Clinical Pathways

Fever and Sepsis Evaluation in the Infant (29-60 days)

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What is a Clinical Pathway?

An evidence-based guideline that decreases unnecessary variation and helps promote safe, effective, and consistent patient care.
Objectives of Pathway

• Decrease variability in care for febrile infants ages 29-60 days
• Decrease unnecessary testing
• Decrease unnecessary antibiotic use
• Decrease rate of hospitalization for well-appearing infants with low risk test results
• Decrease average length of stay of patients admitted as inpatient or placed in observation
Why is Pathway Necessary?

• Fever is a very common reason for visits to ED
  o 500,000 ED visits annually children ≤ 60 days of age
  o Serious Bacterial Infection (SBI) rate: 6-10% in children ≤ 90 days of age
    – UTI 5-9%
    – Bacteremia 1.9-2.2%
    – Meningitis 0.3-0.5%

• There is great variability in care provided to patients in this age group
  o Past Management of febrile infants 29-60 disorder included 3 common algorithms:
    1. Philadelphia Criteria
    2. Rochester Criteria
    3. Boston Criteria
Background

• More and more evidence now exists which supports:
  o Use of clinical pathways for workup and treatment of these infants
  o Lumbar puncture not universally indicated in this age group
  o Hospitalization not necessary for all febrile infants in this age group
  o Shorter length of stay and earlier discontinuation of antibiotics if hospitalized

• Byington et al., 2012: evidence based care practice model for febrile infants 29-90 days old\(^1\):
  o Improved risk stratification
  o Improved rate of appropriate testing
  o Less missed SBI on initial evaluation
  o Less unnecessary antibiotics
  o Shorter hospital length of stay
  o All accomplished across multiple care sites

• Chua et al., 2015\(^2\)
  o Showed no difference in clinical outcomes between institutions with guidelines recommending universal LP compared to institutions where LP was recommended if the patient is not “well appearing” or had high risk laboratory results
Recent literature is more relevant to our inpatient population
- Excludes patients admitted to ICUs, with indwelling hardware, and with histories of intra-abdominal, intracranial or intrathoracic surgeries
- Current automated technology is allowing for earlier detection

97% of blood cultures, 95% of urine cultures and 86% of CSF cultures treated as true pathogens were identified in ≤36 hours

Risk of positive CSF culture >24 hours is low (1.5%) and is 0% in low risk infants (well-appearing, normal laboratory values) (Fielding-Singh, 4)

Most pathogens in blood cultures in febrile bacteremic infants ≤90 days will be identified within 24 hours of collection
- Time to positivity: 91% by 24 hours, 96% by 36 hours, 99% by 48 hours

Newer risk stratification strategies better at predicting “Invasive Bacterial Infection (IBI)” – see next slide
Recent Literature: New Algorithms

Validation of the “Step-by-Step” Approach in the Management of Young Febrile Infants

Borja Gomez, MD, Santiago Mintegi, MD, PhD, Silvia Bressan, MD, PhD, Liviana Da Dalt, MD, Alain Gervaix, MD, Laurence Lacroix, MD, on behalf of the European Group for Validation of the Step-by-Step Approach

Conclusion:
- CBC not very predictive
- ANC better
- PCT most useful

*But using a combination of these is best
Recent Literature: Bacterial Meningitis with Positive UA and Use of Procalcitonin

Rate of bacterial meningitis 0.44% in patients with positive urinalysis (2703 infants) vs 0.5% in patients with a normal urinalysis (10,032)

Additional references re prevalence of meningitis with a positive UA:
Recent Literature: New AAP Infant Fever Guidelines 2021!

Support of Current Practices:
• No LP if screening inflammatory markers are normal
• Discharge of patients w/neg cultures at 24-36 hrs if well appearing, neg cultures

New Practices:
• Do NOT use WBC as inflammatory marker, but rather use ANC. However, this must be used in combination with other inflammatory markers
• Procalcitonin >0.5 is best of independent predictors, however guidelines do not recommend using in isolation for decision-making
• Positive UA alone does not count as a positive inflammatory marker
• May discharge pt from ED on oral abx if pos UA but all inflammatory markers normal – CSF included
• Discharging at 24-36 hrs should include patients with UTI since they may be managed on oral abx
This is the Fever and Sepsis Evaluation in the Infant (29-60 days) Clinical Pathway.

We will be reviewing each component in the following slides.
All infants that are 29-60 days old and ≥37 weeks gestational age with a rectal temp ≥38°C should be included on the pathway, unless specific exclusion criteria exist.

Of note, this pathway is NOT meant for use for infants who are admitted to the NICU.
History and physical exam components are used to classify infant as “well” or “ill”, which will dictate management.

