

**TEXAS CHILDREN'S HOSPITAL**  
**EVIDENCE-BASED OUTCOMES CENTER**

**Fever and Neutropenia in Children Receiving Cancer Treatment or with Blood Disorders**  
**Evidence-Based Guideline**

**Definition:** Fever is a common sign that suggests infection in children. However, signs and symptoms are often absent or minimized in the child with cancer because of inability to evoke an inflammatory response. In this population, fever is defined as a single temperature  $>38.3^{\circ}\text{C}$  ( $101^{\circ}\text{F}$ ) or a temperature  $\geq 38.0^{\circ}\text{C}$  ( $100.4^{\circ}\text{F}$ ) on two occasions one hour apart. Rectal temperatures are not taken in children with cancer. Caregivers should be advised NOT to add a degree to any type of temperature reading. Neutropenia is classified as mild (ANC  $>500$ - $1000/\text{mm}^3$ ), moderate (ANC  $\geq 200$ - $500/\text{mm}^3$ ) or severe (ANC  $<200/\text{mm}^3$ ). (1-2)

**Pathophysiology:** Chemotherapy agents and radiation therapy cause myelosuppression. In addition, certain malignancies that metastasize to the bone marrow (e.g., leukemia, lymphoma, neuroblastoma, sarcomas) cause a decrease in the number of normal blood cell precursors. When the myelosuppressive effect is severe enough, the child becomes predisposed to infection, anemia, or bleeding, depending on which blood cell line is affected. The risk for serious infection in a child receiving treatment for cancer is related to the degree and duration of neutropenia. Children with brief periods of neutropenia (ANC  $\geq 500$ ) and fever ( $<7$  days) respond better than those with moderate to severe neutropenia (ANC  $\leq 500$ ) lasting more than 7 days. Pneumonitis, cellulitis, bacteremia and abscess can occur when the ANC falls below 500. The risk for bacteremia/septicemia increases when the ANC is  $<200$ . (1-2)

**Common Organisms:** Gram + bacteria account for 60-70% of microbial documented infections in children with cancer. (1-2)

**Inclusion Criteria**

Child with fever and neutropenia receiving therapy for cancer  
Child with fever and neutropenia with a blood disorder  
Child with fever after BMT, see p. 4 & BMT algorithm

**Exclusion Criteria**

Patients with shock symptoms (proceed to shock protocol)

**Diagnostic Evaluation**

Because of the high mortality rate associated with untreated infection, all febrile children with cancer who have neutropenia are considered at risk for a life-threatening infection until proven otherwise. Evaluation of a child with fever and neutropenia should be completed as quickly as possible. The child with fever and neutropenia is at risk for septic shock.

**Table 1. Vital Sign Changes of Sepsis (3)**

Age	Heart Rate	Resp Rate	Systolic BP	Temp ( $^{\circ}\text{C}$ )
0d - 1m	$> 205$	$> 60$	$< 60$	$<36$ or $>38$
$> 1\text{m} - 3\text{m}$	$> 205$	$> 60$	$< 70$	$<36$ or $>38$
$> 3\text{m} - 1\text{y}$	$> 190$	$> 60$	$< 70$	$<36$ or $>38.5$
$> 1\text{y} - 2\text{y}$	$> 190$	$> 40$	$< 70 + (\text{age in yr} \times 2)$	$<36$ or $>38.5$
$> 2\text{y} - 4\text{y}$	$> 140$	$> 40$	$< 70 + (\text{age in yr} \times 2)$	$<36$ or $>38.5$
$> 4\text{y} - 6\text{y}$	$> 140$	$> 34$	$< 70 + (\text{age in yr} \times 2)$	$<36$ or $>38.5$
$> 6\text{y} - 10\text{y}$	$> 140$	$> 30$	$< 70 + (\text{age in yr} \times 2)$	$<36$ or $>38.5$
$> 10\text{y} - 13\text{y}$	$> 100$	$> 30$	$< 90$	$<36$ or $>38.5$
$> 13\text{y}$	$> 100$	$> 16$	$< 90$	$<36$ or $>38.5$

