Neutropenic Fever\(^1\) Inpatient Pediatric Treatment  
(Solid Tumors)

Disclaimer: This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson’s specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient’s care. This algorithm should not be used to treat pregnant women.

**Note:** This algorithm should not be used for patients receiving CAR cell therapy.

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**Patient presents with fever or develops fever at MD Anderson**

- **PEWS\(^2\) 6 or greater?**
  - Yes
    - See Pediatric Sepsis Management Algorithm for stabilization information
    - See Antimicrobial Therapy Recommendations (Page 2)
  - No
    - Complete physical exam and history of recent chemotherapy
    - Start IV fluids at maintenance (or less if clinically indicated)
    - CBC with differential, CMP, and lactic acid
    - Blood cultures\(^3\) (with a set collected from each lumen simultaneously if CVAD present and consider one peripheral site); urinalysis with culture
    - Other site specific cultures (e.g., stool studies, respiratory viral PCR panel) only if clinically indicated
    - Chest/abdominal x-ray or other tests as clinically indicated

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**PEWS** = Pediatric early warning score

\(^1\) ANC less than 1 K/microliter and either temperature of at least 38.3°C once or 38.0°C twice separated by at least 1 hour

\(^2\) See **Appendix A for Modified PEWS Tool**; full details available in the Detecting Pediatric Patient Deterioration Using PEWS Algorithm

\(^3\) Do not delay antibiotic administration for blood cultures; antibiotics should be given within one hour

Approved by the Executive Committee of the Medical Staff on 04/24/2018

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Department of Clinical Effectiveness V1
Consider the following when selecting antibiotics (antibiotics should be given within 1 hour):

- Recent culture and sensitivity results
- History of multi-drug resistant organism (MDRO) infection or colonization
- Suspected line infection
- Antibiotic history and prophylaxis
- Source of infection if identified
- Antibiotic allergies
- Organ dysfunction
- Mucositis

### ANTIMICROBIAL THERAPY RECOMMENDATIONS

#### Neutropenic fever

**GRAM NEGATIVE COVERAGE** antibiotics should be given first

<table>
<thead>
<tr>
<th>Condition</th>
<th>Antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Neutropenic fever:</strong></td>
<td></td>
</tr>
<tr>
<td>• Cefepime</td>
<td></td>
</tr>
<tr>
<td>If clinically suspected line infection, bacteremia, skin/soft tissue infection, or MRSA colonization:</td>
<td></td>
</tr>
<tr>
<td>• Add vancomycin</td>
<td></td>
</tr>
<tr>
<td>If relative contraindication exists to vancomycin use, consider linezolid instead</td>
<td></td>
</tr>
<tr>
<td>If indicated for double gram negative coverage, add either:</td>
<td></td>
</tr>
<tr>
<td>• Tobramycin or amikacin or ciprofloxacin (only if no quinolone prophylaxis)</td>
<td></td>
</tr>
<tr>
<td>If mucositis (at least Grade 2), suspected intra-abdominal infection, or other indication for anaerobic coverage:</td>
<td></td>
</tr>
<tr>
<td>• Add metronidazole to cefepime</td>
<td></td>
</tr>
<tr>
<td>If history of MDRO infection:</td>
<td></td>
</tr>
<tr>
<td>• Consider ID consult</td>
<td></td>
</tr>
</tbody>
</table>

#### Neutropenic fever:

- Aztreonam (preferred) or
- Ciprofloxacin (only if no quinolone prophylaxis or therapy in past 90 days)

**Plus:**

- Vancomycin
- If relative contraindication exists to vancomycin use, consider linezolid instead

If mucositis of at least Grade 2, suspected intra-abdominal infection, or other indication for anaerobic coverage:

- Add metronidazole

If history of MDRO infection:

- Consider ID consult

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1. Chills, rigors with infusion through catheter, cellulitis or discharge around the line entry site
2. Consider meropenem if patient has any of the following:
   - Non-IgE-mediated allergy to alternative agents
   - Failed treatment with cefepime or piperacillin/tazobactam
   - Infection with ESBL organism
   - Infection with organism only susceptible to carbapenem
3. Double gram negative coverage should be considered with complicated tissue-based infections, neutropenic enterocolitis, and perirectal infections
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**RE-ASSESSMENT**

**Patient afebrile**

72-hour evaluation

- Identified source of fever?

  - Yes
    - Treat for appropriate duration based on nature of infection (e.g., urinary tract infection, cellulitis)
    - Complete antibiotic regimen and disposition per MD

  - No
    - Re-evaluate antibiotics
    - Repeat cultures
    - Imaging as clinically indicated
    - Evaluate thoroughly for non-infectious causes of fever (e.g., medications, thrombosis, tumor, necrosis)
    - Consult ID
    - Disposition based on ID consult recommendations and/or diagnostic test results

**Patient febrile**

- Identified source of fever?

