Fever in a Patient with Sickle Cell Disease

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Connecticut Children's

MAGNET RECOGNIZED

BEST CHILDREN'S HOSPITAL

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

Background

- 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[2]
- 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.

CLINICAL PATHWAY:

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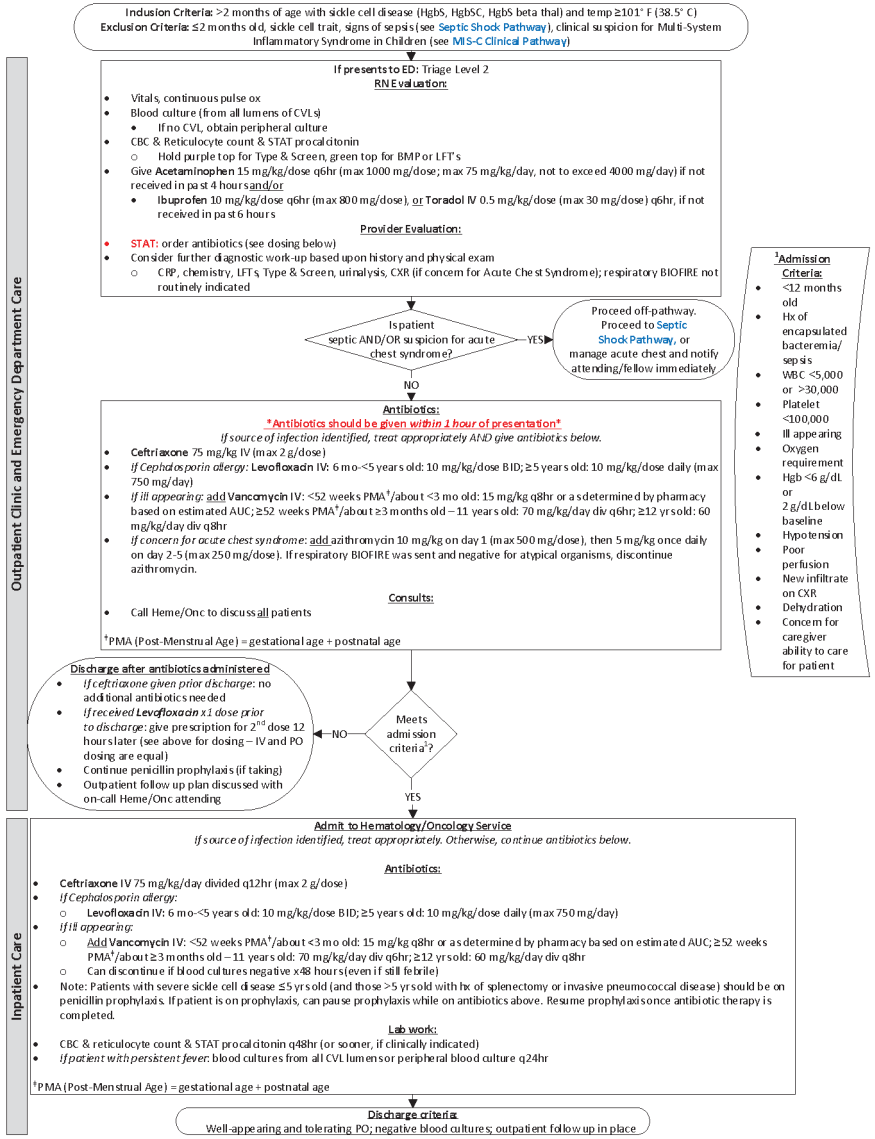
THIS PATHWAY SERVES AS A GUIDE AND DOES NOT REPLACE CLINICAL JUDGMENT.



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- 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.

