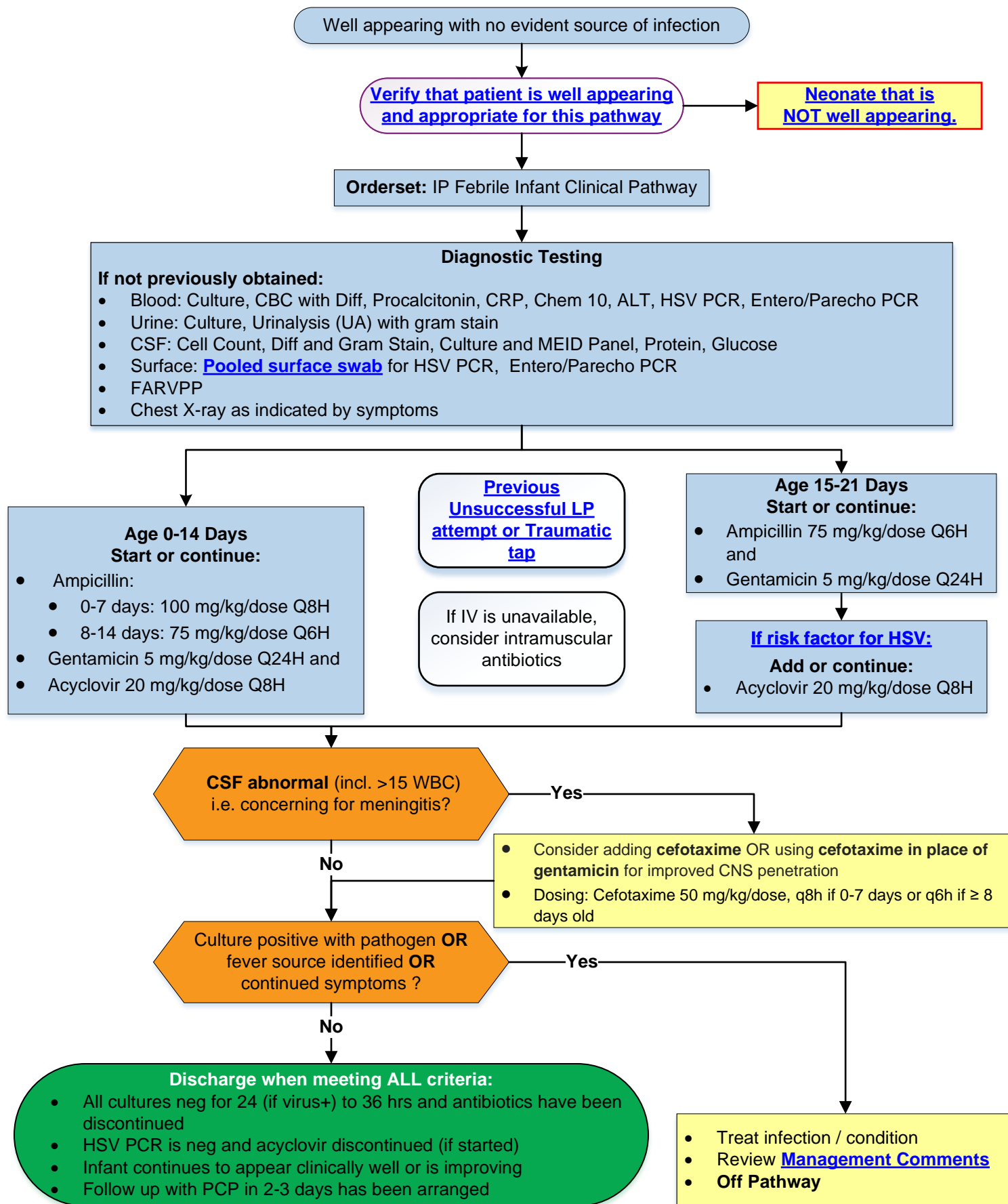