**Table 2. Signs and Symptoms of Shock (3)**

	Exam Abnormalities		
	Cold Shock	Warm Shock	Non-Specific
Peripheral Pulses	Decreased or weak	Bounding	
Capillary Refill (central vs. peripheral)	$\geq 3$ sec	Flash ( $< 1$ sec)	
Skin	Mottled, cool	Flushed, ruddy, erythroderma (other than face)	Petechiae below the nipple, any purpura
Mental Status			Decreased, irritability, confusion, inappropriate crying or drowsiness, poor interaction with parents, lethargy, diminished arousability, obtunded

**History: Assess for**

- Date of last treatment and details of therapy (agents, dose, route)
- Onset of fever and highest temperature (Note: Dexamethasone may mask fever)
- Other symptoms including nausea, vomiting, diarrhea, pain (e.g., mouth, abdomen, perianal), swelling, redness, drainage
- Recent diagnosis of GI or GU tumor
- Exposure to infection (e.g., TB, history of MRSA, recent CVC infection) and seasonal illnesses (i.e., RSV, influenza)
- Recent invasive procedure
- Recent foreign travel
- Renal/Hepatic dysfunction

**Physical Examination: Assess**

- For signs/symptoms of shock (see Tables 1 and 2)
- Entire body for signs, tenderness/pain, induration, redness or discharge from any area; **examine closely the skin, nose, teeth, pharynx, sinuses, joints and extremities, procedure sites, perineal and perirectal areas**
- Central line - note any redness or drainage along tunnel or at exit site
- Mental status and changes in sensorium

**Laboratory Tests:**

- Complete CBC, Chem 7, urinalysis (bagged or clean catch only), blood culture from central and peripheral site of appropriate volume
- **Optional studies to consider:** C-reactive protein (CRP), stool cultures for history of diarrhea, aspirate or biopsy of any suspicious skin lesion after Attending MD consultation
- Urine culture if UA abnormal (non-catheterized)
- CXR in presence of respiratory symptoms, chest pain, tachypnea or decreased pulse oximetry (4-10)

## Critical Points of Evidence

### **Evidence Supports**

Utilize a validated risk stratification rule for patients with fever and neutropenia due to cancer treatment. (2,11-13) – Strong recommendation, moderate quality evidence

Remarks: Evaluation of the evidence does not demonstrate that one prediction rule is more effective over another. Due to the Alexander rule's documented effectiveness for pediatric patients in North America and England, this rule was chosen as best suited for risk stratification of TCH patients presenting to the EC with fever and neutropenia due to cancer treatment.

Manage low risk patients with fever and neutropenia due to cancer treatment outpatient with oral antibiotics ensuring frequent follow-up and monitoring. (2,12,14-16) – Strong recommendation, moderate quality evidence

Empiric antibiotics for patients with fever and neutropenia should be based upon the patient's risk for bacteremia. See below for antibiotic selection: (2,12-13,17) – Strong recommendation, moderate quality evidence

- Outpatient Low Risk - Levofloxacin
- Inpatient Low Risk – Ceftriaxone
- High Risk – Vancomycin and Cefepime
- High Risk with suspicion of GI issues or typhlitis – Add Metronidazole

Administer empirical antifungal therapy to high risk patients with no identified infectious source that have persistent fever after 4 – 7 days of broad spectrum antibiotics. (2,12,18-20) – Strong recommendation, low quality evidence

Remarks: There is no one antifungal agent that has been proven superior for use in this population. Unless the patient has concerns for renal or liver toxicity, the guideline development team would recommend the use of liposomal amphotericin B. An equally equivalent selection would be an echinocandin.