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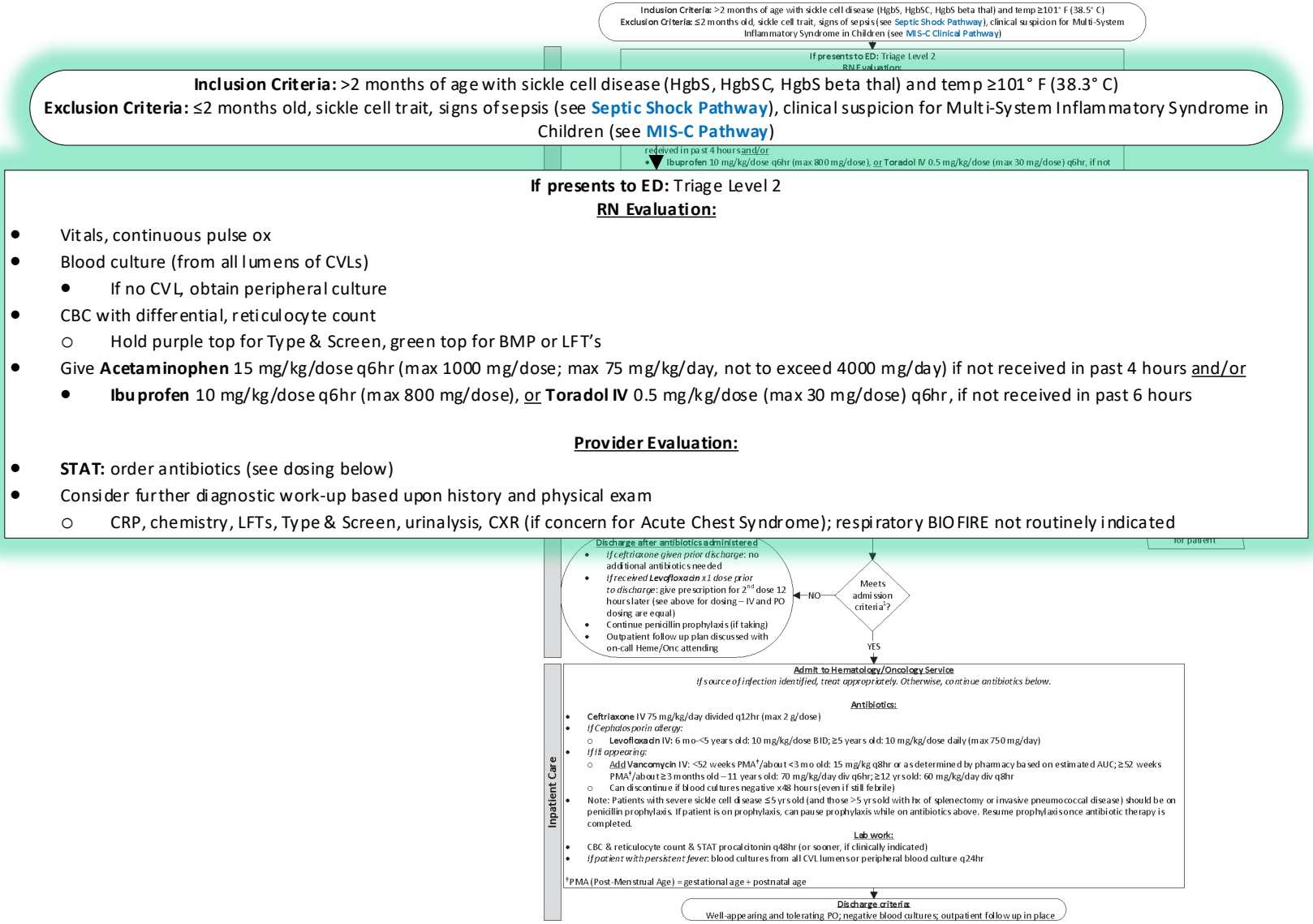

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If presents to ED: Triage Level 2

