Nationwide Children's
When your child needs a hospital, everything matters.

Evaluation & Management of Febrile Infants 22-28 Days Old

Emergency Department

Center for Clinical Excellence

Inclusion Criteria:
Well appearing
infant 22-28 days &
measured temperature
≥ 38° C / 100.4° F

Temperature Measurement

Is patient ill appearing and requiring resuscitation?
See Escalation of Care

Initial Evaluation:
(see Febrile Infant 22-28 Day Order Set)

Confirm vitamin K status

- If no prophylaxis:
  - Counsel family on vitamin K recommendations in newborns and administer if family is agreeable
  - Obtain PT/PTT if LP to be performed

Obtain:

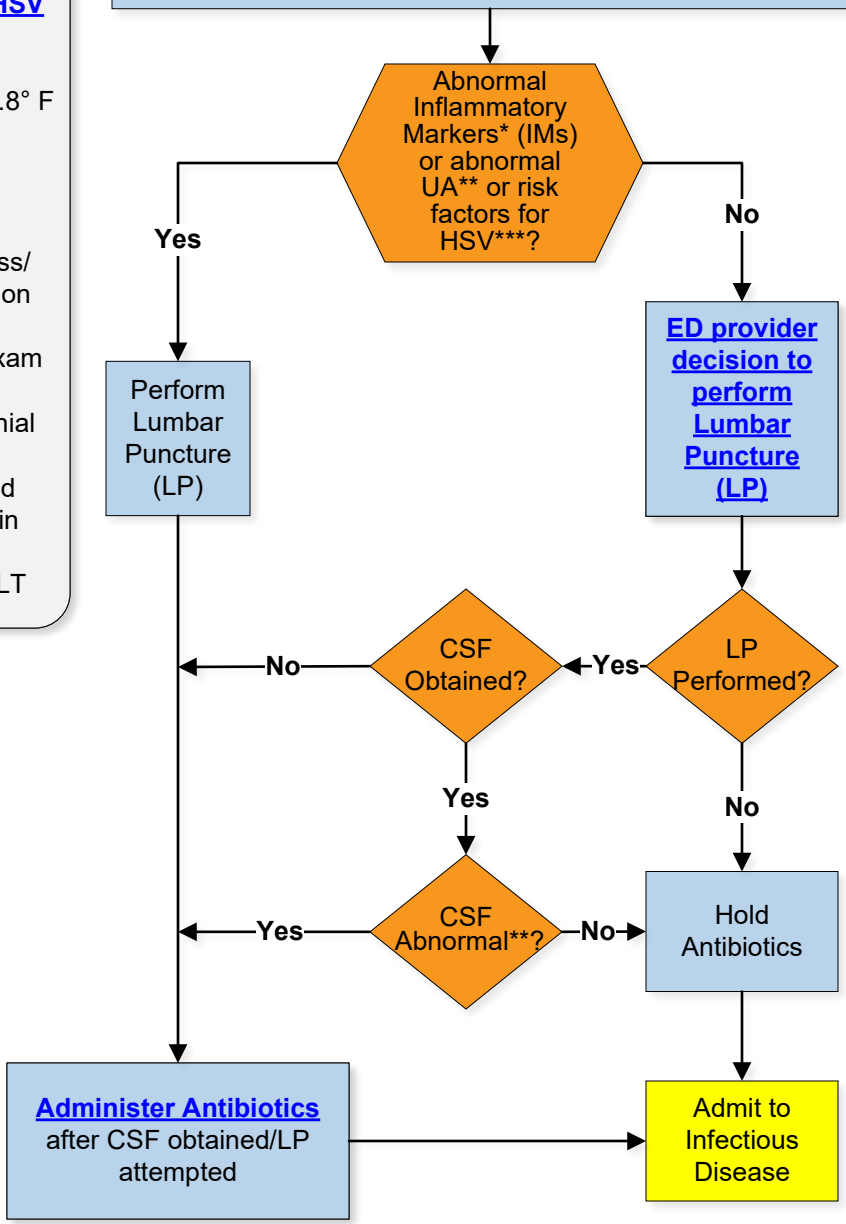
- Blood Culture
- CBC with Diff
- Procalcitonin
- CRP
- ALT
- Chem 10
- Blood HSV PCR
- Blood Entero/Parecho PCR
- Urine Culture
- Urinalysis (UA) with Microscopy
- Viral respiratory panel (FARVPP)
- Chest X-ray as indicated by symptoms

Exclusion Criteria:

