HemOnc BMT Suspected Infection: Emergency Department v10.0

Approval & Citation

Inclusion Criteria
- Any Hematology/Oncology/BMT patient with concern for infection
- Fever (Temp ≥ 38.3°C or greater than 38°C for more than 1 hour) AND
- Recent Myelosuppressive chemotherapy with neutropenia (defined as ANC <2000/mm^3 or dropping ANC). OR presumed/functional neutropenia as determined by the HemOnc/ BMT provider.

Exclusion Criteria
- Benign Hematology Condition
- Sickle Cell Anemia
- Under 1 month old

Summary of Version Changes
- Signs & Symptoms of Sepsis
- Hypotension (MAP ≤ 5th percentile for age)
- Tachycardia
- Poor perfusion
- Reduced urine output
- Tachypnea/ new oxygen requirement
- Mental status changes

Communication Specialist: Prompt the HemOnc/ BMT Provider for the following information

- HemOnc:
  - Is ANC expected to be low (i.e. should patient be on pathway and receive antibiotics before ANC back)?
  - Which empiric antibiotics should be given (see below)?
  - Remind family to apply EMLA to port
- BMT:
  - Is the patient on immunosuppressive therapy?
  - Does the patient have an “Individualized Antibiotic Plan?” If not, which antibiotics should be given.

Are There Signs & Symptoms of Evolving Sepsis?

- ED Sepsis Score of 3 or greater AND provider concern for sepsis / septic shock
- OR Any ill appearing HemOnc/BMT patient

Labs (Do not delay blood cultures if family has not applied EMLA)
- Rapid Neutrophil Count
- Blood cultures: aerobic, anaerobic, fungal from all lumens of central venous catheter
- Other diagnostic tests as clinically indicated
  - Urinalysis and culture: clean catch NO catheterization
  - Rapid Respiratory Virus PCR
  - Chest X-ray

Administer Empiric Antimicrobials

- “Do not delay first dose for any diagnostic evaluations with the exception of blood cultures
- BMT
  - Refer to “INDIVIDUALIZED ANTIBIOTIC PLAN” in CIS “Care Plan” folder.
  - OR if no individualized antibiotic plan present in CIS:
    - Start Meropenem
- HemOnc
  - Start Cefazidime
  - OR, Cefepime for patients with AML, infant ALL, relapsed ALL, history of s. viridans or cefazidime allergy
  - OR, Meropenem for patients allergic to non-Cefazidime 3rd generation cephalosporins
  - Consider history of resistant organisms

Are There Signs & Symptoms of Evolving Sepsis?

No

No

Empiric only

Empiric plus Clindamycin^1 or Metronidazole^2

Empiric plus Clindamycin^3 or Vancomycin^4

Suspected intra-abdominal OR perineal infection?

YES

NO

Skin infection OR severe mucositis?

YES

NO

Assess labs and clinical status. Monitor VS every 15 min until 60 minutes after completion of empiric antibiotic.

Are There Signs & Symptoms of Evolving Sepsis?

No

ANC > 200 AND well-appearing?

No

YES

Off Pathway

Off Pathway

Off Pathway

Off Pathway

Yes:
- Discuss discharge from ED with HemOnc Provider
- *Note: BMT patients almost always require admission; Discuss with BMT provider

 Activate ED Suspected Septic Shock Pathway

Do not delay fluid resuscitation!

For questions concerning this pathway, please contact
HemOncBMTSuspectedInfection@seattlechildrens.org

Seattle Children's Hospital Research Foundation

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Last Updated: September 2020
Next Expected Review: November 2020
HemOnc BMT Suspected Infection: Clinic v10.0

Approval & Citation

ANY ill-appearing HO/BMT patient should receive prompt ANTIBIOTICS WITHIN 1 HOUR & evaluation for sepsis, regardless of fever or ANC

Start antibiotics within 1 hour of arrival

Inclusion Criteria
- Any Hematology/Oncology/BMT patient with concern for infection OR
- Fever (Temp ≥ 38.3°C, or greater than 38°C for more than 1 hour) AND
- Recent Myelosuppressive chemotherapy with neutopenia (defined as ANC <2000/mm³ or dropping ANC), OR presumed functional neutropenia as determined by the HemOnc/ BMT provider.

