Fever in a Patient with Sickle Cell Disease

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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.
Why is the pathway necessary?

- Fever is one of the most common chief complaints bringing patients with sickle cell disease to the Emergency Department at CT Children’s

- A fever in these patients may be the first subtle sign of a serious bacterial infection and necessitates prompt evaluation (including a laboratory work-up and empiric antibiotic therapy) even if another source of fever is identified

- This pathway provides:
  - Specific criteria to risk-stratify patients and determine who warrants inpatient admission versus outpatient management with close follow-up
  - Strict discharge criteria
  - Ability to appropriately divert patients who present with sepsis and/or acute chest syndrome
Objectives of Pathway

• To improve triage and initial management of fever in patients with sickle cell disease in the emergency department and outpatient settings, through consistent application of current best practice

• To decrease the time from initial presentation to first evaluation by a provider and administration of empiric antibiotic therapy

• To decrease the number of patients admitted to the hospital by appropriately discharging patients who can be managed outpatient with close follow-up
Patients with sickle cell disease are often functionally asplenic by age three years of age
  - Are at increased risk of severe bacterial infection, particularly encapsulated bacteria
  - The most notably pathogens include *S. pneumoniae*, as well as *H. influenzae*, *N. meningitidis*, and salmonellae

Although vaccinations and antibiotic prophylaxis has made bacteremia increasingly rare (rates of 0.8% or lower\(^1,8\)), the risk of overwhelming bacterial infection necessitates that infection be ruled out
This is the Fever in a Patient with Sickle Cell Disease Clinical Pathway.

This pathway spans outpatient clinic, emergency department, and inpatient care.

We will be reviewing each component in the following slides.
Inclusion and Exclusion criteria are clearly defined.

Those with Sickle Cell Disease are included while those with Sickle Cell Trait are excluded.

Patients with septic shock and MIS-C should be treated off of this pathway.
• If the patient has a CVL, blood cultures should be obtained from all lumens
  - Otherwise, peripheral blood cultures should be drawn

• Procalcitonin has been shown to be unaffected by vaso-occlusive disease in patients with SCD
  - This can help differentiate between fever due to infection vs inflammation
  - Of note, respiratory BIOFIRE is not routinely indicated

**CLINICAL PATHWAY:**
**Fever in a Patient with Sickle Cell Disease**

**If presents to ED:** Triage Level 2

**RN Evaluation:**
- Vitals, continuous pulse ox
- Blood culture (from all lumens of CVLs)
  - If no CVL, obtain peripheral culture
- CBC & Reticulocyte count & STAT procalcitonin
  - Hold purple top for Type & Screen, green top for BMP or LFTs
- Give Acetaminophen 15 mg/kg/dose q6hr (max 1000 mg/dose; max 75 mg/kg/day, not to exceed 4000 mg/day) if not received in past 4 hours and/or
  - Ibuprofen 10 mg/kg/dose q6hr (max 800 mg/dose), or Toradol IV 0.5 mg/kg/dose (max 30 mg/dose) q6hr, if not received in past 6 hours

**Provider Evaluation:**
- STAT: order antibiotics (see dosing below)
- Consider further diagnostic work-up based upon history and physical exam
  - CRP, chemistry, LFTs, Type & Screen, urinalysis, CXR (if concern for Acute Chest Syndrome); respiratory BIOFIRE not routinely indicated

**Provider Evaluation:**

- Ongoing fever/poor history/abnormal exam
- Discharge
- Re-evaluation
- Monitoring
- Oral antibiotics continued

- CRP level (may be divided by 2 or 3)
- CBC
- Chem panel
- LFT
- BMP
- BMP
- CXR
- STAT

**Note:** Patients with unremitting fever, end stage renal disease, or hepatic failure should be considered for hospitalization.

**Provider Education:**

- Acetaminophen: 15 mg/kg/dose q6hr (max 1000 mg/dose; max 75 mg/kg/day, not to exceed 4000 mg/day)
- Ibuprofen: 10 mg/kg/dose q6hr (max 800 mg/dose)
- Toradol: 0.5 mg/kg/dose q6hr (max 30 mg/dose)
- Acetaminophen is the preferred analgesic.