- Temp < 36° C / 96.8° F
- Preterm < 37 weeks gestation
- Focal bacterial infection (cellulitis, omphalitis, septic arthritis, osteomyelitis, pneumonia)
- Ophthalmia Neonatorum
- Immune compromise
- Congenital/ chromosomal abnormalities
- Technology dependent

***Risk Factors for HSV**

- Known exposure
- Temp < 36° C / 96.8° F
- Toxic appearing/ lethargy/irritability
- Hemodynamically unstable
- Severe resp distress/ apnea/pneumonia on CXR
- Abnormal neuro exam
- Seizure
- Vesicular or petechial rash
- CSF WBC > 15 and negative Gram stain
- Platelet < 150,000
- Any elevation of ALT



***Abnormal Inflammatory Markers (IMs):**

- Procalcitonin > 0.5 ng/mL
- ANC > 4000 or ANC < 1000
- CRP > 2.0 mg/dL

****Abnormal Labs:**

- UA: > 5 WBC or any LE or + nitrites
- CSF: >15 WBC

LP Guidance for Infants without Vitamin K Prophylaxis

Management Comments

Temperature Measurement

Inclusion Criteria:
Well appearing
Infant 22-28 days **&** measured temperature
≥ 38° C / 100.4° F

Rectal thermometry is the most accurate method for measuring temperature in this patient population.

When a non-rectal temperature is obtained, the reported temperature should not be altered.

Algorithm

Escalation of Care

If patient is ill appearing and requiring resuscitation:
Obtain standard initial evaluation labs inclusive of CSF and HSV/EV/PEV studies
Consider sepsis alert/sepsis watcher pathway and order sets

- **Initiate resuscitation**
- **Encourage obtaining blood, urine and CSF cultures prior to antibiotic administration**
- **Obtain HSV and EV/PEV PCRs in blood and CSF**
- **Antibiotics: Refer to Sepsis Pathway**

Algorithm

Risk Factors for HSV

If HSV is suspected, perform lumbar puncture

- Known exposure
- Temp < 36° C / 96.8° F
- Toxic appearing/lethargy/irritability
- Hemodynamically unstable
- Severe resp distress/apnea/pneumonia on CXR
- Abnormal neuro exam
- Seizure
- Vesicular or petechial rash
- CSF WBC >15 and negative Gram stain
- Platelet < 150,000
- Any elevation of ALT

Escalation of Care

- Recommended HSV studies in the Emergency Department are HSV PCR from blood and CSF.
- Surface studies, when time sensitive, may be performed in the ED by infectious disease resident team.
  - **HSV and Enterovirus/PEV surface studies**
    - One swab total: first swab eye, then throat, then rectum in viral transport media
    - Separate HSV PCR swab of vesicle (unroofed) if present

Algorithm

Instructions for Obtaining Surface Swabs for Entero/Parechovirus and HSV PCRs

- Please ask the patient's RN to bring a M6 viral transport media collection kit 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, abdomen, 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. You need to collect only 1 swab.
    - 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 grab the patient's bottom lip to pull down and out to expose the buccal mucosa. Gently rub the swab in a back-and-forth motion on the buccal mucosa for 5 seconds. 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 send it to the lab. *Of note, the specimen needs to be received by lab before 9 am to result on the same day.*

Algorithm

LP in 22-28 Days 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.

Pantell R H, Roberts K B, Adams W G, et al. Evaluation and management of well-appearing febrile infants 8-60 days old. Pediatrics. 2021;148(2):e2021052228

Algorithm

LP Guidance for infants without Vitamin K prophylaxis

Vitamin K is essential for normal blood clotting as factors II, VII, IX and X require vitamin K for activity. Newborns are born with low vitamin K stores, and breast milk contains only small amounts of the vitamin. Additionally, normal newborn gut flora (lactobacillus) does not synthesize vitamin K. For these reasons, infants are at risk of developing Vitamin K Deficiency Bleeding (VKDB), a potentially life-threatening condition, which can be prevented with a single intramuscular (IM) dose of vitamin K at birth. Oral vitamin K, even in higher doses, is not as effective as IM dosing.

There are three forms of VKDB:

- **Early VKDB:** Within 24 hours of birth, associated with maternal medications that interfere with vitamin K.
- **Classic VKDB:** Between days 2–7, especially in exclusively breastfed infants.
- **Late VKDB:** Between 2 weeks and 6 months; often severe, associated with intracranial hemorrhage, and almost exclusively affects infants who did not receive vitamin K at birth.

