

Febrile Infants 0-21 Days

ED Evaluation & Management

Inclusion Criteria: Well appearing

Infant 0-21 days & measured temperature
≥ 38° C / 100.4° F

[Temperature
Measurement](#)

Exclusion Criteria:

- Temp < 36° C / 96.8° F
- Preterm < 37 weeks gestation
- Infants < 2 weeks of age with perinatal complications (maternal fever, infection, or antimicrobial use)
- Focal bacterial infection (cellulitis, omphalitis, osteomyelitis, septic arthritis, pneumonia)
- Concerns for ophthalmia neonatorum
- Immune compromise
- Congenital/chromosomal abnormalities
- Technology dependent

Initial Evaluation:

(See Febrile Infant 0-21 days 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

Obtain:

- Blood Culture
- CBC with Diff
- Procalcitonin
- CRP
- ALT
- Chem 10
- Blood Entero/Parecho PCRs
- Blood HSV PCR
- Urine Culture
- Urinalysis (UA) with Microscopy
- CSF Cell Count, Diff, Glucose, Protein, Gram Stain, Culture and MEID Panel
 - [LP guidance for infants without vitamin K prophylaxis](#)
- Chest X-ray as indicated by symptoms

Is patient ill appearing and requiring resuscitation?

[See Escalation of care](#)

[Vitamin K Prophylaxis](#)

[Risk Factors for HSV](#)

- Age ≤ 14 days old
- 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
- Conjunctivitis
- CSF WBC > 15 and negative Gram stain
- Platelet < 150,000
- Any elevation of ALT

Risk Factors
for HSV?

No

Yes

[Acyclovir
per protocol](#)

[Antimicrobials based on age/CSF
results](#)

Admit to Infectious
Disease

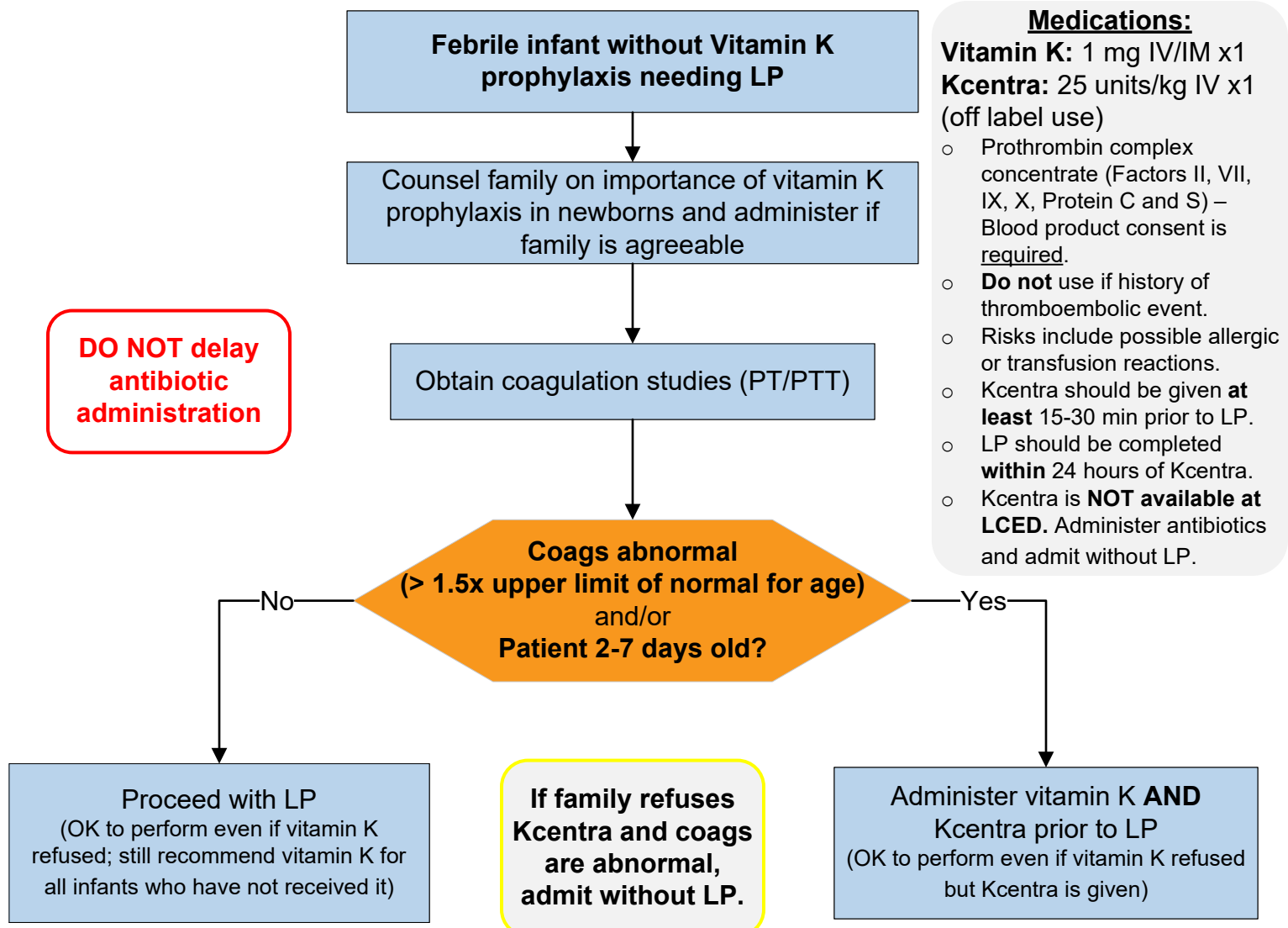
[Management Details](#)