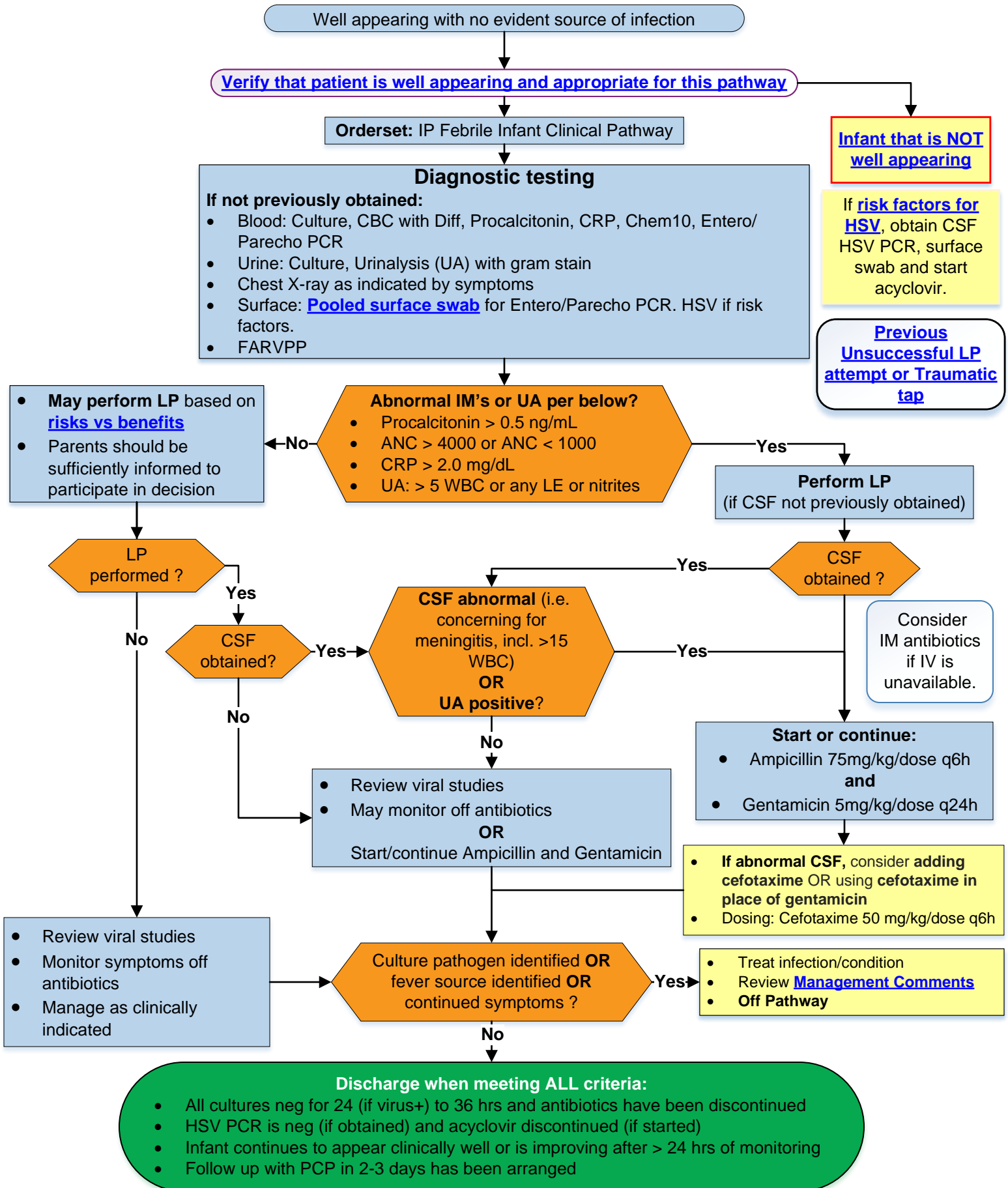