### **Evidence Lacking/Inconclusive**

Draw complete blood counts (CBC) at least every three days. More frequent monitoring may be warranted in for patients who are being assessed for count recovery. – Strong recommendation, very low quality evidence

Perform baseline renal functioning testing at initial presentation. – Strong recommendation, very low quality evidence

Consider liver function tests in patients with clinical concerns for liver dysfunction. – Weak recommendation, very low quality evidence

Use of prolonged steroids greater than 7 days may be associated with a higher risk of infection. (21-23) – Strong recommendation, very low quality evidence

Remarks: Knowledge of the use of prolonged steroids should heighten the clinicians' suspicion for infection; however, management decisions may not be affected. The dose and duration of steroids along with the status of the malignancy and immunodeficiency determine the individual patient's risk for infection.

Repeat sampling for blood cultures should be obtained from the central line, if applicable, after the initial assessment for CLABSI has been performed. (2,24-28) – Strong recommendation, low quality evidence

Remarks: Central and peripheral blood cultures are obtained initially to diagnosis CLABSI using time-to-positivity. Thereafter, repeat sampling of blood cultures can be obtained from one site. If the initial peripheral culture is positive, repeat sampling of blood cultures from the central site allow for monitoring of organism growth from the CLC and decrease the need for peripheral venipunctures in the patient.

Consider galactomannan,  $\beta$ -D-glucan and/or CT scans in the patients with persistent fever and neutropenia. (2,12,29-33) – Weak recommendation, low quality evidence

Consider further diagnostic evaluation such as bronchopulmonary lavage or biopsy in FN patients with pulmonary lesions that suggest invasive fungal infections. Preferred approach should be chosen based on the patient's clinical picture. (12,34-39) – Weak recommendation, low quality evidence

### **Evidence Against**

Only obtain a chest x-ray for the initial assessment of patients with fever and neutropenia if respiratory signs and/or symptoms are present. (4-10) – Strong recommendation, moderate quality evidence

Patients with fever and neutropenia without a clinical change in presentation should not have blood culture sampling repeated daily if adequate volume cultures was obtained on day #1. If initial blood cultures result positive, repeat blood cultures should be obtained until clearance (48 - 72 hours). (12,40-42) – Strong recommendation, low quality evidence

Remarks: If adequate volumes were not obtained on initial cultures, cultures should be repeated the next day ensuring optimal volume. Unnecessary repeat blood cultures can result an increase rate of false positives in commensal organisms, avoidable waste of blood volume and increase attempts to access central lines. Improvements in optimal blood culture volumes and technology has resulted in the vast majority of positive blood cultures exhibiting growth within 24 hours.

## Condition-Specific Elements of Clinical Management

### Risk Assessment at Presentation of FN<sup>(11-12)</sup>

**Patient is considered High Risk if ANY of the following clinical criteria is present:**

- High-risk diagnoses
  - ALL and lymphoma patients who are **not in maintenance therapy**
  - Infant ALL
  - Acute Myeloid Leukemia (AML)
  - Relapsed/Progressive Leukemia
  - Bone Marrow Transplant patients
  - HLH patients
  - Severe aplastic anemia / Bone marrow failure patients
  - Primary Immunodeficiencies patients
- Age <1 year
- Down Syndrome
- 2 normal saline boluses in the ER
- Abnormal vital signs (except temperature) at time of disposition or changes in mental status
- Focal infection (e.g., mucositis, abdominal pain, cellulitis, pneumonia, perianal tenderness)

**Patient should be admitted for Low Risk treatment management if any of the following exclusions are present:**

- Inability to take PO antibiotics
- Allergy to Levofloxacin
- Parents with a history of poor compliance or follow-up
- Absence of working telephone
- Families that live farther than 1 hour/40 miles from the main campus ER of TCH
- Parental preference to be admitted
- If patient cannot be seen in the Oncology Clinic Urgent Care Bay within 3 calendar days of discharge from the ER

**Patient is eligible for Low Risk outpatient management if they have no exclusion above.**

### Early Assessment and Diagnostic Work-up

- Careful, detailed history and thorough physical exam
- Initiate Life Threatening Lab System - CBC, BUN, Cr
- Draw other labs: Lytes, LFTs, urinalysis, blood culture from a central and peripheral site of appropriate volume, site specific cultures as clinically indicated
- Diagnostic Imaging - CXR if respiratory signs/symptoms present including chest pain, tachypnea, decreased pulse oximetry

