al. (2006). "Neonatal herpes simplex virus infections in Canada: results of a 3-year national prospective study." Pediatrics **117**(6): 1955-62.
- Levine, D. A., S. L. Platt, et al. (2004). "Risk of serious bacterial infection in young febrile infants with respiratory syncytial virus infections." Pediatrics **113**(6): 1728-34.
- Mahnert, N., S. W. Roberts, et al. (2007). "The incidence of neonatal herpes infection." Am J Obstet Gynecol **196**(5): e55-6.
- Meehan, W. P., 3rd, E. Fleegler, et al. "Adherence to guidelines for managing the well-appearing febrile infant: assessment using a case-based, interactive survey." Pediatr Emerg Care **26**(12): 875-80.
- Nigrovic, L. E. and V. W. Chiang (2000). "Cost analysis of enteroviral polymerase chain reaction in infants with fever and cerebrospinal fluid pleocytosis." Arch Pediatr Adolesc Med **154**(8): 817-21.
- Oray-Schrom, P., C. Phoenix, et al. (2003). "Sepsis workup in febrile infants 0-90 days of age with respiratory syncytial virus infection." Pediatr Emerg Care **19**(5): 314-9.
- Rittichier, K. R., P. A. Bryan, et al. (2005). "Diagnosis and outcomes of enterovirus infections in young infants." Pediatr Infect Dis J **24**(6): 546-50.
- Spicher, V. M., P. Y. Berclaz, et al. (2000). "Detection of enteroviruses in the cerebrospinal fluid by polymerase chain reaction: prospective study of impact on the management of hospitalized children." Clin Pediatr (Phila) **39**(4): 203-8.
- Teng, C. L., C. J. Ng, et al. (2008). "The accuracy of mother's touch to detect fever in children: a systematic review." J Trop Pediatr **54**(1): 70-3.
- Titus, M. O. and S. W. Wright (2003). "Prevalence of serious bacterial infections in febrile infants with respiratory syncytial virus infection." Pediatrics **112**(2): 282-4.