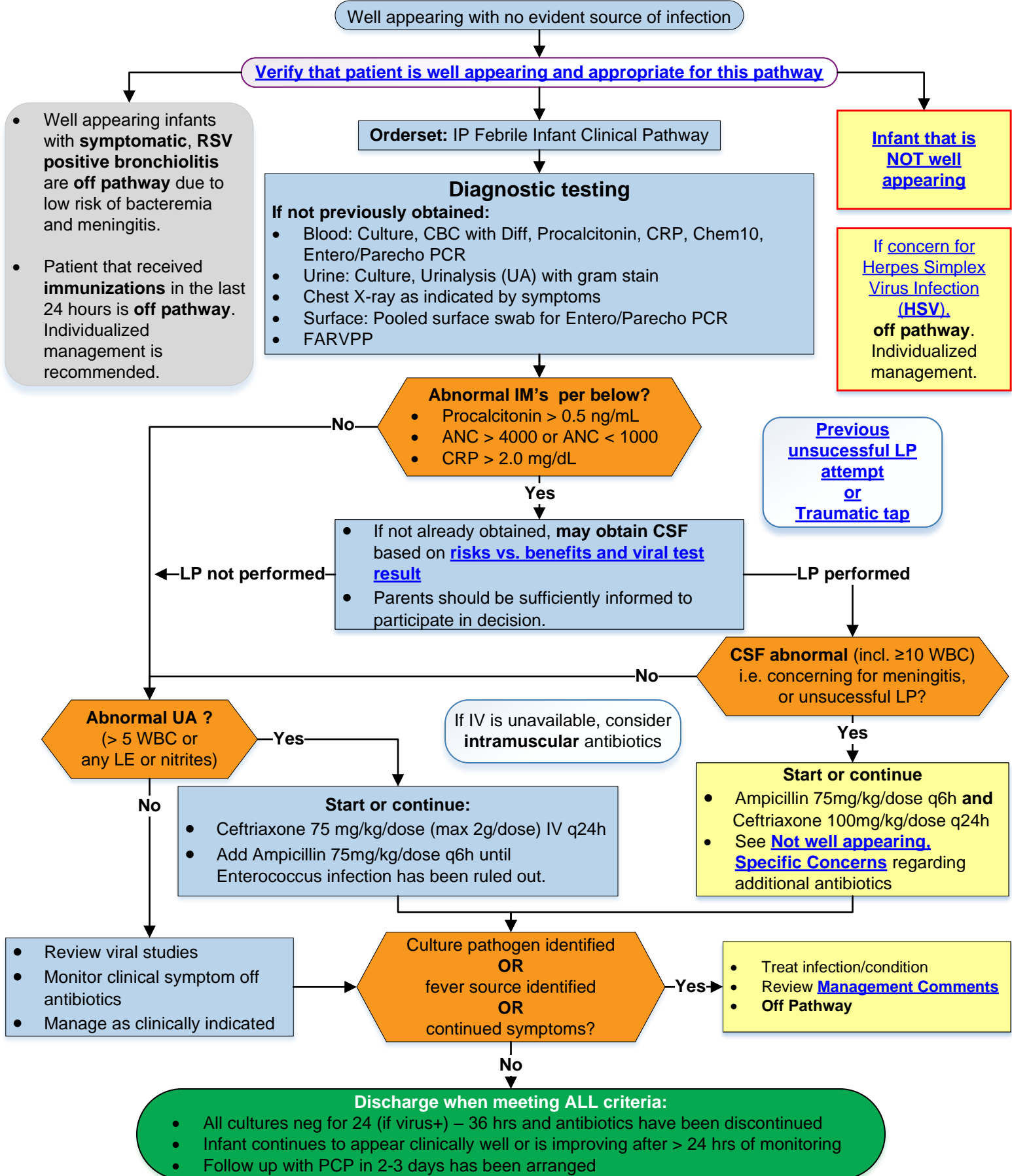
Febrile Neonate 0-21 Days Old Inpatient



Febrile Neonate 22-28 Days Old Inpatient



Febrile Infant 29-60 Days Old Inpatient



Pre-Pathway Validation

Is this a Febrile Infant?

Well appearing infant, 0 – 60 days old with a fever and **no evident source of infection** except respiratory viral symptoms

Typical presentation:

- Well appearing, asymptomatic infant **OR** with congestion, rhinorrhea, cough, diarrhea, otitis media.
- Can progress to altered mental status, seizure, unresponsiveness and death

Diagnostic Criteria for febrile infant.

- Fever $\geq 38^{\circ}\text{C}$ / 100.4°F . Rectal thermometry is the most accurate method for measuring temperature in this patient population. Temperatures measured by non-rectal methods should be interpreted on a case-by-case basis using the overall clinical assessment. When possible, a rectal temperature should be taken. When a non-rectal temperature is obtained, we do NOT recommend disregarding or adjusting the reported temperature.
- Well appearing

Consider other alternate clinical problem and diagnosis when:

- Diagnostic criteria are not met.

Consider a diagnostic timeout ("What else could this be?") or using a diagnostic checklist.



Pathway Inclusion Criteria

- 0 to 60 days old, well-appearing infant with no evident source of infection and temperature $\geq 38^{\circ}\text{C}$ / 100.4°F

Pathway Exclusion Criteria

- Hypothermia
- Preterm < 37 weeks gestation
- Infants < 2 weeks of age with perinatal complications (maternal fever, infection, or antimicrobial use)
- Focal bacterial infection (skin and soft tissue)
- Concerns for ophthalmia neonatorum
- Immune compromise
- Congenital/chromosomal abnormalities
- Technology dependent

Exclusions for 29-60 days old ONLY:

- Concern for Herpes Simplex Virus Infection (HSV)
- Received immunizations in the last 24 hours
- Clinical presentation consistent with bronchiolitis

[Return to 0-21 Days Algorithm](#)



