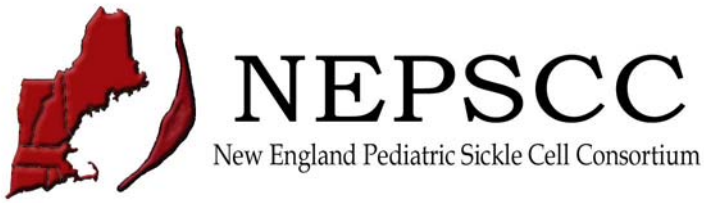
New England Pediatric Sickle Cell Consortium



Evaluation and Management of Fever in Pediatric Patients with Sickle Cell Disease

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Disclaimer Statement:

- Hospital clinical pathways are designed to assist clinicians by providing an analytical framework for the diagnosis and treatment of specific medical problems. They may be used for patient education and to assist in planning future care. They are not intended to replace a physician's judgment or to establish a protocol for all patients with a particular condition. The ultimate decision regarding the care of any patient should be made in respect to the individual circumstances presented by the patient.
- Any specific medications and dosing must always be reviewed carefully for each patient in view of any history of drug allergy or adverse reactions.
- This document was based on available research and clinical experience at time of its compilation.
- The following protocol is a regional guideline, and may be adapted by individual institutions as needed.

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FEVER

Inclusion:

- Children and adolescents > 3 months of age with sickle cell disease (Hb S with variant Hb)
- Fever > 101.5°F /38.5°C documented or by history.

I. Introduction

- Children and adolescents with sickle cell disease (SCD) are prone to invasive infections with encapsulated organisms.[1] They should be assumed to be functionally asplenic, even if their spleens have not been surgically removed.
- Aggressive evaluation and empiric treatment is necessary to reduce both mortality and morbidity for febrile sickle cell patients. The goal of rapid triage and parenteral antibiotic coverage is to reduce the occurrence of sepsis.
- Pneumococcal sepsis is the leading cause of mortality in younger children with sickle cell anemia. Pulmonary complications, including those from infections, are the leading cause of mortality for adolescents and adults.
- Antibiotic prophylaxis from infancy until at least 5 years of age decreases the risk of bacteremia. [2]
- Vaccine compliance with pneumococcal conjugate (PCV7, Prevnar™) and pneumococcal polysaccharide (PPV23, Pneumovax™) vaccines also decreases risk of bacteremia.[3] The AAP Red Book recommends meningococcal polysaccharide vaccine be administered to asplenic children 2 years of age and older. [4] There is not consensus among providers regarding meningococcal vaccine, however most would agree to administration prior to splenectomy or residential living.
- Even those patients compliant with antibiotic prophylaxis or over age 5 years should be considered high-risk for bacteremia, osteomyelitis, acute chest syndrome and overwhelming sepsis.
- Children with an obvious source of infection (otitis, gastroenteritis) should still receive full evaluation and treatment.
- Patients with acute chest syndrome may not initially present with respiratory symptoms, but may subsequently develop significant respiratory compromise. [5, 6] Therefore most febrile sickle cell patients should have a chest x-ray.
- In continuously monitored laboratory systems positive blood cultures for pathogens are available in an average of less than 18 hours[7]. Practitioner must be familiar with their local microbiology lab capabilities before determining adequate length of empiric therapy.