Exclusion Criteria
- Benign Hematology/Condition
- Sickle Cell Anemia
- Under 1 month old

Summary of Version Changes

Signs & Symptoms of Sepsis
- Hypotension (MAP ≤ 5th percentile for age)
- Tachycardia
- Poor perfusion
- Reduced urine output
- Tachypneic/new oxygen requirement
- Mental status changes

Communication Specialist: Prompt the HemOnc/ BMT Provider for the following information

- **HemOnc:**
  - Is ANC expected to be low (i.e. should patient be on pathway and receive antibiotics before ANC back)?
  - Which empiric antibiotics should be given (see below)?
  - Remind family to apply EMLA to port

- **BMT:**
  - Is the patient on immunosuppressive therapy?
  - Does the patient have an “Individualized Antibiotic Plan?” If not, which antibiotics should be given.

If yes, In addition to HOBSI do the following:

- Call RRT for signs of sepsis that require ICU presence within 30 minutes
- Call code blue for imminent cardiac or pulmonary failure or neurologic emergency

Are There Signs & Symptoms of Evolving Sepsis?
(includes any hypotension with MAP ≤ 5th percentile AND provider concern for sepsis/sepsis shock)

Labs (Do not delay blood cultures if family has not applied EMLA)
- Rapid Neutrophil Count
- Blood cultures: aerobic, anaerobic, fungal from all lumens of central venous catheter
- Other diagnostic tests as clinically indicated
  - Urinalysis and culture: clean catch NO catheterization
  - Rapid Respiratory Virus PCR
  - Chest X-ray

**Administer Empiric Antibiotics**

- **BMT**
  - Refer to “INDIVIDUALIZED ANTIBIOTIC PLAN” in CIS “Care Plan” folder.
  - Or if no individualized antibiotic plan present in CIS:
    - Start Meropenem

- **HemOnc**
  - Start Ceftazidime
  - OR, Cefepime for patients with AML, infant ALL, relapsed ALL, history of a viridans or cefazidime allergy
  - OR, Meropenem for patients allergic to non-Ceftazidime 3rd generation cephalosporins
  - Consider history of resistant organisms

Administer Additional Site Directed Antibiotics

- Suspected intra-abdominal OR perineal infection?
  - YES
    - Empiric plus Clindamycin¹ or Metronidazole²
  - NO

- Skin infection OR severe mucositis?
  - YES
    - Empiric plus Clindamycin³ or Vancomycin⁴
  - NO

- Empiric only

- **Assess labs and clinical status. Monitor VS every 15 min until 60 minutes after completion of initial antibiotic dose.

Evaluate for Signs & Symptoms of Evolving Sepsis

ANC > 200 AND well-appearing?

- YES
- Evaluate for Signs & Symptoms of Evolving Sepsis
- NO

Stable for 60 minutes after completion of initial empiric antibiotics & NS boluses. Proceed with admission to the Cancer Care Unit

- **Severity of Sepsis**
  - Stable for 60 minutes after completion of initial empiric antibiotics & NS boluses.
  - Proceed with admission to the Cancer Care Unit

Sepsis Management during RRT:

Refer to ED Septic Shock Pathway Algorithm for guidance

- Call RRT or Code Blue
- Assess airway, breathing, circulation
- Provide supplemental oxygen
- Reassess frequent vital signs
- Obtain additional labs (eg, VBG, lactate, iCa, glucose)
- Order & deliver PROMPT antibiotics:
  - Empiric antimicrobials PLUS Gentamicin AND Vancomycin for recurrent or refractory hypotension despite 40cc/kg IV fluid resuscitation OR sooner if signs of severe sepsis
  - Rapid fluid resuscitation (Each 20mL/kg NS boluses over 20 minutes or less)

- **Concern for Necrotizing Soft Tissue Infection**
  - Call RRT and Urgently consult the General Surgery Fellow.
  - Refer to GOC: Necrotizing Soft Tissue Infection