Diagnostic Timeout

Red Flags

- Vesicular rash
- Somnolence or lethargy
- Hypothermia
- Seizure-type activity



Diagnostic Timeout

Differential Diagnosis

- Meningitis
- Bacteremia
- UTI
- Viral illness
- Focal bacterial infection
- CNS condition with autonomic dysfunction with hyper- or hypothermia

[Return to 22-28 Days Algorithm](#)

[Return to 29-60 Days Algorithm](#)

0-60 day old infant that is NOT well appearing

- Patient is **Off Febrile Infant clinical pathway**. Use guidance below as clinically appropriate for the specific patient.
- Follow Sepsis Alert and Watcher process
- Obtain blood, urine and CSF cultures prior to antibiotic administration if deemed safe
- If <29 days old or concern for HSV, add on HSV by PCR, blood and CSF.
- Administer **High Risk antibiotics** according to **Age** and **Specific Concerns** below:

Age: Neonate 0-28 days

- **Ampicillin:**
 - 0-7 days: 100mg/kg/dose Q6H
 - 8-21 days: 75mg/kg/dose Q6H
and
- **Gentamicin** 5mg/kg/dose
and
- **Cefotaxime** 50mg/kg/dose, q8h if 0-7 days
and q6h if ≥ 8 days old

Age: Infant 29-60 days

- **Ampicillin** 75mg/kg/dose Q6H
and
- **Ceftriaxone** 100mg/kg/dose q24h
(or **Cefotaxime** 50mg/kg/dose Q6H if on calcium containing IVFs).

Specific Concerns

- *Strep. pneumoniae* (pneumococcus) infection suspected based on Gram stain or MEID, or concern for *Staph. aureus* infection: Add **Vancomycin** 20mg/kg/dose Q6H
- <29 days or risk factors for HSV: Add **Acyclovir** 20 mg/kg/dose Q8H
- GNR seen on CSF or any specific organism concern: Discuss with ID.

- **If IV unavailable**, consider IM antibiotics with *Exception: Do not give Vancomycin IM*
- **Re-evaluate** potential source of infection and adjust antibiotic regimen accordingly

[Return to 0-21
Days Algorithm](#)

[Return to 22-28
Days Algorithm](#)

[Return to 29-60
Days Algorithm](#)

Risk Factors for HSV

- Age \leq 14 days old
- Known exposure

Symptoms and Exam findings:

- Vesicular or petechial rash
- Conjunctivitis
- Hypothermia (Temp $< 36^{\circ}$ C (96°F))
- Toxic appearing/lethargy/irritability
- Hemodynamically unstable
- Severe resp distress/apnea/PNA on CXR
- Abnormal neuro exam
- Seizure

Lab findings:

- CSF WBC > 15 and negative Gram stain
- Platelet $< 150,000$
- Any elevation of ALT

Infants 29-60 days

- Perinatally acquired HSV **can** present as late as 6 weeks, but **most** do within **first 3 weeks**
- **CNS disease** more likely; disseminated HSV is unlikely at this age
- Infants can still acquire HSV beyond the neonatal period
- Vesicular rash has likely developed if skin disease
- Mild, isolated pleocytosis (without additional symptom and exam findings), is NOT an indication for routine Acyclovir

[Return to 0-21
Days Algorithm](#)

[Return to 22-28
Days Algorithm](#)

[Return to 29-60
Days Algorithm](#)

0-21 Days Old, Management Comments

This clinical pathway is based on the American Academy of Pediatrics (AAP)
Clinical Practice Guideline: Evaluation and Management of Well-Appearing Febrile Infants 8-60 Days Old (2021).

The following NCH team consensus modifications were made to the AAP CPG recommendations to contextualize care for NCH:

- **Inclusion of infants 1-7 days old:** Care of these infants outside of the NCH Newborn Nursery/NICU does not differ from recommendations for infants 8-14 days old.
- Neonates with **clinical bronchiolitis are not excluded** due to risk of invasive bacterial infections in this age group.
- Specific NCH recommendations on HSV evaluation and treatment facilitate inclusion of infants with **high suspicion for HSV** in this specific clinical pathway.
- Infants > 14 days of age **on oral antibiotics** should follow the guidelines in this pathway: NCH team consensus is that there is insufficient evidence to support that oral antibiotics decrease the risk of invasive disease in this age group enough to forgo the recommended evaluation.
- **Obtain Inflammatory Markers (IM):** While the results of IM will not determine initial treatment, there is potential to impact ongoing clinical decisions.
- NCH team consensus recommendation that **age < 14 days is an indication for HSV testing and empiric treatment with Acyclovir** even in the absence of additional risk factors.
- Recommended HSV studies in the Emergency Department are **HSV PCR from blood and CSF; surface studies are obtained as inpatient**