### Empiric Antibiotic Selection<sup>(2,12-17,43-45)</sup>

- **High Risk Inpatient Intravenous Treatment:** Vancomycin and Cefepime (Table 3)
- **High Risk Inpatient with GI issues and/or typhlitis:** Add Metronidazole (Table 3)
- **Low Risk Inpatient Intravenous Treatment:** Ceftriaxone (Table 3)
- Initiate antibiotics ASAP (preferably within ONE HOUR of arrival)
- All antibiotics should be rotated among the different CVC lumens, so all lumens are exposed to all antibiotics. If only one lumen has a positive blood culture, all antibiotics should then be administered through that lumen <sup>(1-2)</sup>

### Treatment and Ongoing Management

- Be prepared to start IV or access CVC and draw blood
- Normal saline bolus for hypotension
- Blood product support if needed
- Daily evaluate: Central venous catheter site(s), surgical incisions, other breaks in skin, oral mucosa, peri-rectal area
- With continued fever, repeat urine, stool, and tissue cultures, obtain diagnostic imaging as clinically indicated

### Monitoring

- Careful monitoring should continue as long as the child is neutropenic
- Complete blood count with differential at least every 3 days <sup>(2)</sup>
- Baseline renal function testing at initial presentation
- Monitor liver function tests if clinical concern for liver dysfunction
- Serum chemistries at least every 3 days - monitor for electrolyte depletion <sup>(2)</sup>
- Monitor creatinine daily if rises over baseline
- Urine samples – monitor for glycosuria, hematuria, and albuminuria, sodium and potassium, as clinically indicated
- Patients with history of renal dysfunction calculate antibiotic dosing with creatinine clearance method below

### Specific monitoring:

- **Aminoglycosides:** Serum drug peak and trough to be obtained with the 3<sup>rd</sup> to 5<sup>th</sup> dose
- **\*Creatinine Clearance estimation method by Modified Schwartz equation:**  

$$\text{GFR (mL/min/1.73 m}^2\text{)} = 0.413 \times \text{length (cm)}/\text{serum creatinine (mg/dL)}$$

### Preserving/Removing the Central Line<sup>(2,46-48)</sup>

The benefits of catheter removal must be weighed against the difficulty of obtaining alternate venous access for each individual patient. Prompt removal of the central line should be considered when any of the following conditions and/or organisms exists:

- Severe sepsis
- Endocarditis
- Bloodstream infection that continues despite >72 h of antimicrobial therapy to which the infecting microbes are susceptible
- Infections due to *S. aureus*, gram-negative bacilli including *P. aeruginosa*, *Bacillus* species, and/or enterococci

Prompt removal of the catheter is necessary in cases of:

- Infections due to mycobacteria and/or fungi
- Tunnel site infection (e.g., redness, inflammation along catheter line, purulent drainage)
- Suppurative thrombophlebitis

Consider removal of the central line when the integrity of the line is compromised as evidence by broken, cracked or clotted lumens.

**Management of Persistent Fever**

- If patient continues fever >48 h and on monotherapy, add Vancomycin (2)
- If patient continues fever >48 h and on double antibiotics, consider changing/adding antibiotics (2)
- If fever continues on broad spectrum antibiotics for >4 - 7 days, begin antifungal agents and perform evaluation for invasive fungal disease. (2,12,18-20) Consider monitoring galactomannan,  $\beta$ -glucan and/or CT scans and consider ID consult. (2,12,29-33)
- CT evaluations to assess fungal infection should include scans of the lungs and other areas as clinically indicated. CT scans of the sinuses can be considered in children two years of age or older. (2)
- In patients with pulmonary lesions suggestive of fungal infection, consider further diagnostic evaluation such as bronchopulmonary lavage or biopsy. Preferred approach should be chosen based on the patient's clinical picture. (12)
- If there is clinical or laboratory evidence of HSV, administer antiviral treatment. (2)
- Consider culture for HSV in patients with mucositis.