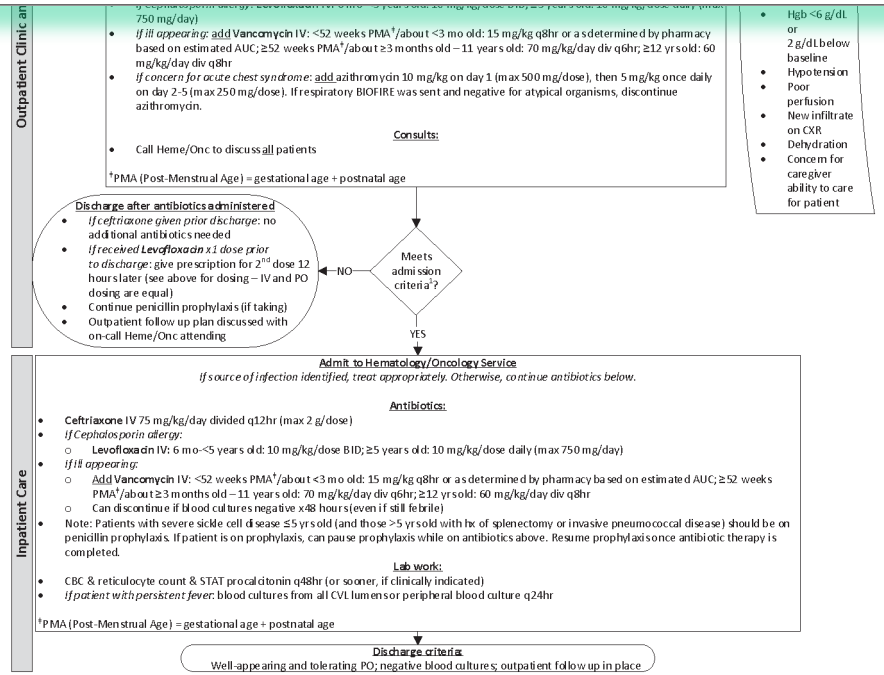
RN Evaluation:

- 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

- If the patient has a CVL, blood cultures should be obtained from all lumens
  - Otherwise, peripheral blood cultures should be drawn
- Of note, respiratory BIOFIRE is not routinely indicated