II. Evaluation: Rapid Triage and Assessment

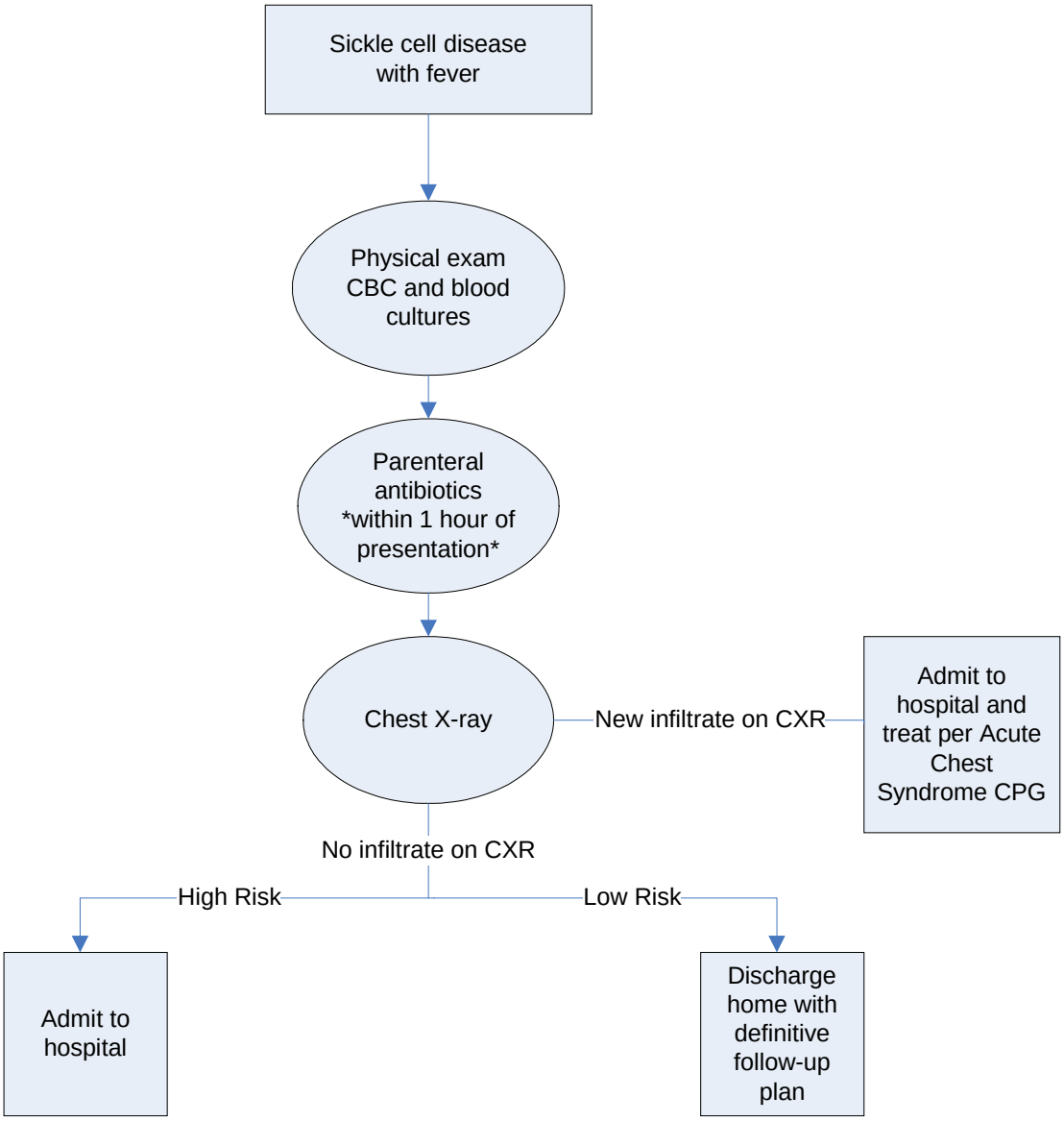
DO NOT DELAY ANTIBIOTICS. GIVE IMMEDIATELY AFTER OBTAINING BLOOD CULTURES, NO LONGER THAN 1 HOUR AFTER PRESENTATION TO ED/CLINIC.

- Vital signs including room air pulse oximetry.
- History and physical examination.
- Assessment of medication allergies.
- Placement of peripheral IV or access of central venous access device for CBC with differential, reticulocyte count, blood cultures, and type & screen.
  - If patient has central line or implanted port, blood cultures must be drawn off this line and peripheral cultures are not routinely required.
- Consider room air ABG if pulse oximetry is not consistent with clinical presentation.
- Chest X-ray - PA and lateral
  - CXR required of most patients, especially those with tachypnea, cough, hypoxemia, thoracic pain, and history of asthma or history of ACS. In some institutions all febrile sickle cell patients undergo CXR.
- Urinalysis and urine culture required for all males <6 months and females <2 years.
- Throat culture, LP, stool specimens, respiratory studies (viral panel if URI symptoms in children under three years between November and April) and other studies, as clinically indicated.

III. Management: Parenteral Antibiotics

- All patients require parenteral coverage for the first 24 hours.
- Those with an infiltrate on CXR also need a macrolide added to empiric antibiotics and admission as per CPG for ACS.
- Ceftriaxone (Rocephin™) [8, 9] 50 mg/kg IV (may use IM if no IV access) to a max of 1-2 grams/day per institutional guidelines. Use meningitis dosing of 100mg/kg q12 hours BID to a max of 2 grams/day if CNS infection is suspected.
  - If new infiltrate on CXR, add macrolide (see Acute Chest Syndrome CPG).
  - If a CVL is present, must administer antibiotics via this route.
- Options for patients allergic to Ceftriaxone (Rocephin™)
  - Vancomycin for sepsis, meningitis or toxic appearance. Consider in patients with central line/port and history or infection with resistant organisms. [10, 11]
  - Other antibiotic to complete coverage for 1st 24 hours. Possibilities include:
    - Azithromycin
    - Clindamycin
    - Quinolones (Gatafloxacin, Levofloxacin)