## THE BMT PATIENT WITH FEVER AND SUSPECTED INFECTION

**Definition:** Fever is a common sign that suggests infection in children. However, signs and symptoms are often absent or minimized in the child following BMT because of inability to evoke an inflammatory response. In this population, fever is defined as a single oral temperature  $\geq 38.0^{\circ}\text{C}$  ( $100.5^{\circ}\text{F}$ ). Rectal temperatures are NOT taken in BMT patients. Caregivers should be advised to NOT add a degree to any type of temperature reading. Neutropenia is classified as mild (ANC  $>500$ - $1000/\text{mm}^3$ ), moderate (ANC  $\geq 200$ - $500/\text{mm}^3$ ) or severe (ANC  $<200/\text{mm}^3$ ). (1-2)

**Pathophysiology:** After allogeneic BMT, there is a loss of both innate and acquired immunity, which persists for more than 12 months, and even longer in patients receiving immunosuppressive medications. Consequently, BMT patients are particularly at risk for not only bacterial, but fungal and viral infections post-transplant. Oftentimes, BMT patients may have systemic infection in the absence of neutropenia. In fact, the vast majority of BMT patients will not be neutropenic but may still present with bacterial sepsis, especially those with indwelling central catheters and active GvHD. While the risk for serious infection in a neutropenic child is related to the degree and duration of neutropenia, BMT patients may have serious infection with normal neutrophil counts. Judicious use of fluid resuscitation is necessary in BMT patients as they have a high incidence of capillary leak and pulmonary disease and can easily be fluid overloaded. (49-51)

**Rationale:** Because of the high-risk of infection post BMT (bacterial, fungal or viral), patients who present to the EC with or without fever, should be promptly triaged and isolated from other patients. Children with underlying immunodeficiencies, such as SCID, should be in reverse isolation at all times. Blood cultures and labs should be promptly obtained and appropriate antibiotics given within 60 minutes. The BMT physician on call should be notified immediately upon arrival of any BMT patient. In general, patients who are less than 100 days post BMT are at a much higher risk of serious bacterial infection and should be considered for admission after appropriate antibiotics given. Children who are hemodynamically unstable or exhibiting even mild signs of early shock (including chills) should be admitted with triple antibiotic coverage. (52)

**Common Organisms:** Gram positive bacteria account for 60-70% of microbial documented infections (1-2)

Gram positive	Gram negative
<i>Staphylococcus E. coli</i>	<i>Enterobacter</i>
<i>Streptococcus</i>	<i>Klebsiella</i>
<i>Enterococcus</i>	<i>Pseudomonas</i>

**Diagnostic Evaluation:** Because of the high mortality rate associated with untreated infection, all febrile children who have received a BMT are considered at risk for a life threatening infection until proven otherwise. Additionally, BMT patients experiencing chills, who may not yet have fever, also should be considered at risk for a life-threatening infection until proven otherwise. Evaluation of a BMT patient with suspected infection should be completed as quickly as possible as they are at risk for septic shock. Signs and symptoms include:

- Fever and/or chills or rigors
- Tachypnea
- Pulse oximetry  $< 95\%$
- Early - warm, flushed, dry skin
- Tachycardia
- Hypotension
- Decreased urine output
- Late - cool, clammy skin