[Return to 0-21 Days Algorithm](#)

LP in 22-28 Day Old, Risk vs Benefit Assessment

Clinicians **MAY** obtain a CSF analysis on infants 22 to 28 days of age even if all of the following criteria are met: (1) urinalysis result is negative or positive; (2) no IM obtained is abnormal; (3) blood and urine cultures have been obtained; and (4) infant is hospitalized. Evidence Quality: B; Moderate Recommendation

Benefits of testing	Early detection of bacterial meningitis. Detection of CSF pleocytosis or elevated protein attributable to HSV infection. Early treatment may decrease neurologic morbidity. Identification of pathogen from CSF to target type and duration of antimicrobial treatment. A normal CSF analysis helps in the decision whether to discharge infants at 24–36 h. Avoids unnecessarily prolonged antimicrobial therapy if CSF was obtained after antimicrobial agents started and diagnosis of meningitis is uncertain. This situation may occur if a blood culture grows a pathogen in 24 h and clinical circumstances suggest an LP is indicated.
Benefits of not testing	Avoids consequences of LP: discomfort or harm. Avoids further medical interventions because of false-positive results from CSF pleocytosis or bacterial contaminants. Avoids unnecessary or prolonged hospitalizations because of false-positive culture results. Avoids cost of procedure and unnecessary hospitalization. Avoids transient respiratory compromise resulting from positioning.
Risk, harm, cost of testing	Discomfort for infant. Potential for transient respiratory compromise during positioning for LP. Traumatic LPs yielding uninterpretable CSFs have been documented to prolong length of stay for hospitalized infants. ¹³² Unnecessary prolongation of hospitalization from false-positive bacterial culture result. Substantial cost if hospitalizing because of ambiguous CSF or prolonged hospitalization for bacterial contaminant. Parental anxiety.
Risks, harm, cost of not testing	In otherwise low-risk infants, delayed recognition of bacterial meningitis with increased risk of morbidity. Prolonged treatment if delay in obtaining CSF raises concern for partially treated meningitis.
Benefit–harm assessment	Benefit in specified situations.
Shared decision-making	Parents must provide consent for this procedure. An option by the committee to not obtain CSF for analysis is based on a consensus regarding the rate and risks of meningitis and benefit–harm assessment. Parents should be sufficiently informed to participate in this decision.
Key references	17–20, 22, 60, 106, 148

[Return to 22-28 Days Algorithm](#)

[See also 22-28 Days Management Comments](#)

22-28 Days Old, Management Comments

This clinical pathway is based on the American Academy of Pediatrics (AAP)
Clinical Practice Guideline: Evaluation and Management of Well-Appearing Febrile Infants 8-60 Days Old (2021).

The following NCH team consensus modifications were made to the AAP CPG recommendations to contextualize care for NCH:

- Infants with clinical **bronchiolitis** are not excluded.
- Infants with the following symptoms/signs should still be **included**: congestion, rhinorrhea, cough, diarrhea, otitis media.
- The risks of invasive bacterial infection (IBI) in infants < 28 days with a **positive viral test** is high enough to warrant management per this clinical pathway. In the literature, the risk of invasive bacterial infection in infants < 28 days with a positive viral test ranges from 0.8%-2.1%.
- Infants > 14 days of age **on oral antibiotics** should follow the recommendations in this pathway: NCH team consensus is that there is insufficient evidence to support that oral antibiotics decrease the risk of invasive disease in this age group enough to forgo the recommended evaluation.
- Urinalysis (UA) and urine culture ordered simultaneously: This is consistent with NCH current practice and avoids the potential need for an additional urine specimen and possible delay in starting antibiotics.
- A **positive UA** result **without elevation of inflammatory markers (IM)** is an indication for lumbar puncture to obtain cerebrospinal fluid (CSF). It is NCH team consensus that the risk of bacterial meningitis in an infant in this age group with a positive UA is sufficient to warrant analysis of CSF.
- An infant in this age group with reassuring **IM and UA without CSF obtained** should be observed in the hospital but does not require empiric antibiotic therapy.
- All infants in this age group **should be admitted** to the hospital: It is NCH team consensus that the combined risk of deterioration in this age group and challenges to ensure ideal outpatient follow-up justifies observation in the hospital setting.