- Yes: Discuss discharge from clinic with HemOnc Provider
- Note: BMT patients will typically require admission; Discuss with BMT provider
- Off Pathway

For questions concerning this pathway, please contact HemOncBMTSuspectedInfection@seattlechildrens.org

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Last Updated: September 2020
Next Expected Review: November 2020
**HemOnc BMT Suspected Infection: Inpatient v10.0**

**Approval & Citation**
- ANY ill-appearing HO/BMT patient should receive prompt ANTIBIOTICS WITHIN 1 HOUR & evaluation for sepsis, regardless of fever or ANC

**Inclusion Criteria**
- Any Hematology/Oncology/BMT patient with concern for infection
  - Fever (Temp < 38.3°C, or greater than 38°C for more than 1 hour) AND
  - Recent Myelosuppressive chemotherapy with neutropenia (defined as ANC <200/mm³ or dropping ANC). OR presumed/functional neutropenia as determined by the HemOnc/BMT provider.

**Exclusion Criteria**
- Benign Hematology Condition
- Sickle Cell Anemia
- Under 1 month old

**Summary of Version Changes**

**Signs & Symptoms of Sepsis**
- Hypotension (MAP ≤ 5th percentile for age)
- Tachycardia
- Poor perfusion
- Reduced urine output
- Tachypnea/new oxygen requirement
- Mental status changes

**Are There Signs & Symptoms of Evolving Sepsis?**
- (includes any hypotension with MAP ≤ 5th percentile AND provider concern for sepsis/sepsis shock)

- Labs
  - CBC with diff
  - Blood cultures: aerobic, anaerobic, fungal from all lumens of central venous catheter
  - Other diagnostic tests as clinically indicated
    - Urinalysis and culture: clean catch NO catheterization
    - Rapid Respiratory Virus PCR
    - Chest X-ray

**Administer Empiric Antimicrobials**
- **“Do not delay first dose for any diagnostic evaluations with the exception of blood cultures**
- **BMT**
  - Refer to “INDIVIDUALIZED ANTIBIOTIC PLAN” in CIS “Care Plan” folder.
  - Or if no individualized antibiotic plan present in CIS:
    - Start Meropenem
- **HemOnc**
  - Start Ceftazidime
  - OR, Cefepime for patients with AML, infant ALL, relapsed ALL, history of vridiants or cefalosorin allergy
  - OR, Meropenem for patients allergic to non-Ceftazidime 3rd generation cephalosporins
  - Consider history of resistant organisms

**Are There Signs & Symptoms of Evolving Sepsis?**

- **Are There Signs of Evolving Sepsis?**
  - Yes, initiate team huddle
  - **Activate Inpatient New Septic Shock Pathway** and call RRT
  - Do not delay fluid resuscitation!

- **Administer Empiric Antimicrobials**
  - IVF bolus as clinically indicated

- **Administer Additional Site Directed Antibiotics**
  - Yes
    - **Suspected intra-abdominal OR perineal infection?**
      - Empiric plus Clindamycin¹ or Metronidazole
      - **Skin infection OR severe mucositis?**
        - Empiric plus Clindamycin³ or Vancomycin
      - Empiric only
    - YES
  - NO
  - YES
  - NO

**Assess labs and clinical status. Monitor VS every 15 min until 60 minutes after completion of empiric antibiotic.**

**Are There Signs & Symptoms of Evolving Sepsis?**

- ANC > 200 AND well-appearing?
  - Yes, discuss continuing antibiotics with fellow/attending/hospitalist
  - Off Pathway if antibiotics discontinued

**Guidance for ongoing Infectious disease management:**
- **BMT:** See MEROPENEM DE-ESCALATION POLICY & FHCRC Standard Practice
- **HemOnc:** MANAGEMENT OF SUSPECTED INFECTION OR FEVER AND NEUTROPENIA IN PEDIATRIC ONCOLOGY PATIENTS

For questions concerning this pathway, please contact HemOncBMTSuspectedInfection@seattlechildrens.org

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Last Updated: September 2020
Next Expected Review: November 2020
Inclusion and Exclusion Criteria

**Inclusion Criteria**
- Any Hematology/Oncology/BMT patient with concern for infection OR
- Fever (Temp ≥ 38.3°C, or greater than 38°C for more than 1 hour)
- Recent Myelosuppressive chemotherapy with neutropenia (defined as ANC <200mm³ or dropping ANC), OR presumed/functional neutropenia as determined by the HemOnc/BMT provider.