- Potential signs of an ill infant are listed
- Infants with HSV risk factors are also considered ill

Ill Infant (potential signs):
- Poor feeding
- Excessive sleeping
- Decreased responsiveness
- Inconsolability
- Respiratory distress
- Cyanosis
- Petechial rash
- Seizures
- Parental concern
- Provider concern

Risk Factors for HSV:
- Ill appearing infant (including hypothermia and severe respiratory distress)
- Seizure history
- Conjunctivitis
- Vesicles on skin exam
- Hepatosplenomegaly
- Elevated AST or ALT
- Thrombocytopenia
- CSF pleocytosis
- Negative CSF gram stain
- Interstitial pneumonitis
- Post-natal HSV contact

Maternal risk factors:
- Hx of maternal genital lesions at delivery
- Maternal fever at delivery
- Current/past sexual partners with hx of genital/oral HSV
- New sexual partner during pregnancy
- Maternal sores
- Risky sexual behavior
Well Infant:

Once infant is determined to be well, determine if they have abnormal inflammatory markers as below:

- Includes: blood and urine only
- May include: stool studies, CXR and viral studies as indicated
- Based upon recent literature, screening labs for well appearing infants are to include procalcitonin, CBC (to obtain ANC), urinalysis
- If there is no procalcitonin available, should obtain CRP

**Diagnostic Tests**
- Blood: CBC w/diff, procalcitonin, culture
- Urine: (cath) UA, culture

**Consider:**
- Stool BIOFIRE (if diarrhea)
- Chest X-ray (if significant respiratory signs and sx)
- Nasal RSV and Influenza PCR (if symptoms and late fall/winter season)

**Risk Factors for HSV:**
- Ill appearing infant (including hypothermia and severe respiratory distress)
- Seizure history
- Conjunctivitis
- Vesicles on skin exam
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**Maternal risk factors:**
- Hx of maternal genital lesions at delivery
- Maternal fever at delivery
- Current/past sexual partners with hx of genital/oral HSV
- New sexual partner during pregnancy
- Maternal sores
- Risky sexual behavior
If the infant has normal inflammatory markers, may discharge patient home:

- ANC ≤ 4000 or ≥ 500
- Procalcitonin < 0.5 ng/ml

If procalcitonin unavailable, may substitute following inflammatory markers:

- Fever ≤ 38.5°C
- CRP < 2 mg/dL
- ANC ≤ 4000 or ≥ 500

***Any abnormal inflammatory marker should lead to further workup***

If there is a positive UA, but otherwise normal inflammatory markers, may also discharge patient home with treatment for UTI:

- **Ceftriaxone IV/IM** 50 mg/kg in the ED
- RBUS in ED if able (otherwise, notify PCP to schedule as outpatient)
- Prescribe **Cephalexin PO** 75-100 mg/kg/day divided 4 times daily for 10-14 days

Discharge Instructions:

- Call PCP to inform of work-up
- PCP or ED follow up patient in 24 hours
- If barriers to follow up, consider placing in observation

If UTI:

(U/A with positive leukocyte esterase or nitrates, and/or > 5 WBC and bacteria)

- Ceftriaxone IV/IM 50 mg/kg
- RBUS in ED if able (otherwise, notify PCP to schedule as outpatient)
- Prescribe Cephalexin PO 75-100 mg/kg/day divided 4 times daily for 10-14 days

Diagnostic Tests

- Blood: CBC w/diff, procalcitonin, culture
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- Stool BIOFIRE (if diarrhea)
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Well Infant:

If the has abnormal inflammatory markers, they will be treated like an infant who is “ill”

***Any abnormal inflammatory marker should lead to further workup***

Abnormal inflammatory markers:
- ANC >4000 or <500
- Procalcitonin >0.5 ng/ml

If procalcitonin unavailable, may substitute following inflammatory markers:
- Fever >38.5°C
- CRP >2 mg/dL
- ANC > 4000 or <500
Ill Infant and/or well infants with abnormal inflammatory markers:

- A complete evaluation including blood, urine and CSF studies is recommended.

If risk factors for HSV infection:

- HSV studies per AAP Red Book

Consider additional studies as indicated by clinical scenario

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Diagnostic Tests

- **Blood:** CBC w/ diff, procalcitonin, culture, AST, ALT
- **Urine:** (cath) UA, culture
- **CSF:** culture, glucose, protein, cell count, gram stain
  - Add enterovirus PCR (if June-Oct)

If risk factors for HSV:

- **Blood:** HSV PCR
- **Skin:** HSV PCR (swab mouth, conjunctiva, rectum) AND HSV PCR of unroofed vesicles if present
- **CSF:** HSV PCR
- Place on contact precautions

Consider:

- Stool BIOFIRE (if diarrhea)
- Chest X-ray (if significant respiratory signs and sx; not required if exam consistent with bronchiolitis)
- Nasal RSV and Influenza PCR (if symptoms and late fall/winter season)
Ill Infant and/or well infants with abnormal inflammatory markers:

- Begin immediate empiric antimicrobials:
  - Ceftriaxone IV/IM
  - Vancomycin, if concern for meningitis
  - Acyclovir if risk factors for HSV

- Infant will be admitted to the hospital

Note: The pharmacy’s vancomycin protocol was updated in Feb 2021.