[Return to 22-28 Days Algorithm](#)

Instructions for Obtaining Surface Swabs for Entero/parechovirus & HSV

- You will only need to collect 1 swab. Both tests can be run off of the same swab.
- The swab to collect the sample is the M6 media (the same swab for the FARVPP test). Please ask the patient's RN to bring a swab to bedside for you since they are stored in the refrigerator.
- You will need to write your initials and employee ID number on the collection tube. This is how the lab documents who collected the swab.
- Undress the patient to expose their face and diaper area.
- Wash your hands and apply gloves.
- Remove the sterile M6 swab from its packaging. Do not place the swab down on any surfaces in order to prevent contamination.
- Swab the conjunctiva first. Gently pull the lower eyelid down and rub the swab in a back-and-forth motion on the conjunctiva for 5 seconds. Please take care not to rub the cornea.



- Next, gently swab the patient's throat. It is okay if food material gets on the swab.
- Finally, gently use one hand to pick up the patient's legs to help expose their anus. Gently rub both sides of perianal area for 5 seconds. It is okay if stool gets on the swab.
- Place the swab in the fluid of the collection tube. There is a perforated line on the end of the swab that you can bend and break on the collection tube. Discard this piece of plastic in the trash.
- Screw the lid of the collection tube on the tube. Place the closed tube in the biohazard bag and leave on the computer stand.
- Take off and discard your gloves. Wash your hands. Please notify the patient's RN that you have collected the swab, and they will bring it to the lab. *Of note, the specimen needs to be received by lab before 9 am to result on the same day.*

[Return to 0-21
Days Algorithm](#)

[Return to 22-28
Days Algorithm](#)

LP in 29-60 Day Old, Viral Test Result & Risk vs Benefit Assessment

- Infants 29-60 days old who are overall well appearing with **clinical bronchiolitis** and a **positive RSV** test are at low risk for bacteremia and meningitis and therefore are excluded from this pathway.
- A **positive viral test** does not **preclude** entry into this pathway, BUT for this age group it may be considered in individualizing evaluation and management decisions. **Bacteremia rate has been shown to be significantly lower in viral-positive infants** compared to viral-negative infants (0.6% versus 1.8%). Specifically, rhinovirus positivity has been associated with a lower prevalence of bacteremia (1.4%) compared to virus negative infants (3.7%) in this age group.

Clinicians may obtain CSF for analysis if any IM obtained is abnormal. Evidence Quality: C; Weak Recommendation

Benefits	The prevalence of meningitis in this age group is 0.12–0.32. ^{17,22,24,61,94}
	Early detection of meningitis.
	Early treatment may lead to decreased neurologic morbidity. Identification of pathogen from CSF to target type and duration of antimicrobial treatment.
	Avoids unnecessarily prolonged antimicrobial therapy if CSF was obtained after antimicrobial agents started and diagnosis of meningitis is uncertain.
Risks, harm, cost	Discomfort for infant.
	Potential for transient respiratory compromise during positioning for LP.
	Traumatic LPs have been documented to prolong length of stay for hospitalized infants.
	Unnecessary prolongation of hospitalization from false-positive bacterial culture result.
	Substantial cost if hospitalizing because of ambiguous CSF or prolonged hospitalization for bacterial contaminant.
Benefit–harm assessment	Parental anxiety.
	Preponderance of benefit if CSF obtained.
Shared decision-making	Because parents must consent for this procedure, shared decision-making is required and their risk tolerances a consideration. KAS 4 extensively discusses rates and consequences of unsuccessful LPs, uninterpretable CSF analysis, and false-positive bacterial culture rates. If, for whatever reason, a parent is resistant or unwilling to consent to an LP, risk of meningitis, the evidence quality, benefit/harm assessment, and value judgments should be communicated to the parent to foster informed decision-making. The potential need for a future LP, depending on further clinical information and progress, is an important part of the discussion. These discussions should be documented.
Key references	17, 22, 24, 106, 132, 148

[Return to 29-60 Days Algorithm](#)

[See also 29-60 Days Management Comments](#)

29-60 Days Old, Management Comments

This clinical pathway is based on the American Academy of Pediatrics (AAP)
Clinical Practice Guideline: Evaluation and Management of Well-Appearing Febrile Infants 8-60 Days Old (2021).

The following NCH team consensus modifications were made to the AAP CPG recommendations to contextualize care for NCH:

- If LP attempted but **CSF unobtainable or uninterpretable**, there are insufficient data for the AAP CPG to make specific recommendations. NCH pathway team recommends admission, with or without IV antibiotics based on individualized risk assessment, under these circumstances
- Infants with the following symptoms/signs should still be **included**: congestion, rhinorrhea, cough, diarrhea, otitis media.
- Infants 29-60 days old who are overall well appearing with **clinical bronchiolitis** and a **positive RSV test** are at low risk for bacteremia and meningitis and therefore are excluded from this pathway. Risk of **UTI** is still significant however with rates from 5 to 14% reported. UA and urine culture should be considered in this population.
- A **positive viral test** does not preclude entry into this pathway, but for this age group may be considered in individualizing evaluation and management decisions. Bacteremia rate has been shown to be significantly lower in viral-positive infants compared to viral-negative infants (0.6% versus 1.8%). Specifically, rhinovirus positivity has been associated with a lower prevalence of bacteremia (1.4%) compared to virus negative infants (3.7%) in this age group.