**Table 1. Vital Sign Changes of Sepsis (3)**

Age	Heart Rate	Resp Rate	Systolic BP	Temp ( $^{\circ}\text{C}$ )
0d - 1m	$> 205$	$> 60$	$< 60$	$<36$ or $>38$
$> 1\text{m} - 3\text{m}$	$> 205$	$> 60$	$< 70$	$<36$ or $>38$
$> 3\text{m} - 1\text{y}$	$> 190$	$> 60$	$< 70$	$<36$ or $>38.5$
$> 1\text{y} - 2\text{y}$	$> 190$	$> 40$	$< 70 + (\text{age in yr} \times 2)$	$<36$ or $>38.5$
$> 2\text{y} - 4\text{y}$	$> 140$	$> 40$	$< 70 + (\text{age in yr} \times 2)$	$<36$ or $>38.5$
$> 4\text{y} - 6\text{y}$	$> 140$	$> 34$	$< 70 + (\text{age in yr} \times 2)$	$<36$ or $>38.5$
$> 6\text{y} - 10\text{y}$	$> 140$	$> 30$	$< 70 + (\text{age in yr} \times 2)$	$<36$ or $>38.5$
$> 10\text{y} - 13\text{y}$	$> 100$	$> 30$	$< 90$	$<36$ or $>38.5$
$> 13\text{y}$	$> 100$	$> 16$	$< 90$	$<36$ or $>38.5$

**Table 2. Signs and Symptoms of Shock (3)**

Exam Abnormalities			
	Cold Shock	Warm Shock	Non-Specific
Peripheral Pulses	Decreased or weak	Bounding	
Capillary Refill (central vs. peripheral)	$\geq 3$ sec	Flash ( $< 1$ sec)	
Skin	Mottled, cool	Flushed, ruddy, erythroderma (other than face)	Petechiae below the nipple, any purpura
Mental Status			Decreased, irritability, confusion, inappropriate crying or drowsiness, poor interaction with parents, lethargy, diminished arousability, obtunded

### History: Assess

- Date of BMT and time post BMT ( $<$  or  $>$  100 days)
- Onset of fever and highest temperature
- Presence of central line
- Medications, such as immunosuppressants (tacrolimus, cyclosporine, prednisone and MMF most common)
- Other symptoms including nausea, vomiting, diarrhea, pain (e.g., mouth, abdomen, perianal), swelling, redness, drainage
- Recent invasive procedure
- Renal/Hepatic dysfunction

### Physical Examination: Assess

- For signs/symptoms of shock (Tables 1 and 2)
- Pulse oximetry
- Entire body for signs of infection, including tenderness/pain, induration, redness or discharge from any area; **examine closely the skin, nose, teeth, pharynx, sinuses, joints and extremities, procedure sites, perineal and perirectal areas**
- Central line note any redness or drainage along tunnel or at exit site
- Mental status and changes in sensorium

### Diagnostic and Laboratory Studies: Assess

- Complete CBC, Chem 10, LFTs
- Blood culture (CVC-all lumens, include portacath)
- Nasal wash for RSV, flu, viral culture and "respiratory viral panel" in patients with rhinorrhea
- Diarrheal stools for bacteria, ova/parasites, viral particles and Clostridium difficile toxin
- UA, U/C (bagged or clean catch only)
- Chest x-ray

**Considerations for Discharge**

- Afebrile  $\geq 24$  hours
- Negative blood cultures for 48 hours
- No signs of focal infection (examples include: mucositis, abdominal pain, cellulitis, pneumonia)
- Rising ANC
- 24 hour caregiver available at home, able to take temperature, live within 1 hour of accessible medical care, phone and transportation access

**Measures**

**Process**

- Antibiotic administration initiated within one hour of patient arrival to EC or TXCH
- Frequency of adequate volume blood cultures
- Frequency of optimal volume blood cultures
- Method of diagnosis of fungal infections