**Exclusion Criteria**
- Benign Hematology Condition
- Sickle Cell Anemia
- Under 1 month old

Criterial for presumed or functional neutropenia

In addition to recent chemotherapy with neutropenia, the referring hem/onc or BMT provider may request that the following patients receive antibiotics regardless of ANC and therefore antibiotics administration should not be delayed while awaiting ANC results. **Note: this determination should be made only by the referring hem/onc or BMT provider.**

- Any patient between 7 and 14 days from the **start** of any inpatient chemo regimen, OR **start of any outpatient cyclophosphamide-containing regimen** (ie any ALL patient in second half of DI, and HR ALL in consolidation),
- Any ALL patient (new diagnosis or relapsed) in **induction** or any ALL patient in delayed intensification (DI) between day 8 and 29
- Any **infant** ALL patient on therapy.
- Any AML patient on therapy
- Any patient with relapsed leukemia (ALL, AML, JMML, CML) at any time during therapy
- Any newly diagnosed oncology patient at presentation
- Any BMT patient undergoing conditioning or on immunosuppressive therapy. Patients with active graft versus host disease (GVHD) who are also on prednisone are particularly at risk.
Key Recommendations for the ED

- For patients with fever and neutropenia or ill appearance, the goal is to **administer** antibiotics **WITHIN ONE HOUR OF ED ADMISSION.**
- When family notices child is febrile, they will call the HemOnc fellow, BMT provider or clinical team.
- The HemOnc/ BMT provider will call the Communication Specialist (CS) nurse and will direct whether or not patient should be put on pathway. CS nurse will complete the standardized template and place “HemOnc BMT Suspected Infection ON PATHWAY” on FirstNet.
- If the family has not applied EMLA prior to arrival, **DO NOT** apply LMX before accessing line. Fever is an emergency in these patients. It is not safe to wait. Families will be counseled about this in clinic.
- If the patient is on pathway, they must get empiric antibiotics as soon as line is accessed and blood is drawn for culture. Order the first dose of empiric antibiotics (Ceftazidime, Cefepime or Meropenem) when the patient arrives.
- **DO NOT WAIT** for ANC result or call the fellow again before giving the first dose of antibiotics.
- The Rapid Neutrophil Count should be ordered for these patients (as indicated in the orderset). You do **NOT** need a CBC with diff also. The Rapid Neutrophil Count **includes**: Hematocrit, Platelets, White Blood Cell Count, and Absolute Neutrophil Count.
- Patients with presumed or evolving severe sepsis or refractory hypotension despite 40ml/kg NS require addition of gentamicin and vancomycin **AND a PICU consult.**
- Patients will stay in the ED for one hour after administration of empiric antibiotics and fluid boluses in order to allow time for assessment of possible clinical deterioration. Prior to admission to the HemOnc/BMT unit, a patient must demonstrate resolution of any hypotension as detailed in the hypotension/MAP slide attached.
- For BMT patients, BMT provider must evaluate patient before they leave the ED.
## Definition of hypotension & resuscitation goals