[Return to 29-60 Days Algorithm](#)

LP & CSF Complications

Previous unsuccessful LP attempt and/or spine US indications:

- Rehydrate if evidence of dehydration
- Insufficient evidence to make routine recommendation about lumbar spine US prior to repeat LP and when US guided LP is indicated.
- A risk/benefit assessment in consultation with IR is recommended, considering patient size and anatomy, number of previous attempts, risk of lumbosacral hematoma and other patient specific circumstances.
- When CSF volume is small/insufficient for LP on spine US, IR recommends waiting 48 hours before reassessing with repeat US.

Traumatic tap

If traumatic tap or subarachnoid hemorrhage is suspected, send 1st and 4th tube for cell count and ask lab to evaluate for xanthochromia (Ref: The Harriet Lane Handbook)

WBC/RBC ratio is an **unreliable** indicator for clinical decision making

[Return to 0-21 Days Algorithm](#)

[Return to 22-28 Days Algorithm](#)

[Return to 29-60 Days Algorithm](#)

Quality Measures

Goals:

1. To implement use of inflammatory markers to identify infants 22-60 days old who are at risk for serious bacterial infection.
2. To promote evidence-based use of broad-spectrum antimicrobials for well-appearing febrile infants.

Metrics 0-21 Days:

Process measures:

1. IP Order Set utilization

Outcome measures:

1. IP length of stay
2. IP: Percent of patients with positive viral studies and negative cultures at 24 hours with active antibiotic orders.
3. IP: Percent of patients with negative cultures at 36 hours with active antibiotic orders.

Balancing measure:

1. ED/IP: Percent of patients aged 15-21 days with HSV who did not receive empiric acyclovir.
 - a. Any positive HSV PCR (Blood, CSF, or Surface Swabs)
2. IP: 72 hour return visit to ED/UC
3. IP: 7-day readmission rate

Metrics 22-28 Days:

Process measures:

1. IP Order Set utilization
2. ED/IP: Rate of LP in patients with normal inflammatory markers and normal UA
 - i. Procalcitonin >0.5
 - ii. ANC >4000 or ANC <1000
 - iii. CRP >2
 - iv. UA: > 5 WBC or any LE or nitrites

Outcome measures:

1. IP length of stay
2. ED/IP: Rate of empiric antimicrobial use in patients with normal UA, inflammatory markers, and CSF.
3. IP: Percent of patients with positive viral studies and negative cultures at 24 hours with active antibiotic orders.
4. IP: Percent of patients with negative cultures at 36 hours with active antibiotic orders.

Balancing measure:

1. ED/IP: Percent of patients aged 22-28 days with HSV who did not receive empiric acyclovir.
 - a. Any positive HSV PCR (Blood, CSF, or Surface Swabs)
2. ED/IP: Rate of UTI, bacteremia, or bacterial meningitis in patients with a normal UA and inflammatory markers who did not receive empiric antibiotics.
3. IP: 72 hour return visit to ED/UC
4. IP: 7-day readmission rate

Metrics 29-60 Days:

Process measures:

1. IP Order Set utilization

Outcome measures:

1. IP length of stay
2. Rate of LP in patients with normal inflammatory markers and normal UA
 - i. Procalcitonin >0.5
 - ii. ANC >4000 or ANC <1000
 - iii. CRP >2
 - iv. UA: > 5 WBC or any LE or nitrites
3. Rate of empiric antimicrobial use in patients with normal UA, inflammatory markers and CSF
4. IP: Percent of patients with positive viral studies and negative cultures at 24 hours with active antibiotic orders.
5. IP: Percent of patients with negative cultures at 36 hours with active antibiotic orders.

