INCLUSION CRITERIA (*All of the following*):

- Receiving treatment for cancer (within the preceding 12 months) or any time post stem cell transplantation
- Temperature (taken by any method) ≥ 100.4ºF (>38ºC) within the preceding 24 hrs **OR** Clinical concern for sepsis, pneumonia or meningitis, regardless of temperature
- Absolute Neutrophil Count (ANC) known or suspected to be <1000/μL

INITIAL APPROACH:

1. **Expedited Triage process:**
   - Clinical assessment
   - Vitals including temperature and pulse oximetry. Note: No rectal temperatures.

2. **STAT Collection:**
   - CBC with manual differential
   - History (esp. last chemotherapy or radiation therapy, central line, new symptoms)
   - Physical Examination (esp. lungs, abdomen, skin, perirectal area)
   - Blood culture (at least 3mL from each lumen of central line; use Adult culture bottles for patients weighing ≥ 40kg). Collect peripheral blood culture if unable to obtain adequate volume from central line.
   - Draw/hold tubes for type/cross, biochemistries, CRP if possible, without 2nd needle stick
   - Urinalysis and culture only if clinically indicated
   - CXR (PA+lateral) only for active cough or lung findings on examination.
   - Stool for C. difficile, if diarrhea is present

3. **Frequent vital signs**, as directed by level of illness

4. **Notify Pediatric Hematology attending or NP immediately if changes** in VS or deteriorating consciousness level

5. **Administer antibiotics *within 1 hour of arrival*;** do *not* wait for laboratory results.
   - If ANC >100 or unknown: Ceftriaxone 50 mg /kg IV (per weight-based dosing Table 5, page 5)
   - If ANC <100: Cefepime 50 mg/kg/dose (Maximum 2000 mg/dose) every 8 hours
   - if allergic to cephalosporins,consider Levofloxacin (per age and weight-based dosing Table 6, page5)
   - if allergic to cephalosporins, but without anaphylaxis, consider Ampicillin 100 mg/kg/dose q6 hours (Max 2000mg/dose)

6. **Risk-based Disposition** (See Table 1, page 2)

Table 1. DISPOSITION by RISK CATEGORY

***Note*: Presence of a central venous catheter is NOT considered an automatic indication for hospital admission.**

HIGH RISK (any High Risk features, Table 2)	LOW RISK (all others)
• **Admit** to Pediatric Hematology Oncology Service • See Inpatient Management Guidelines (Table 3)	• Arrange **follow up** for re-evaluation in 12 to 24 hours • **Observe** 1-2 hours post antibiotics • **Discharge** to home • **See** Outpatient Management Guidelines (Table 4)

Table 2. High Risk Criteria -- *ANY of the following:*

History
- Toxic appearing, rigors, severe abdominal pain, or clinically unstable
- Age < 12 months
- Persistent fever >72 hours despite outpatient antibiotic management
- Acute Leukemia (i.e. AML or ALL), not in remission (e.g still in Induction phase or in active relapse).
- Stem cell transplantation within the past 12 months, OR on treatment for chronic Graft vs Host Disease (GvHD)
- Concurrent organ dysfunction (e.g pancreatitis) or comorbidity (e.g. uncontrolled diabetes)
- Conditions preceding cancer diagnosis with increased risk of severe infection (e.g. Trisomy 21, immunodeficiency)
- Mucositis interfering with oral intake
- Systemic corticosteroid course > 10 days in the past month
- Currently enrolled on Phase 1 clinical trial, with treatment < 30 days prior to presentation

Physical Examination
- Temperature > 103°F (≥ 39.5°C)
- Evidence of significant localized infection (tunnel catheter infection, perirectal abscess, cellulitis)

Laboratory Parameters
- Absolute neutrophil count < 100/μL
- Anticipated duration of neutropenia ≥ 7 days
- Platelets < 10K/μL
- Hemoglobin < 5gm/dL

Social Factors raising concerns about ability to follow up within 24 hours
- Prolonged delay (e.g. > 12 hours) in initial contact and/or seeking medical care after the onset of fever
- No phone
- Uncertain transportation, including excessive distance from hospital
- Frequent missed appointments
- Prior nonadherence with medical advice

Table 3. Suggested Inpatient Management Guidelines:

1. Initial Management
   - Admit to Pediatric Oncology Service
   - Continue IV Cefepime 50mg/kg/dose (maximum 2000 mg/dose)) q8H.
   - Daily evaluation of symptoms and physical findings
   - Monitor blood counts for ANC recovery
   - Daily Blood culture while febrile for up to the first 3 days of fever
   - Acetaminophen may be administered for fever, *if the patient is uncomfortable due to fever*.