<table>
<thead>
<tr>
<th>Age</th>
<th>Critical Hypotension (MAP ≤ 1% for age)</th>
<th>Hypotension (MAP ≤ 5% for age)</th>
<th>Resuscitation Goal (Minimum MAP ≥ 10% for age)</th>
<th>Normotension (Median for Age) (MAP = 50% for age)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-30 days</td>
<td>32</td>
<td>≤ 39</td>
<td>≥ 42</td>
<td>57</td>
</tr>
<tr>
<td>30-90 days</td>
<td>37</td>
<td>≤ 44</td>
<td>≥ 47</td>
<td>62</td>
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<tr>
<td>91 days-1 year</td>
<td>41</td>
<td>≤ 48</td>
<td>≥ 52</td>
<td>68</td>
</tr>
<tr>
<td>&gt;1-2 years</td>
<td>41</td>
<td>≤ 48</td>
<td>≥ 53</td>
<td>70</td>
</tr>
<tr>
<td>&gt;2-4 years</td>
<td>41</td>
<td>≤ 50</td>
<td>≥ 55</td>
<td>70</td>
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<tr>
<td>&gt;4-6 years</td>
<td>43</td>
<td>≤ 51</td>
<td>≥ 56</td>
<td>70</td>
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<tr>
<td>&gt;6-10 years</td>
<td>46</td>
<td>≤ 54</td>
<td>≥ 58</td>
<td>72</td>
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<tr>
<td>&gt;10-13 years</td>
<td>47</td>
<td>≤ 55</td>
<td>≥ 60</td>
<td>74</td>
</tr>
<tr>
<td>&gt;13 years</td>
<td>48</td>
<td>≤ 57</td>
<td>≥ 61</td>
<td>76</td>
</tr>
</tbody>
</table>

Resolution of hypotension = Two blood pressure measurements obtained 15 minutes apart with MAP ≥10 %ile
Sepsis Score

Pediatric Sepsis Score: Adapted from the Pediatric septic shock collaborative patient identification tool. Currently validated for ED use only.

One point is given for presence of each concerning symptom:
- High risk condition (immunocompromised/central line)
- Vital sign abnormalities based on age:
  - Temperature
  - Hypotension
  - Tachycardia
  - Tachypnea
- Abnormal capillary refill
- Abnormal mental status
- Abnormal pulse
- Abnormal skin exam
Approved by the CSW HemOnc BMT Suspected Infection for December 14, 2016 go-live

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The authors have checked with sources believed to be reliable in their efforts to provide information that is complete and generally in accord with the standards accepted at the time of publication.

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Readers should confirm the information contained herein with other sources and are encouraged to consult with their health care provider before making any health care decision.
Summary of Version Changes

**Version 1.0 (8/29/2012):** Go live for Emergency Department Fever & Neutropenia pathway

**Version 2.0 (8/23/2013):** Go Live for Heme/Onc Suspected Infection Pathway in ED, Heme/Onc Clinic and Heme/Onc Inpatient Unit

**Version 3.0 (10/7/2015):** Updated each phase to coincide with the new septic shock pathway that was also implemented on October 7, 2015.

**Version 4.0 (12/14/2016):** Updated each phase to coincide with the New Septic Shock pathway that was also updated on December 14, 2016. Revision of Septic Shock Score Trigger; Inclusion of BMT in Hem/Onc Suspected Infection pathway (renamed Hem/Onc BMT Suspected Infection - HOBSI)

**Version 5.0 (2/28/2017):** Added recommendation to the inpatient phase to initiate a team huddle if there are signs and symptoms of evolving sepsis.

**Version 6.0 (5/22/2017):** Updated Fever definition (Fever (temperature GREATER THAN OR EQUAL TO 38.3 C, or GREATER THAN 38 C for more than 1 hour)

**Version 6.1 (12/26/2017):** Updated Management of Suspected Infection or Fever and Neutropenia in Ped. Onc patients link

**Version 7.0 (5/18/2018):** Updated the recommendations for empiric therapy from pip/tazo to cefepime.

**Version 8.0 (5/6/2019):** Updated to remove modalities of temperature slide and link HemOnc Management of suspected infection or fever and neutropenia in pediatric oncology patients to 2018.

**Version 9.0 (1/31/2020):** Updated Clinic, ED and Inpatient Algorithm to clarify and standardize guidance for Necrotizing Soft Tissue Infection; updated GOC: Necrotizing Soft Tissue Infection and HOBSI Metrics links.

**Version 10.0 (9/8/2020):** Updated Empiric Antibiotic Plan - Cefepime for patients with AML, infant ALL, relapsed ALL, history of s viridans or ceftazidime allergy