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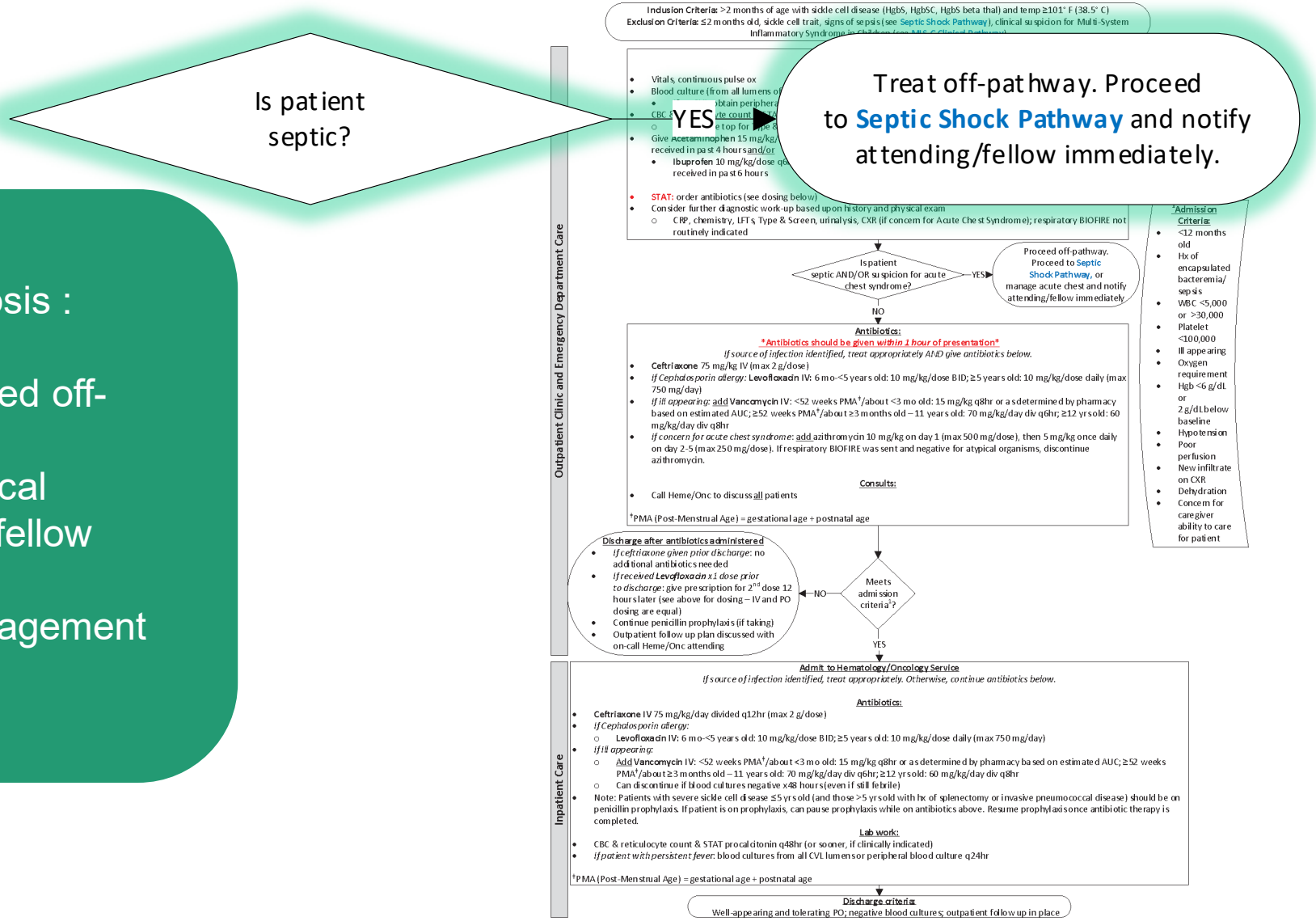
If there is concern for sepsis :

- The patient should be managed off-pathway
- Proceed to Septic Shock clinical pathway Notify the attending/fellow immediately
- Timely identification and management are important!



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If there is no suspicion of septic, the patients can proceed with this pathway

- **Antibiotics should be given within 1 hour of presentation**
- **If possible, ensure blood cultures collected prior to antibiotic administration**
- All patients should receive empiric antibiotic therapy, **even if the source of the fever has been identified**, with additional appropriate treatment based on infection source
- Heme/Onc should be consulted to discuss **all** patients

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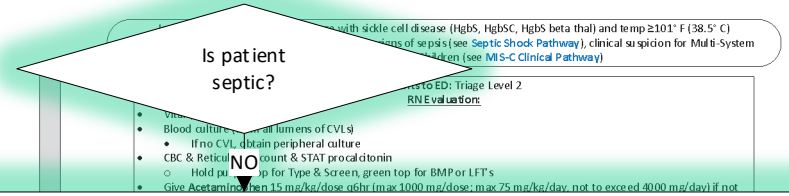


Antibiotics:

Antibiotics should be given *within 1 hour* of presentation

Send cultures before starting antibiotics, if possible.