Febrile infant without Vitamin K prophylaxis needing LP

↓

Counsel family on importance of vitamin K prophylaxis in newborns and administer if family is agreeable

↓

Obtain coagulation studies (PT/PTT)

↓

Coags abnormal (> 1.5x upper limit of normal for age)?

DO NOT delay antibiotic administration

Medications:

Vitamin K: 1 mg IV/IM x1

Kcentra: 25 units/kg IV x1 (off label use)

- Prothrombin complex concentrate (Factors II, VII, IX, X, Protein C and S) – Blood product consent is required.
- **Do not** use if history of thromboembolic event.
- Risks include possible allergic or transfusion reactions.
- Kcentra should be given **at least** 15-30 min prior to LP.
- LP should be completed **within** 24 hours of Kcentra.
- Kcentra is **NOT available at LCED.** Administer antibiotics and admit without LP.

No → Proceed with LP
(OK to perform even if vitamin K refused; still recommend vitamin K for all infants who have not received it)

If family refuses Kcentra and coags are abnormal, admit without LP.

Yes → Administer vitamin K **AND** Kcentra prior to LP
(OK to perform even if vitamin K refused but Kcentra is given)

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 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.

Algorithm

NCH Intravenous Medication Recommendations

See Febrile Infant 22-28 Days Order Set

Abnormal CSF or LP indicated but not successful/uninterpretable

- Cefotaxime 50mg/kg/dose &
- Ampicillin 75mg/kg/dose

Abnormal IMs and normal CSF

- Gentamicin 5mg/kg/dose &
- Ampicillin 75mg/kg/dose

Add Acyclovir 20 mg/kg/dose if CSF WBC > 15 and negative Gram stain or if risk factors for HSV present.

Add Vancomycin if concerned for Streptococcus pneumoniae or Staphylococcus aureus on Gram stain or MEID.

Neonatal Vancomycin Dosing (Meningitic)	
Postmenstrual Age (PMA)	**Dose**
< 30 weeks	12.5 mg/kg/dose
30 weeks – 43 weeks, 6 days	15 mg/kg/dose
≥ 44 weeks	20 mg/kg/dose

If Gram negative rods seen on CSF or any other specific organism concerns, discuss with Infectious Disease

If IV unavailable, consider intramuscular antibiotics
(do not give Vancomycin or Acyclovir IM)

Algorithm

Quality Measures

Goals:
- To implement use of inflammatory markers to identify infants 22-28 days old who are at risk for serious bacterial infection.
- To promote evidence-based use of broad-spectrum antimicrobials for well appearing febrile infants

Process measures:
- ED/UC Order set utilization
- Rate of lumbar puncture in patients with normal inflammatory markers and a normal urinalysis

Outcome measures:
- UC length of stay
- ED length of stay
- Rate of empiric antimicrobial use in patients with normal urinalysis, inflammatory markers, and CSF studies

Balancing measure:
- Percent of patients 22-28-days old with confirmed HSV infection who did not receive empiric acyclovir
- Rate of UTI, bacteremia, or bacterial meningitis in patients with a normal urinalysis and inflammatory markers who did not receive empiric antibiotics

Algorithm

References

1.) Pantell RH, Roberts KB, Adams WG, et al. Evaluation and management of well-appearing febrile infants 8-60 days old. *Pediatrics*. 2021;148(2) .doi:10.1542/peds.2021-052228.

2.) Niven DJ, Gaudet JE, Laupland KB, et al. Accuracy of peripheral thermometers for estimating temperature: a systematic review and meta-analysis. *Ann Intern Med*. 2015;163(10):768. doi:10.7326/M15-1054.

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4.) Scott K, Miller E, Culhane JF, et al. Trends in Vitamin K Administration Among Infants. JAMA. 2026;335(3):272–274. doi:10.1001/jama.2025.21460

5.) Ivan Hand, Lawrence Noble and Steven Abrams. COMMITTEE ON FETUS AND NEWBORN, SECTION ON BREASTFEEDING, COMMITTEE ON NUTRITION. Pediatrics (2022) 149 (3): e2021056036.

6.) Burstein B, Waterfield T, Umana E, Xie J, Kuppermann N. Prediction of Bacteremia and Bacterial Meningitis Among Febrile Infants Aged 28 Days or Younger. JAMA. 2026;335(5):425–433. doi:10.1001/jama.2025.21454

Algorithm

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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 associates 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.

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Algorithm