Balancing measure:

1. ED/IP: Rate of UTI, bacteremia, or bacterial meningitis in patients with a known viral source and abnormal inflammatory markers and who did not have an LP performed and/or did not receive empiric antibiotics
2. IP: 24 hour return visit to ED/UC
3. IP: 7-day readmission rate

[Return to 0-21
Days Algorithm](#)

[Return to 22-28
Days Algorithm](#)

[Return to 29-60
Days Algorithm](#)

References

1. Pantell RH, Roberts KB, Adams WG, et al. Evaluation and Management of Well-Appearing Febrile Infants 8 to 60 Days Old [published correction appears in *Pediatrics*. 2021 Nov;148(5):e2021054063. doi: 10.1542/peds.2021-054063]. *Pediatrics*. 2021;148(2):e2021052228. doi:10.1542/peds.2021-052228
2. Niven DJ, Gaudet JE, Laupland KB, Mrklas KJ, Roberts DJ, Stelfox HT. Accuracy of peripheral thermometers for estimating temperature: a systematic review and meta-analysis. *Ann Intern Med*. 2015;163(10):768-777. doi:10.7326/M15-1150
3. Thomson J, Sucharew H, Cruz AT, et al. Cerebrospinal Fluid Reference Values for Young Infants Undergoing Lumbar Puncture. *Pediatrics*. 2018;141(3). doi:https://doi.org/10.1542/peds.2017-3405
4. The Harriet Lane Handbook, 22nd Edition, The Johns Hopkins Hospital & Keith Kleinman & Lauren McDaniel & Matthew Molloy [2021]
5. Levine DA, Platt SL, Dayan PS, et al. Risk of serious bacterial infection in young febrile infants with respiratory syncytial virus infections. *Pediatrics*. 2004;113(6):1728-1734. doi:10.1542/peds.113.6.1728
6. Hendaus MA, Alhammadi AH, Khalifa MS, Muneer E, Chandra P. Risk of urinary tract infection in infants and children with acute bronchiolitis. *Paediatr Child Health*. 2015;20(5):e25-e29. doi:10.1093/pch/20.5.e25
7. Mahajan P, VanBuren JM, Tzimenatos L, et al. Serious Bacterial Infections in Young Febrile Infants With Positive Urinalysis Results. *Pediatrics*. 2022 Oct;150(4):e2021055633. DOI: 10.1542/peds.2021-055633.

[Return to 0-21
Days Algorithm](#)

[Return to 22-28
Days Algorithm](#)

[Return to 29-60
Days Algorithm](#)

Team & Process

Pathway Development Team

Leader(s):

Infectious Disease:

Cristina Tomatis Souverbielle MD

Hospital Pediatrics:

Gerd McGwire MD, PhD

Members:

Emergency Medicine:

Berkeley L. Bennett, MD, MS

Maegan Reynolds MD

Infectious Disease:

Guliz Erdem, MD

Infectious Disease & Informatics:

Juan Chaparro, MD

Infectious Disease & Neonatology:

Alexandra Medoro, MD

Hospital Pediatrics:

Alana Painter, MD

Ashleigh Slemmer, MD

Pediatric Resident:

Jennifer Springer, MD

Clinical Pathways Program:

Medical Director – Emergency Medicine:

Berkeley Bennett, MD, MS

Medical Director – Hospital Pediatrics:

Gerd McGwire, MD, PhD

Medical Director – Clinical Informatics & Emergency Medicine:

Laura Rust, MD, MPH

Business & Development Manager:

Rekha Voruganti, MBOE, LSSBB

Program Coordinators:

Tara Dinh, BS

Clinical Pathway Approved

Medical Director – Associate Chief Quality Officer, Center for Clinical Excellence:

Ryan Bode, MD, MBOE

Advisory Committee Date: *September, 2022*

Origination Date: *March, 2023*

Last Revision Date: *April, 2024*

Next Revision Date: *March, 2027*

Clinical Pathway Development

This clinical pathway was developed using the process described in the NCH Clinical Pathway Development Manual Version 6, 2022. Clinical Pathways at Nationwide Children's Hospital (NCH) are standards which provide general guidance to clinicians. Patient choice, clinician judgment, and other relevant factors in diagnosing and treating patients remain central to the selection of diagnostic tests and therapy. The ordering provider assumes all risks associated with care decisions. NCH assumes no responsibility for any adverse consequences, errors, or omissions that may arise from the use or reliance on these guidelines. NCH's clinical pathways are reviewed periodically for consistency with new evidence; however, new developments may not be represented, and NCH makes no guarantees, representations, or warranties with respect to the information provided in this clinical pathway.

Copyright © 2023. Nationwide Children's Hospital. All rights reserved. No part of this document may be reproduced, displayed, modified, or distributed in any form without the express written permission of Nationwide Children's Hospital.

For more information about our pathways and program please contact:
ClinicalPathways@NationwideChildrens.org

[Return to 0-21
Days Algorithm](#)

[Return to 22-28
Days Algorithm](#)

[Return to 29-60
Days Algorithm](#)