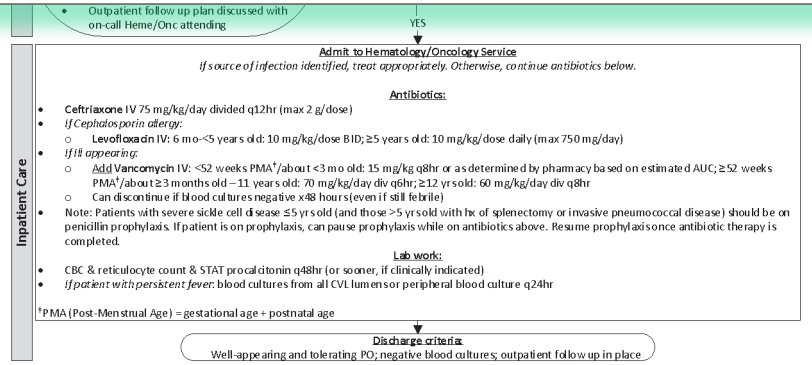
If source of infection identified, treat appropriately AND give antibiotics below.

- **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 renal dysfunction present, 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



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- Ceftriaxone provides good coverage for the most common invasive organisms, including S. pneumococcus and H. influenza
- If there is anaphylaxis to cephalosporins, levofloxacin can be used
- For non-anaphylactic reaction to cephalosporins, may use ampicillin
- If concern for sepsis, add vancomycin
- Antibiotics for acute chest syndrome (ACS) are listed here as well as instructions to notify attending and order appropriate ACS treatments

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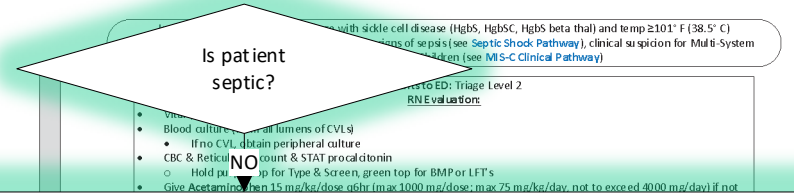

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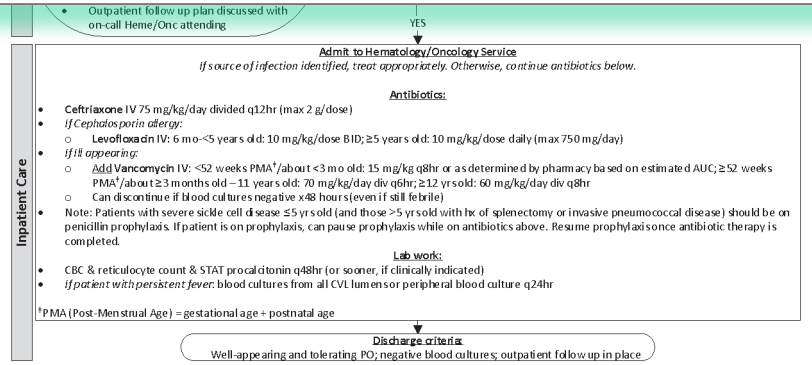

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- Patients who do **not** meet admission criteria can be discharged home after receiving empiric antibiotics
  - Those who received ceftriaxone may be discharged home without additional antibiotics
  - Those who received levofloxacin must be given an 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

