Neutropenic Fever[1] Inpatient Pediatric Treatment (Solid Tumors)

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

PATIENT PRESENTATION

Patient presents with fever or develops fever during hospitalization

PEWS[2] ≥ 6?

MANAGEMENT

Yes

- See Pediatric Sepsis Management algorithm for evaluation and treatment of sepsis
- See Page 2 for Antimicrobial Therapy Recommendations

No

- Complete physical exam and history of recent chemotherapy
- Start IV fluids at maintenance rate (or less if clinically indicated)
- CBC with differential, complete metabolic panel, and lactic acid
- Blood cultures[3] x 2 sets (one set collected from each lumen simultaneously if CVAD present and consider one peripheral site)
- See Page 2 for Antimicrobial Therapy Recommendations
- 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

→ See Page 3 for Re-assessment

CAR = chimeric antigen receptor
CVAD = central venous access device
PEWS = pediatric early warning score

[1] ANC < 1 K/microliter and either temperature of at least 38.3°C once or 38°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 of order

Neutropenic Fever Inpatient Pediatric Treatment (Solid Tumors)

MANAGEMENT

Consider the following when selecting antibiotics (antibiotics should be given within 1 hour of order):

- Recent culture and sensitivity results
- History of MDRO infection or colonization
- Suspected line infection[1]
- Antibiotic history and prophylaxis
- Source of infection if identified
- Antibiotic allergies
- Organ dysfunction
- Mucositis

Documented beta-lactam allergy (*i.e.*, hives or anaphylaxis)?

ANTIMICROBIAL THERAPY RECOMMENDATIONS

See Appendix B: Dosing Information

Gram negative coverage antibiotics should be given first

No

- **Neutropenic fever:**
  - Cefepime[2]
- **If clinically suspected line infection[1], bacteremia, skin/soft tissue infection, or MRSA colonization:**
  - Add vancomycin
  - If relative contraindication exists to vancomycin use, consider linezolid instead
- **If indicated for double gram negative coverage[3], add either:**
  - Tobramycin **or** amikacin **or** ciprofloxacin (only if no quinolone prophylaxis)
- **If mucositis (at least Grade 2), suspected intra-abdominal infection, or other indication for anaerobic coverage:**
  - Add metronidazole to cefepime
- **If history of MDRO infection:**
  - Consider Infectious Disease consult

Yes

- **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 Infectious Disease consult

See Page 3 for Re-assessment

ESBL = extended spectrum beta-lactamase
MDRO = multi-drug resistant organism
MRSA = methicillin-resistant *staphylococcus aureus*

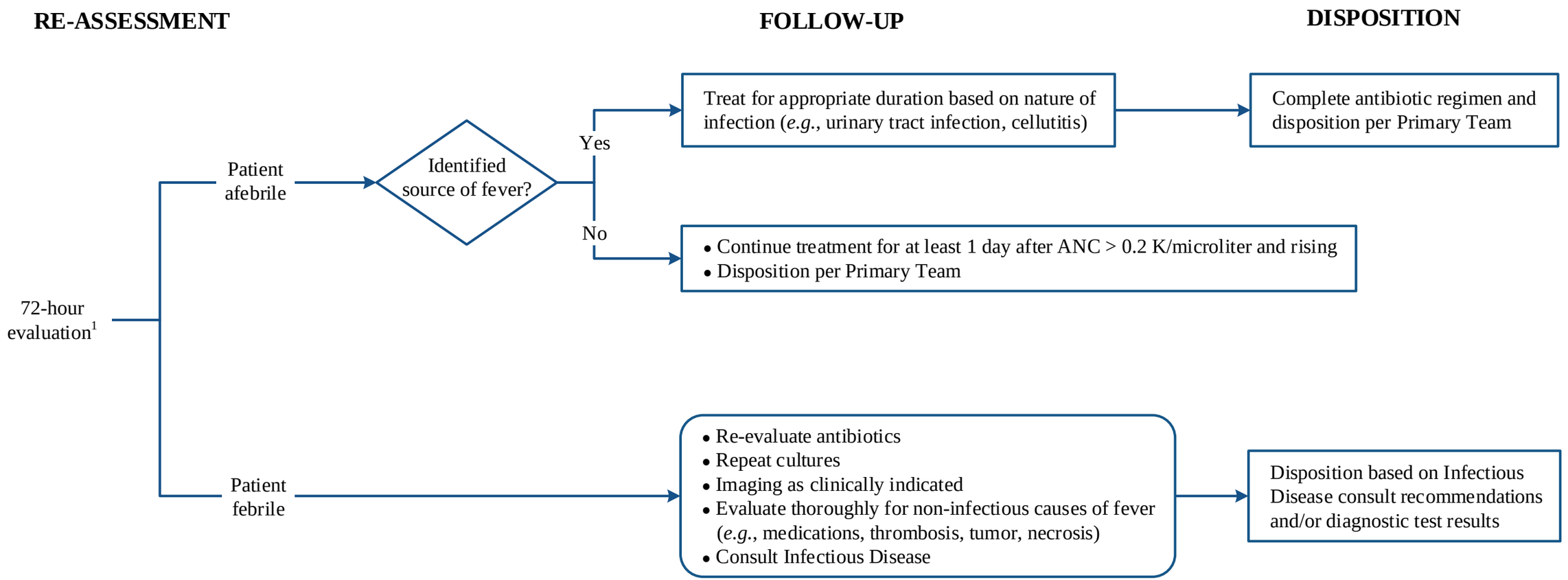
[1] Chills, rigors with infusion through catheter, cellulitis or discharge around the line entry site