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.



Temperature Measurement

Inclusion Criteria:

Well appearing

Infant 0-21 days & measured temperature
 $\geq 38^{\circ}\text{C} / 100.4^{\circ}\text{F}$

- 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](#)

Risk Factors for HSV

- Age < 14 days old
- 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
- Conjunctivitis
- 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](#)

Escalation of Care

If patient is ill appearing and requiring resuscitation:

Obtain standard 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

NCH Intravenous Medication Recommendations

Normal CSF

0-14 Days

- Acyclovir 20 mg/kg/dose &
- Gentamicin 5 mg/kg/dose &
- Ampicillin:
 - 0-7 days: 100 mg/kg/dose
 - 8-14 days: 75 mg/kg/dose

15-21 Days

- Gentamicin 5 mg/kg/dose &
- Ampicillin 75 mg/kg/dose &
- Acyclovir 20 mg/kg/dose (if HSV risk factors)

Abnormal CSF or LP not successful/ uninterpretable

- Acyclovir 20 mg/kg/dose &
- Cefotaxime 50 mg/kg/dose &
- Ampicillin:
 - 0-7 days: 100 mg/kg/dose
 - 8-14 days: 75 mg/kg/dose

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

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](#)

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.
- Infants with **clinical bronchiolitis are not excluded** due to risk of invasive bacterial infections in this age group
- Infants > 14 days of age **on oral antibiotics** should follow the guidelines in this pathway: NCH team consensus is that oral antibiotics do not decrease the risk of invasive disease in this age group enough to forgo the recommended evaluation.
- NCH team consensus is to **include well appearing infants with risk factors for HSV** on this specific pathway in order to decrease risk of missed HSV in this population. Age < 14 days is an indication for **HSV testing** and empiric treatment with Acyclovir: NCH team consensus recommendation even in the absence of additional risk factors.
- **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.
- The risks of invasive bacterial infection (IBI) in infants < 28 days with a **positive viral test** is high enough to warrant completing the recommendations in 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%.
- **Obtain Inflammatory Markers (IM):** While the results of IM will not determine initial treatment, there is potential to benefit ongoing clinical decisions.

[Algorithm](#)

Quality Measures

Goals:

- To promote evidence-based use of broad-spectrum antimicrobials for well appearing febrile infants
- To implement use of inflammatory markers to identify infants 0-21 days old who are at risk for serious bacterial infection.

Process measure:

ED/UC Order set utilization

Outcome measures:

- UC length of stay
- ED length of stay

Balancing measure:

Percent of patients 15-21 days with a positive HSV PCR (blood, CSF or surface swabs) who did not receive empiric acyclovir

[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.
3. Thomson J, Sucharew H, Cruz AT, et al. Cerebrospinal fluid reference values for young infants undergoing lumbar puncture. *Pediatrics*. 2018;141(3) .doi:10.1542/peds.2017-3405.
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 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.

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[Algorithm](#)