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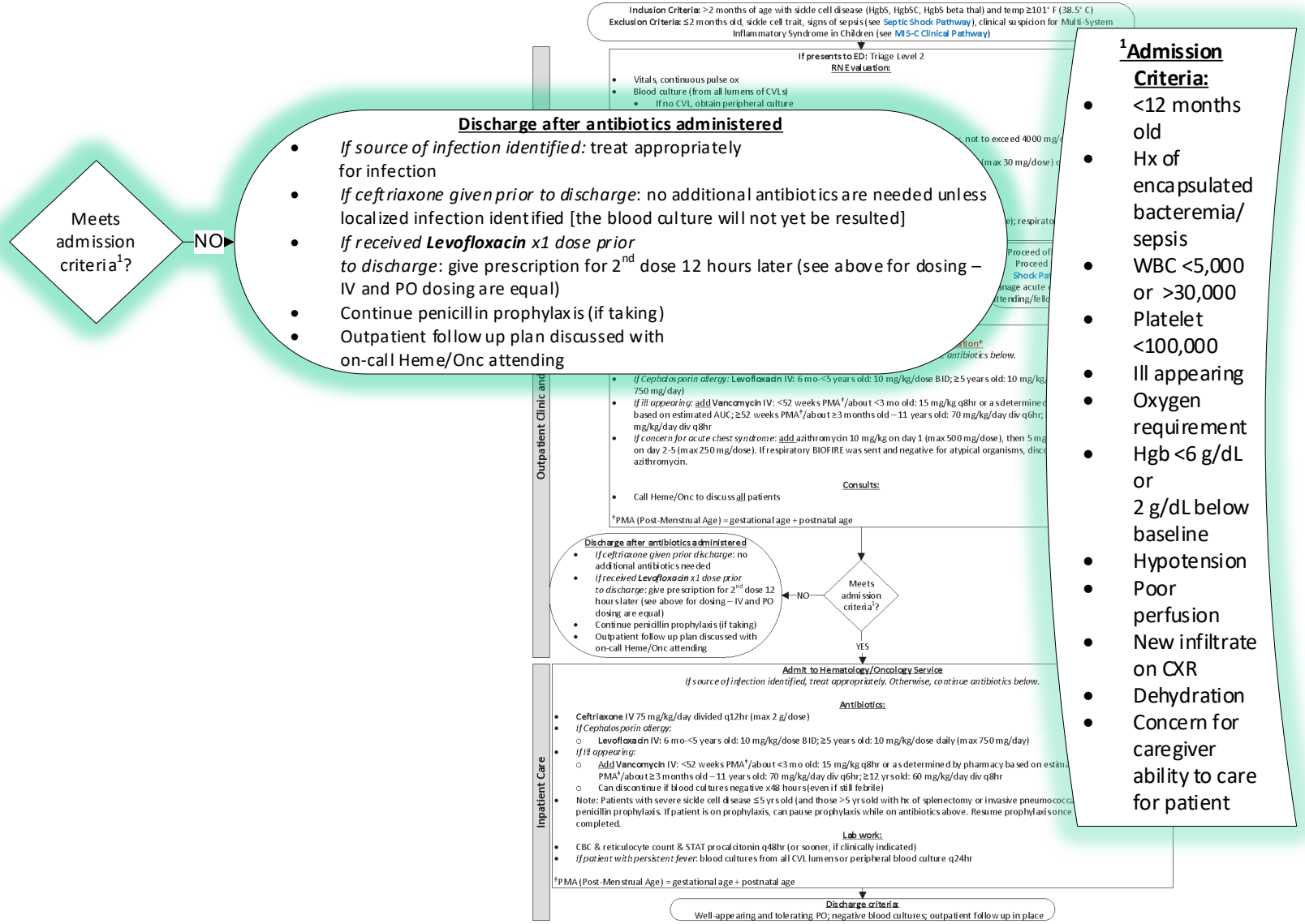

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- Patients who meet ANY ONE of the admission criteria must be admitted to the Heme/Onc service
- If the source of fever has been identified, treat based on infection source
- If the source not identified, continue empiric antibiotics
- Patients who require penicillin prophylaxis can pause their prophylaxis while on inpatient antibiotics and resumed once antibiotic therapy is completed.
- If blood cultures are negative at 36 hours, reassess clinical status and discuss ongoing need for antibiotics
- If 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

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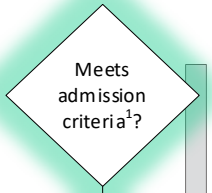

Inclusion Criteria: >2 months of age with sickle cell disease (HgbS, HgbSC, HgbS beta thal) and temp ≥101° F (38.5° C)
Exclusion Criteria: ≤2 months old, sickle cell trait, signs of sepsis (see Septic Shock Pathway), clinical suspicion for Multi-System Inflammatory Syndrome in Children (see MIS-C Clinical Pathway)

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 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

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

Inpatient Care

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

Antibiotics:

- **Ceftriaxone** IV 75 mg/kg/day 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 q24hr