**CONTRACTS:**
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If there is concern for sepsis AND/OR suspicion for acute chest syndrome:

- The patient should be managed off-pathway.
- Proceed to Septic Shock Clinical Pathway or manage acute chest
- Notify the attending/fellow immediately
- Timely identification and management are important!
Antibiotics should be given within 1 hour of presentation.

All patients should receive empiric antibiotic therapy, even if the source of the fever has been identified, with additional appropriate treatment based on source.

Heme/Onc should be consulted to discuss all patients.

**Antibiotics:**

- **Ceftriaxone** 75 mg/kg IV (max 2 g/dose)
- If Cephalosporin allergy: **Levofoxacin IV:** 6 mo–<5 years old: 10 mg/kg/dose BID; ≥5 years old: 10 mg/kg/dose daily (max 750 mg/day)
- If ill appearing: add **Vancomycin IV:** <52 weeks PMA†/about <3 mo old: 15 mg/kg q8hr or as determined by pharmacy based on estimated AUC; ≥52 weeks PMA†/about ≥3 months old – 11 years old: 70 mg/kg/day q6hr; ≥12 yrs old: 60 mg/kg/day q8hr
- If concern for acute chest syndrome: add azithromycin 10 mg/kg on day 1 (max 500 mg/dose), then 5 mg/kg once daily on day 2-5 (max 250 mg/dose). If respiratory BIOFIRE was sent and negative for atypical organisms, discontinue azithromycin.

**Consults:**

- Call Heme/Onc to discuss all patients

†PMA (Post-Menstrual Age) = gestational age + postnatal age

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**CLINICAL PATHWAY:**

Fever in a Patient with Sickle Cell Disease

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**NO**

- Proceed to empiric antibiotics

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**YES**

- Is patient septic AND/OR suspicion for acute chest syndrome?

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**YES**

- Add appropriate antibiotics

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**NO**

- Discharge patient

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**Is patient septic AND/OR suspicion for acute chest syndrome?**

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**Antibiotics should be given within 1 hour of presentation**

- If source of infection identified, treat appropriately AND give antibiotics below.

**Ceftriaxone** 75 mg/kg IV (max 2 g/dose)

- If Cephalosporin allergy: **Levofoxacin IV:** 6 mo–<5 years old: 10 mg/kg/dose BID; ≥5 years old: 10 mg/kg/dose daily (max 750 mg/day)

- If ill appearing: add **Vancomycin IV:** <52 weeks PMA†/about <3 mo old: 15 mg/kg q8hr or as determined by pharmacy based on estimated AUC; ≥52 weeks PMA†/about ≥3 months old – 11 years old: 70 mg/kg/day q6hr; ≥12 yrs old: 60 mg/kg/day q8hr

- If concern for acute chest syndrome: add azithromycin 10 mg/kg on day 1 (max 500 mg/dose), then 5 mg/kg once daily on day 2-5 (max 250 mg/dose). If respiratory BIOFIRE was sent and negative for atypical organisms, discontinue azithromycin.

**Consults:**

- Call Heme/Onc to discuss all patients

†PMA (Post-Menstrual Age) = gestational age + postnatal age
• Ceftriaxone provides good coverage for the most common invasive organisms, including strep pneumo and H. influenzae

• If there is a cephalosporin allergy, levofloxacin can be used.
  • Note: dosing has been updated to be in line with Lexicomp and current susceptibility patterns

• If ill appearing, add vancomycin

• If concerns for acute chest syndrome, azithromycin should be added.

\[\text{Is patient septic AND/OR suspicion for acute chest syndrome?}\]

**Antibiotics:**

*Antibiotics should be given within 1 hour of presentation*

- **Ceftriaxone** 75 mg/kg IV (max 2 g/dose)
- If **Cephalosporin allergy**: **Levofloxacin** IV:
  - 6 mo - <5 years old: 10 mg/kg/dose BID; ≥5 years old: 10 mg/kg/dose daily (max 750 mg/day)
  - If ill appearing: add **Vancomycin** IV: <52 weeks PMA/ about <3 mo old: 15 mg/kg q8hr or as determined by pharmacy based on estimated AUC; ≥52 weeks PMA/ about ≥3 months old – 11 years old: 70 mg/kg/day div q6hr; ≥12 yrs old: 60 mg/kg/day div q8hr
  - If concern for acute chest syndrome: add azithromycin 10 mg/kg on day 1 (max 500 mg/dose), then 5 mg/kg once daily on day 2-5 (max 250 mg/dose). If respiratory BOFIRE was sent and negative for atypical organisms, discontinue azithromycin.