  - Yes
    - Complete antibiotic regimen and disposition per MD

  - No
    - Continue treatment for at least 1 day after ANC is greater than 0.2 K/microliter and rising
    - Disposition per MD

1 Consider narrowing therapy based on cultures and sensitivities (e.g., discontinue vancomycin if no gram positive organisms are identified and patient does not have cellulitis)
### APPENDIX A: Modified PEWS Tool

<table>
<thead>
<tr>
<th></th>
<th>Behavior</th>
<th>Cardiovascular System</th>
<th>Respiratory System</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Score&lt;sup&gt;1&lt;/sup&gt;</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Playing</td>
<td>Tachycardia less than 20 above normal for age</td>
<td>Tachypnea 10-19 above normal parameters for age</td>
</tr>
<tr>
<td></td>
<td>Appropriate</td>
<td>Pale or dusky</td>
<td>Mottled</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Capillary refill 3 seconds</td>
<td>Capillary refill 4 seconds</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tachycardia 20-29 above normal for age</td>
<td>Tachypnea at least 20 above normal parameters for age with retractions</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mottled</td>
<td>Moderate retraction/accessory muscle use (including tracheal tugging)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Capillary refill 4 seconds</td>
<td>Oxygen required to maintain normal&lt;sup&gt;2&lt;/sup&gt; SpO&lt;sub&gt;2&lt;/sub&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>FiO&lt;sub&gt;2&lt;/sub&gt; 40-49%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tachycardia at least 30 above or bradycardia at least 10 below normal for age</td>
<td>Bradypnea at least 5 below normal parameters for age with retractions</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gray</td>
<td>Severe retraction/accessory muscle use (including tracheal tugging) and grunting</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Oxygen required to maintain normal&lt;sup&gt;2&lt;/sup&gt; SpO&lt;sub&gt;2&lt;/sub&gt;</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>FiO&lt;sub&gt;2&lt;/sub&gt; of at least 50%</td>
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<tr>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Lethargic</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Confused</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Reduced response to pain</td>
<td></td>
</tr>
</tbody>
</table>

<sup>1</sup> Add 2 extra points if patient requires frequent interventions (e.g., suctioning, positioning, change in O<sub>2</sub> needs, multiple IV attempts required, or every 15-minute or continuous nebulized treatments) or has persistent post-op vomiting.

<sup>2</sup> As defined in patient’s orders.

<sup>3</sup> Includes home BiPAP/CPAP or home ventilator at baseline settings.
APPENDIX B: Antibiotic Dosing Information

Note: Adjust dose for patients with renal/hepatic dysfunction
Therapeutic drug monitoring should be performed to ensure safety and efficacy when possible

- Amikacin 15 mg/kg IV once and then repeat per pharmacokinetic data
- Aztreonam 30 mg/kg (maximum 2 g) IV every 8 hours
- Cefepime 50 mg/kg (maximum 2 g) IV every 8 hours
- Ciprofloxacin 10 mg/kg (maximum 400 mg) IV every 8 hours
- Linezolid
  - Less than 12 years old: 10 mg/kg (maximum 600 mg) IV every 8 hours
  - Greater than or equal to 12 years old: 600 mg IV every 12 hours
- Meropenem 20 mg/kg (maximum 1 gram) IV every 8 hours
- Metronidazole 7.5 mg/kg (maximum 500 mg) IV every 6 hours
- Piperacillin and tazobactam 100 mg/kg piperacillin (maximum 4 grams) IV every 8 hours
- Sulfamethoxazole and trimethoprim (TMP) 5 mg/kg TMP IV or oral every 8 hours
- Tobramycin 7 mg/kg IV once and then repeat per pharmacokinetic data
- Vancomycin
  - Less than 6 years old: 20 mg/kg IV every 6 hours
  - 6-11 years old: 15 mg/kg IV every 6 hours
  - Greater than 11 years old: 15 mg/kg IV every 8 hours
SUGGESTED READINGS


This practice consensus statement is based on majority opinion of the Pediatric Neutropenic Fever work group at the University of Texas MD Anderson Cancer Center for the patient population. These experts included:

- Patricia Amado, BSN, RN (Nursing G9)
- Natalie J.M. Dailey Garnes, MD (Infectious Disease)
- Suzanne Gettys, PharmD (Pharmacy Clinical Programs)
- Douglas Harrison, MD (Pediatrics – Patient Care)
- Victor Mulanovich, MD (Infectious Disease)
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Core Development Team Lead
Clinical Effectiveness Development Team