- All patients who have vancomycin IV ordered will be followed by the clinical pharmacist to help determine appropriate dosing parameters.
- Providers will order initial doses per pathway/order set and provide indication within the order.
- IV vancomycin dosing and recommended labs will be managed by pharmacy in conjunction with primary teams.

Abnormal Inflammatory Markers:

- ANC >4000 or <500*
- Procalcitonin >0.5 ng/ml
If procalcitonin unavailable, may substitute following Inflammatory Markers:

- Fever >38.5°C
- CRP >2 mg/dL
- ANC >4000 or <500*

Risk Factors for HSV:

- Ill appearing infant (including hypothermia and severe respiratory distress)
- Seizure history
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Diagnostic Tests:

- Blood: CBC w/diff, procalcitonin, culture, AST, ALT
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Consider:

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Ill Infant and/or well infants with abnormal inflammatory markers or risk factors for HSV:

• If a focal infection is identified, treat appropriately
• Consider Infectious Disease Consult if needed
• If UTI identified, may still d/c home at 24-36 hrs if well appearing and blood and CSF cultures are negative (do not need to wait for sensitivities)

• If no focal infection is identified, but the patient is not improving on empiric antimicrobials, further evaluation is needed

If UTI identified?
- May still d/c home at 24-36 hrs if well appearing and blood and CSF cultures are negative (do not need to wait for sensitivities)
- Consider Infectious Disease Consult
- If no focal infection is identified, but the patient is not improving on empiric antimicrobials, further evaluation is needed

If improving?
- No
- Yes

If focal infection identified?
- Treat as indicated
- Consider Infectious Disease Consult
- If UTI, may still d/c home at 24-36 hrs if well appearing and blood and CSF cultures are negative (do not need to wait for sensitivities)
If there is no focal infection and the patient is improving on empiric antimicrobials, the patient can be discharged when these discharge criteria are met.

**Discharge Criteria:**

- Infant well appearing, improving clinically and tolerating feeds well
- Blood, urine, CSF culture results negative after 36 hours for well appearing + high risk lab results
- Blood, urine, CSF culture results negative after 24 hours for well appearing + low risk lab results
- CSF HSV PCR negative
- No new symptoms of concern
- Family understands discharge instructions and ongoing infant needs
- Follow-up provider identified; discharge plan and close follow-up arranged
Clinical pathways helps standardize work up and treatment for this age group.
Workup and treatment is based on history, physical and risk stratification.
Using a group of more sensitive and specific inflammatory markers can help identify those patients at higher risk for bacterial infection.
Lumbar punctures are not universally indicated in this age group.
Newer literature shows isolated UTI with normal inflammatory markers in a well appearing infant is not a high risk condition that necessarily warrants hospitalization.
Shorter length of stay and earlier discontinuation of antibiotics (for hospitalized infants) is supported.
Quality Metrics

- Percentage of eligible patients treated per pathway
- Percentage of patients with order set usage
- Percentage of patients for whom recommendations for lumbar puncture followed
- Percentage of patients for whom recommendations regarding antimicrobials followed
- Average length of stay for ED patients
- Average length of stay for inpatient and observation patients (excluding those with positive cultures)
- Returns to ED within 2 days
Pathway Contacts

- Ilana Waynik, MD
  - Connecticut Children’s Pediatric Hospital Medicine
- Eric Hoppa, MD
  - Connecticut Children’s Emergency Department
References


About Connecticut Children’s Clinical Pathways Program

The Clinical Pathways Program at Connecticut Children’s aims to improve the quality of care our patients receive, across both ambulatory and acute care settings. We have implemented a standardized process for clinical pathway development and maintenance to ensure meaningful improvements to patient care as well as systematic continual improvement. Development of a clinical pathway includes a multidisciplinary team, which may include doctors, advanced practitioners, nurses, pharmacists, other specialists, and even patients/families. Each clinical pathway has a flow algorithm, an educational module for end-user education, associated order set(s) in the electronic medical record, and quality metrics that are evaluated regularly to measure the pathway’s effectiveness. Additionally, clinical pathways are reviewed annually and updated to ensure alignment with the most up to date evidence. These pathways serve as a guide for providers and do not replace clinical judgment.