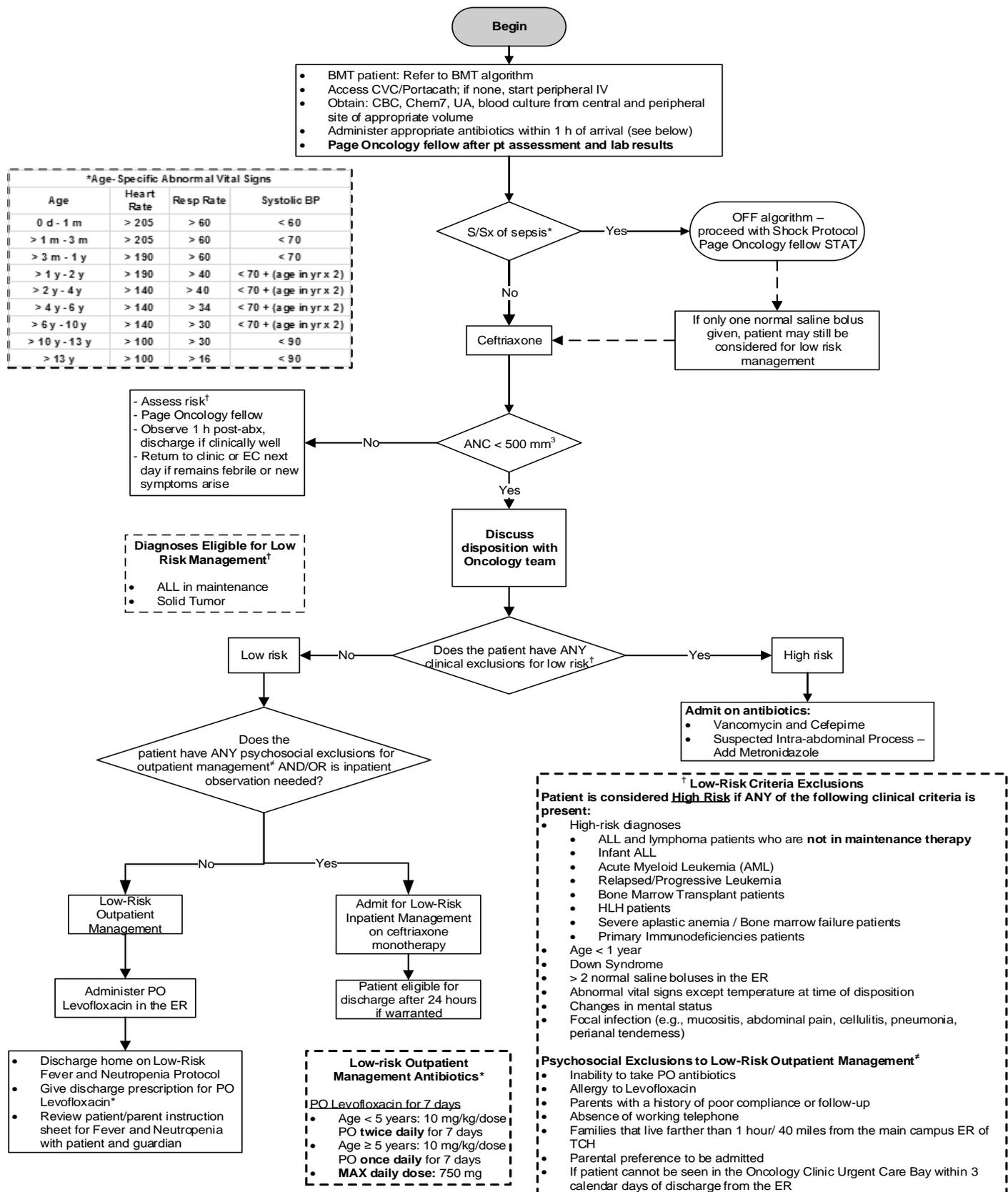
**Outcome**

- Readmission through EC or TXCH triage for fever and neutropenia
- Patients transferred to PICU within 72 hours of admission
- Patients admitted for monotherapy whose antibiotics were changed
- Admission due to positive blood culture after discharge from EC or TXCH triage
- Rate of bacteremia for low risk patients
- Admission rate for low risk patients discharged home from the EC