ALL PATIENTS MUST BE REVIEWED WITH HEMATOLOGY STAFF PRIOR TO DISPOSITION


Sickle cell disease with fever
Physical exam CBC and blood cultures
Parenteral antibiotics *within 1 hour of presentation*
Chest X-ray
New infiltrate on CXR
Admit to hospital and treat per Acute Chest Syndrome CPG
No infiltrate on CXR
High Risk
Low Risk
Admit to hospital
Discharge home with definitive follow-up plan

IV. Disposition

A. High Risk:

1. Emergency Room/Outpatient Disposition [12, 13]

Consider admission for inpatient management if **any** of the following high-risk criteria are present:

- Age < 6 months
- Constitutional Findings
  - Toxic appearance, concern for sepsis
  - Hypotension or poor perfusion
  - History of previous infection with resistant organism
  - Unable to maintain oral hydration
- New onset of abnormal neurological findings (See Stroke CPG)
- Respiratory Findings
  - New hypoxia (Room Air O2 sat > 3% points below baseline, or <92% if baseline not known)
  - New pulmonary infiltrate on CXR (See Acute Chest Syndrome CPG)
  - RAD exacerbation
- Hematological Findings
  - Hct ≤18% or ≥ 5% points below baseline
- Other
  - History of non-compliance with medical care or keeping appointments.
  - Poor likelihood of outpatient follow-up (e.g. no phone, no transportation).
  - Known to have missing / delayed immunizations (Prevnar™, Pneumovax™, Hib).
  - Under age 5 and not compliant with antibiotic prophylaxis.
  - Increase in spleen size suggestive of evolving splenic sequestration.
  - Multiple ED/Clinic visits for same episode of illness.
  - Unable to receive initial 24 hours of coverage from single dose of medication due to allergies or use of Vancomycin for other reason.

2. Inpatient Management [See individual institutional protocol for admission order set]

- Ensure adequate parenteral antibiotic coverage for the 1st 24 hours. Hold antibiotic prophylaxis while on parenteral antibiotics. Patient does not necessarily need to remain in the hospital for the full 24 hours if a longer acting antibiotic has been administered.
- If new CXR infiltrate add macrolide (See Acute Chest Syndrome CPG).
- Supportive care
  - Correct fluid deficits then IV + PO at 100-125% maintenance. Avoid over hydration, especially on older adolescents and patients with history of CHF.
  - O_2 only for documented hypoxemia or respiratory distress. Consider ABG for new hypoxemia.
  - Treat other complications as appropriate (VOC, splenomegaly).
  - Isolation precautions as indicated if any concern of aplastic crisis (Parvovirus B19)
  - Aggressive encouragement of ambulation / activity.
  - Incentive spirometry 10x / hour
- Additional testing:
  - CXR for any respiratory deterioration or drop on pulse oximetry
  - Consider CBC with differential and reticulocyte count 24 hours after admission if labs below baseline from ED or if clinical concern.
  - If fever recurs re culture only if unsure of CVL sterility or if clinical concern of ongoing sepsis.
- If source identified, treat appropriately.

- If blood culture positive for pneumococcus, obtain CXR.
- If blood culture positive for salmonella species or staphylococcus aureus, obtain bone scan.
- If blood culture positive for staphylococcus non-aureus, and patient has indwelling CVL/port, add vancomycin and consider echocardiogram.
- If osteomyelitis of a concern (ongoing fever, persistent focal pain) consider Orthopedics consultation for invasive diagnostics.
- On discharge complete full course of antibiotics for patients with positive blood culture or focus of infection (e.g. acute chest syndrome/pneumonia, osteomyelitis, strep throat)

B. Low Risk: Consider discharge home after receiving antibiotic if no admission criteria are met.
All Patients must be observed for a minimum of one hour following antibiotics.

- Instructions to page hematology provider or return immediately for symptoms of worsening illness, including:
  - Temperature > 103F (39.4C) or if fevers persist after 48 hours
  - Increased respiratory symptoms, and difficulty breathing
  - Dehydration / Reduced oral intake / Increased losses.
  - Lethargy
  - Pain
- Instructions given re: use of antipyretics and need for PO fluids
- Discharge with clear instructions for the next day's follow up either in ED, clinic or by phone
- Identify practitioner to check all cultures at 24 hours

V. REFERENCES:

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