CLINICAL PATHWAY:
Fever in a Patient with Sickle Cell Disease

THIS PATHWAY SERVES AS A GUIDE AND DOES NOT REPLACE CLINICAL JUDGMENT.

Inclusion Criteria: >2 months of age with sickle cell disease (HgbS, HgbSC, HgbS beta thal) and temp ≥101° F (38.3° C)
Exclusion Criteria: ≤2 months old, sickle cell trait, signs of sepsis (see Septic Shock Pathway), clinical suspicion for Multi-System Inflammatory Syndrome in Children (see MIS-C Pathway)

Outpatient Clinic and Emergency Department Care

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 with differential, reticulocyte count
  - Hold purple top for Type & Screen, green top for BMP or LFT's
- 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

Is patient septic? — YES → Treat off-pathway. Proceed to Septic Shock Pathway and notify attending/fellow immediately.

NO

Antibiotics:

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

Send cultures before starting antibiotics, if possible.

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

- **Ceftriaxone** 75 mg/kg IV (max 2 g/dose) x 1 dose
- ***If anaphylaxis to cephalosporins:*** **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 non-anaphylactic reaction to any cephalosporin:* **Ampicillin** 200 mg/kg/day div q6hr (max 2 g/dose)
- ***If concern for sepsis:*** Refer to Septic Shock Pathway and consider adding **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 (max 3 g/day); ≥12 yrs old: 60 mg/kg/day div q8hr (max 3 g/day)
  - If acute kidney injury[2], substitute vancomycin with linezolid IV: <12 yrs old: 30 mg/kg/day div q8hr (max 600 mg/dose); ≥12 yrs old: 600 mg q12hr (if ≥12 yrs old and <45 kg: 20 mg/kg/day div q12hr, max 600 mg/dose)
- ***If concern for acute chest syndrome:*** add **azithromycin** 10 mg/kg on day 1 (max 500 mg/dose), and send respiratory BioFire. If respiratory BioFire negative, then discontinue azithromycin. If BioFire positive atypical organisms, then continue azithromycin 5 mg/kg/ once daily on day 2-5 (max 250 mg/dose). **Note: Do not need azithromycin if already on levofloxacin. Notify attending and order appropriate acute chest syndrome treatments.**

Consults:

- Call Heme/Onc to discuss all patients

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

[1]Admission Criteria:

- <12 months old
- Hx of encapsulated bacteremia/ sepsis
- WBC <5,000 or >30,000
- Platelet <100,000
- Ill appearing
- Oxygen requirement
- Hgb <6 g/dL or 2 g/dL below baseline
- Hypotension
- Poor perfusion
- New infiltrate on CXR
- Dehydration
- Concern for caregiver ability to care for patient

[2]Definition of Acute Kidney Injury

(It should be noted that this definition does not apply to children <1 year of age)

AKI is defined by having ***either***:

- At least a 50% increase in Scr above baseline* **and** new Scr ≥0.5 mg/dL **OR**
- An increase by 0.3 mg/dL from baseline*, **and** new Scr ≥0.5 mg/dL

**If a baseline creatinine is unknown, estimate baseline Cr using the Schwartz Calculation (baseline creatinine = (0.413 * height cm)/120 GFR). For patients with Chronic Kidney Disease (CKD), use the CKiD U25 Calculator.*

Meets admission criteria[1]? — NO → **Discharge after antibiotics administered**

- *If source of infection identified:* treat appropriately for infection
- *If ceftriaxone given prior to discharge*: no additional antibiotics are needed unless localized infection identified [the blood culture will not yet be resulted]
- *If received **Levofloxacin** x1 dose prior to discharge*: give prescription for 2nd dose 12 hours later (see above for dosing – IV and PO dosing are equal)
- Continue penicillin prophylaxis (if taking)
- Outpatient follow up plan discussed with on-call Heme/Onc attending

YES

Inpatient Care

Admit to Hematology/Oncology Service

If source of infection identified, treat appropriately. Otherwise, continue antibiotics below.

Antibiotics:

- **Ceftriaxone** 75 mg/kg/day IV divided q12hr (max 2 g/dose)
  - *If anaphylaxis to cephalosporins:* **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 non-anaphylactic reaction to any cephalosporin:* **Ampicillin** 200 mg/kg/day div q6h (max 2 g/dose)
  - *If concern for sepsis:* treat off pathway *and* refer to **Septic Shock Pathway** and consider adding **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
- Note: Patients with 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.
- If blood cultures are negative at 36 hours, reassess clinical status and discuss ongoing need for antibiotics

Repeat Labs:

- CBC with differential, reticulocyte count, CBC q48hr (or sooner, if clinically indicated)
- *If patient clinically unstable or concern for sepsis*: repeat blood cultures ONCE from all CVL lumens or peripheral blood culture 24 hours after initial blood culture. If persistently febrile, consult Infectious Diseases

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

Discharge criteria: Well-appearing and tolerating PO; negative blood cultures; outpatient follow up in place

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