[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

Department of Clinical Effectiveness V2
Approved by the Executive Committee of the Medical Staff on 03/24/2020

Neutropenic Fever Inpatient Pediatric Treatment (Solid Tumors)



[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

	Score[1]			
	0	1	**2**	**3**
Behavior	• Playing • Appropriate	• Irritable, but consolable	• Irritated, but not consolable	• Lethargic • Confused • Reduced response to pain
Cardiovascular System				
Rate	• Within normal parameters for age	• Tachycardia < 20 above normal for age	• Tachycardia 20-29 above normal for age	• Tachycardia ≥ 30 above **or** bradycardia ≥ 10 below normal for age
Color	• Pink	• Pale **or** dusky	• Mottled	• Gray
Perfusion	• Capillary refill 1-2 seconds	• Capillary refill 3 seconds	• Capillary refill 4 seconds	• Capillary refill ≥ 5 seconds
Respiratory System				
Rate	• Within normal parameters for age	• Tachypnea 10-19 above normal parameters for age	• Tachypnea ≥ 20 above normal parameters for age with retractions	• Bradypnea ≥ 5 below normal parameters for age with retractions
Effort	• No retractions	• Mild retractions/accessory muscle use	• Moderate retractions/accessory muscle use (including tracheal tugging)	• Severe retractions/accessory muscle use (including tracheal tugging) **and** grunting
Oxygen	• N/A	• Oxygen required to maintain normal[2] SpO_2 ◦ FiO_2 24-40% ◦ O_2 2 L/minute • Any assisted ventilation[3] or initiation of O_2	• Oxygen required to maintain normal[2] SpO_2 ◦ FiO_2 40-49% ◦ O_2 ≥ 3 L/minute	• Oxygen required to maintain normal[2] SpO_2 ◦ FiO_2 ≥ 50%

[1] Add 2 extra points if patient requires frequent interventions (*e.g.*, suctioning, positioning, change in O_2 needs, multiple IV attempts required, or every 15-minute or continuous nebulized treatments) or has persistent post-op vomiting
[2] As defined in patient's orders
[3] Includes home bilevel positive airway pressure (BiPAP)/continuous positive airway pressure (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
  - < 12 years old: 10 mg/kg (maximum 600 mg) IV every 8 hours
  - ≥ 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
  - < 6 years old: 20 mg/kg IV every 6 hours
  - 6-11 years old: 15 mg/kg IV every 6 hours
  - > 11 years old: 15 mg/kg IV every 8 hours

SUGGESTED READINGS

Freifeld, A., Bow, E., Sepkowitz, K., Boeckh, M., Ito, J., Mullen, C., . . . Wingard, J. (2011). Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the Infectious Diseases Society of America. *Clinical Infectious Diseases, 52*(4), e56-e93. doi:10.1093/cid/cir073

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