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

[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

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Once patient meets discharge criteria, they may be sent home with close follow up in place

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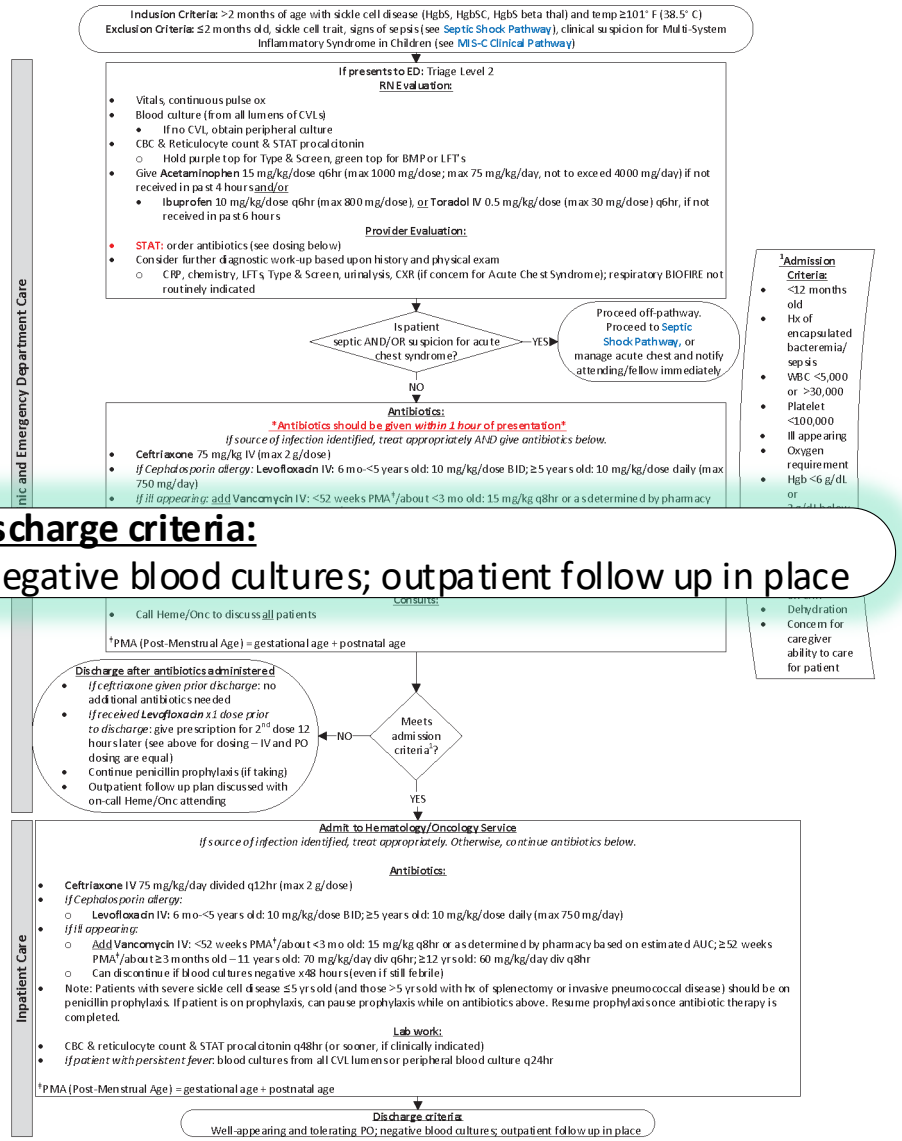

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Review of Key Points

- 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
- If blood cultures are negative at 36 hours, reassess clinical status and discuss ongoing need for antibiotics

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

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

References

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5. Loberger J, Polley K. Improving the Time to Antibiotics in Febrile Children with Sickle Cell Disease in the Emergency Department. *Pediatrics*. 2018;141(1).
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Thank You!

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.