**Consults:**

- Call Heme/Onc to discuss all patients

\[\text{PMA (Post-Menstrual Age) = gestational age + postnatal age}\]
Patients who do **not** meet admission criteria can be discharged home after receiving empiric antibiotics

- Those who received ceftriaxone may be discharged home without additional antibiotics
- Those who received levofloxacin must be given a Rx for a 2nd dose to cover a total of 24 hours

- If the patient is on penicillin prophylaxis, they should continue taking it
- Outpatient follow up plans should be discussed with the on-call Heme/Onc attending
Patients who meet ANY ONE of the admission criteria must be admitted to the Heme/Onc service.

If the source of fever has been identified, treat based on infection source.

If the source has not been identified, continue with empiric antibiotics.

Note that patients who require penicillin prophylaxis can pause their prophylaxis while on inpatient antibiotics. It should be resumed once antibiotic therapy is completed.

**Admission Criteria:**
- <12 months old
- Hx of encapsulated bacteremia/sepsis
- WBC < 5,000 or > 30,000
- Platelet < 100,000
- Ill appearing
- Oxygen requirement
- Hypotension
- Poor perfusion
- New infiltrate on CXR
- Dehydration
- Concern for caregiver ability to care for patient

**Antibiotics:**
- Ceftriaxone IV 75 mg/kg/dose divided q12hr (max 2 g/dose)
- If Cephalosporin allergy:
  - Levofloxacin IV: 6 mo - <5 years old: 10 mg/kg/dose BID; ≥ 5 years old: 10 mg/kg/dose daily (max 750 mg/day)
  - If ill appearing:
    - Add Vancomycin IV: <52 weeks PMA/≥ about < 3 mo old: 15 mg/kg q8hr or as determined by pharmacy based on estimated AUC; ≥52 weeks PMA/≥ about 3 months old – 11 years old: 70 mg/kg/day div q6hr; ≥12 yrs old: 60 mg/kg/day div q8hr
    - Can discontinue if blood cultures negative x48 hours (even if still febrile)

- Note: Patients with severe sickle cell disease ≤ 5 yrs old (and those > 5 yrs old with hx of splenectomy or invasive pneumococcal disease) should be on penicillin prophylaxis. If patient is on prophylaxis, can pause prophylaxis while on antibiotics above. Resume prophylaxis once antibiotic therapy is completed.

**Lab work:**
- CBC & reticulocyte count & STAT procalcitonin q48hr (or sooner, if clinically indicated)
- If patient with persistent fever: blood cultures from all CVL lumens or peripheral blood culture q48hr

1PMA (Post-Menstrual Age) = gestational age + postnatal age
Once patient meets discharge criteria, they may be sent home with close follow up in place.

**Discharge criteria:**
Well-appearing and tolerating PO; negative blood cultures; outpatient follow up in place.
Review of Key Points

• Administration of antibiotics within 1 hour of presentation is very important

• If a source of fever is identified, give empiric antibiotics in addition to treating the source

• Patients who meet any of the admission criteria must be admitted to the Hematology-Oncology service
Quality Metrics

- Percentage of eligible patients treated per clinical pathway
- Length of time from arrival to ED/clinic to administration of antibiotics OR length of time from first fever documented, while inpatient, to administration of antibiotics
- Percentage of patients receiving appropriate antibiotic at correct dose
- Length of stay in ED/clinic (minutes) and hospital (days)
- Percentage of patients appropriately admitted to the hospital
Pathway Contacts

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  - Division of Hematology/Oncology
- Donna Boruchov, MD  
  - Division of Hematology/Oncology


About Connecticut Children’s Pathways Program

Clinical pathways guide the management of patients to optimize consistent use of evidence-based practice. Clinical pathways have been shown to improve guideline adherence and quality outcomes, while decreasing length of stay and cost. Here at Connecticut Children’s, our Clinical Pathways Program aims to deliver evidence-based, high value care to the greatest number of children in a diversity of patient settings. These pathways serve as a guide for providers and do not replace clinical judgment.