2. Re-evaluate antimicrobial coverage
   - Adjust antimicrobial coverage for any positive cultures
   - Consider Vancomycin for patients with expected gram positive infection (20 mg/kg/dose, maximum 1000 mg/dose, q6H)
   - Consider adding an aminoglycoside for double gram negative coverage if hemodynamically unstable (e.g. gentamicin 7.5 mg/kg/dose q24H)
   - Consider piperacillin/tazobactam for suspected perirectal abcess or typhlitis (75 mg of piperacillin /kg/dose; max 3000 mg piperacillin/dose; q6H).
   - Consider metronidazole for suspected perirectal abcess or typhlitis (10 mg/kg/dose, maximum 500 mg/dose, q8H).
   - Consider micafungin for patients with known prior fungal infection or severe mucositis (2 mg/kg/dose; maximum 100 mg; q24H)
   - Consider stopping vancomycin and/or aminoglycoside after 48 hours, if afebrile and clinically stable with negative blood cultures

3. Management of persistent fever (>3-5 days) or Recurrent fever after 3 days of antibiotics
   - Thorough reevaluation including history and physical examination
   - Repeat blood culture, with fungal cultures if fever is recurrent (new fever after 24 hours afebrile).
   - Consider fungal assays (T2 assay for candida; fungitell)
   - Start empiric antifungal therapy (e.g. liposomal amphotericin 3-5 mg/kg/dose IV q24h or micafungin 2 mg/kg/dose, max 100 mg, q24h)
   - Consider imaging studies for occult infection:
     - CT Chest abdomen and pelvis
     - CT sinuses if symptoms or physical findings suggest sinusitis
     - CT head if mental status changes
     - Echocardiogram
   - Consider Lumbar puncture for symptoms or signs of meningitis
   - Consider Ophthalmology evaluation, looking for fungal infection

4. Discharge criteria
   - Afebrile > 24 hours
   - ANC $\geq$ 150 /μL and rising
   - No signs of active infection
   - No positive blood cultures
   - Clinically well-appearing

Table 4. Suggested Outpatient Management Guidelines:

Day 2 re-evaluation: History and Physical Examination**.** CBC, diff, and blood cultures *if febrile*.

- If any High Risk features (see Table 2) are present, ADMIT.
- If ANC < 500/µL, give second dose of antibiotics, *even if afebrile;* arrange for Day 3 follow up visit.
- If ANC ≥ 500/µL:

  If fever has continued > 12 hours after first dose, give second dose of antibiotics; arrange Day 3 follow up visit.

  If afebrile, encourage family to call if fever recurs; return at next scheduled visit.

Day 3 re-evaluation: History and Physical Examination**.** CBC, diff, and blood cultures *if febrile*.

- If any High Risk features (see Table 2) are present, ADMIT.
- If ANC < 500/µL, give third dose of antibiotics, *even if afebrile*.

  Encourage family to call if fever recurs

  Follow-up at next scheduled visit
- If ANC ≥ 500/µL:

  If fever has continued > 12 hours after second dose, give third dose of antibiotics.

  If afebrile, encourage family to call if fever recurs; return at next scheduled visit.

Day 4:

- If any High Risk features (see Table 2) are present, ADMIT.
- If fever has persisted > 72 hours, ADMIT.

Table 5. Ceftriaxone Dosing Table

Typical dosing is 50-75 mg/kg given IV or IM once daily.

Patient Weight	Recommended Ceftriaxone Dose
< 15kg	50 mg/kg/dose, once daily
15kg to 20kg	1000 mg, once daily
> 20kg to < 30 kg	1500 mg, once daily
≥ 30kg	2000 mg, once daily

Table 6. Levofloxacin Dosing Table

Typical dosing is 8-10mg/kg/dose, IV or PO,
given once daily for children ≥ 5 years old, twice daily for children < 5 years old.

Patient Age	Weight	Recommended Levofloxacin Dose
< 5 years	< 47 kg	8 mg/kg/dose, twice daily
	≥ 47 kg	375 mg/dose, twice daily
≥ 5 years	< 50 kg	8 mg/kg/dose, once daily
	50 kg to 64 kg	500 mg daily
	≥ 64 kg	750 mg daily

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