

Inclusion Criteria: Well appearing

infant 29-60 days & measured
temperature
≥ 38° C / 100.4° F

Temperature Measurement

Exclusion Criteria:

- Hypothermia (< 36° C / 96.8° F)
- Preterm < 37 weeks gestation
- Clinical presentation consistent with bronchiolitis
- Focal bacterial infection (cellulitis, omphalitis, septic arthritis, osteomyelitis, pneumonia)
- Concern for Herpes Simplex Virus infection (HSV)
- Immune compromise
- Congenital/chromosomal abnormalities
- Technology dependent
- Received immunizations in last 24 hours

Management Comments

Positive Viral Test

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
- Urine Culture
- Urinalysis (UA) with microscopy
- Consider Blood Entero/Parecho PCRs
- Consider viral respiratory panel (FARVPP)
- Chest Xray as indicated by symptoms

Is patient ill appearing and requiring resuscitation?
See escalation of care

*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: ≥ 10 WBC

Abnormal
Inflammatory
Markers*
(IMs)?

No

Yes

May obtain CSF based on:

risks vs. benefits and viral test result

Parents should be sufficiently informed to participate in decision.

LP Guidance for Infants without Vitamin K Prophylaxis

LP Performed

CSF abnormal** or
unobtainable or
uninterpretable?

Yes

No

LP
Deferred

UA
Abnormal**?

Yes

No

Ceftriaxone
IV/IM

Admit
for observation?
*Shared decision
making with family*

Admit to
Infectious
Disease

No

UA
Abnormal**?

Yes

Discharge

- No antibiotics
- Follow-up within 24 hours

Discharge

- Oral antibiotics
- Follow-up within 24 hours

Discharge

- If not completed already, consider FARVPP
- Follow-up within 24 hours

No

Yes

Discharge Criteria

- Adequate PO intake
- Parents & provider comfortable
- Reliable phone and transportation
- Follow-up in 24 hours

Viral Test Result

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.

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 for RSV positive infants, however, and should be considered during evaluation.*

[Algorithm](#)

LP in 29-60 day old Risk vs Benefit Assessment

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. Parental anxiety.
Benefit–harm assessment	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

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](#)

Temperature Measurement

Inclusion Criteria:**Well appearing**

Infant 29-60 days & measured temperature
 $\geq 38^{\circ}\text{C}$ / 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

- Known exposure
- Temp < 36° C / 96.8°F
- Toxic appearing/lethargy/irritability
- Hemodynamically unstable
- 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](#)

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

- 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](#)

NCH Medication Recommendations

See Febrile Infant 29-60 Days Order Set

Abnormal Inflammatory Markers

Abnormal CSF or LP not successful/uninterpretable

- Ceftriaxone 100 mg/kg/dose IV &
- Ampicillin 75 mg/kg/dose IV

LP deferred or normal CSF but + concern for UTI

- Ampicillin 50 mg/kg/dose IV &
- Gentamicin 5 mg/kg/dose IV

LP deferred or normal CSF and NO concern for UTI (prior to discharge or admission)

- Ceftriaxone 75 mg/kg/dose IM/IV

Normal Inflammatory Markers

Oral treatment of UTI

Cephalexin 25 mg/kg/dose Q8 hours for 7 days

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

Add Vancomycin if CSF is cloudy, purulent or there is concern for Streptococcus pneumoniae or Staphylococcus aureus

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

[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)?

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)

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.

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 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 are at low risk for bacteremia and meningitis and therefore are excluded from this pathway. *Risk of UTI is still significant, however, and should be considered during evaluation.*
- 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.
- If **CSF is felt to be indicated by the care team but is unobtainable or uninterpretable**, there are insufficient data for the AAP CPG to make specific recommendations. NCH pathway team recommends intravenous antibiotics and admission in these circumstances.

[Algorithm](#)

Quality Measures

Goals:

- To implement use of inflammatory markers to identify infants 22-60 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

Outcome measures:

- UC length of stay
- ED length of stay
- Rate of LP in patients with normal inflammatory markers and normal UA
- Rate of empiric antimicrobial use in patients with normal UA, inflammatory markers and CSF

Balancing measure:

- Rate of UTI, bacteremia, or bacterial meningitis in patients with a known viral source and abnormal inflammatory markers
- 7 day return visit to ED/UC
- UC to ED transfer rate

[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) Mahajan P, VanBuren JM, Tzimenatos L, et al. Serious bacterial infections in young febrile infants with positive urinalysis results. *Pediatrics*. 2022;150(4) .doi:10.1542/peds.2021-055633
- 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):1728-34. doi:10.1542/peds.113.6.1728. PMID: 15173498.
- 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) .doi:10.1093/pch/20.5.e25. PMID: 26175566; PMCID: PMC4472059.

[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](#)