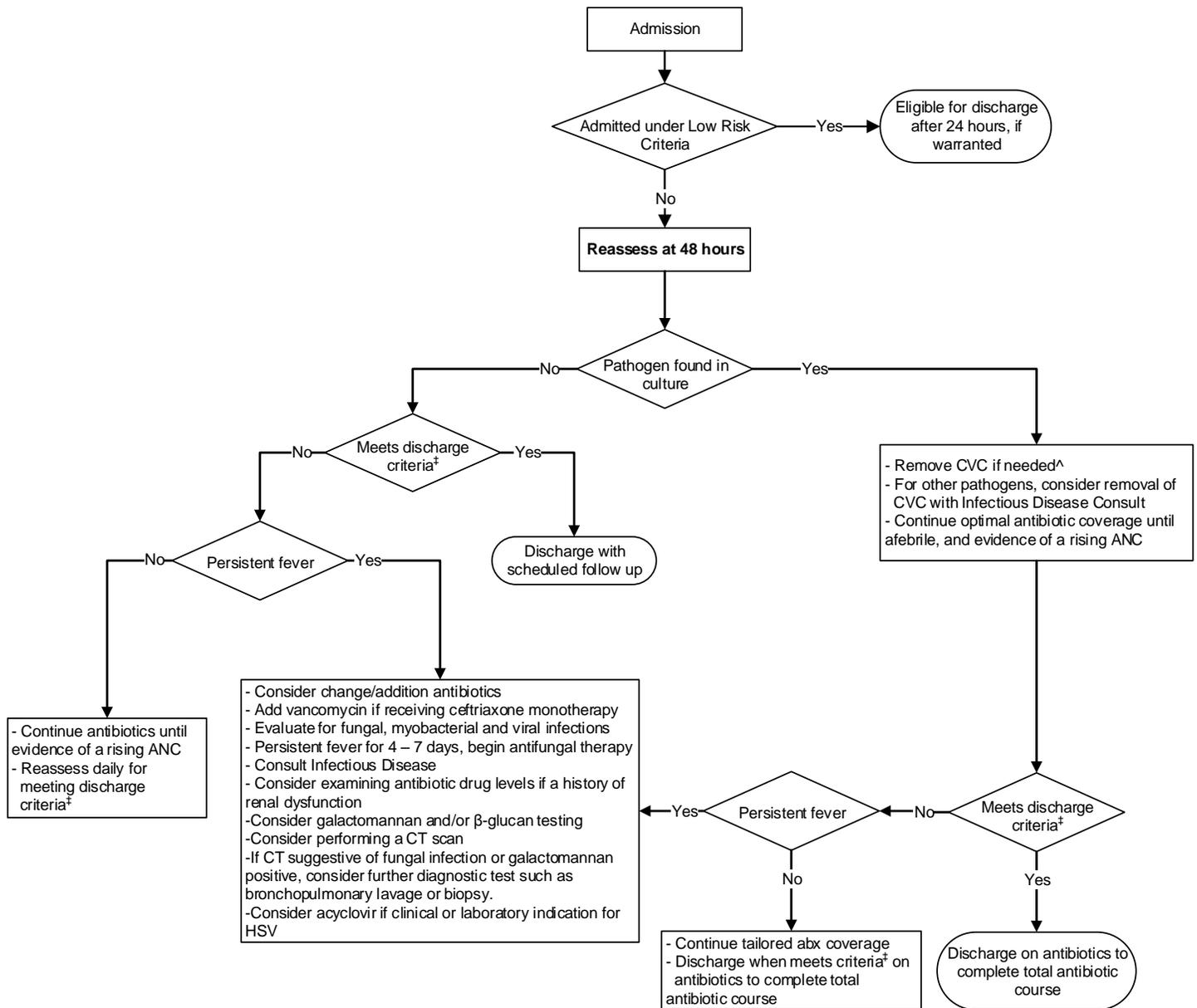
**Table 3. Antibiotic Therapy (2,12-17,43-45)**  
**(For Hematology/Oncology and BMT Patients)**

Patient Class	Medications	Dose and Frequency
<b>On Arrival in EC or TXCH Clinic</b>	Ceftriaxone	50 mg/kg/dose IV for one dose <b>MAX:</b> 2 grams/dose
<b>Outpatient Low Risk Treatment</b> (refer to Patient <u><b>Risk Assessment</b></u> for eligibility)	Levofloxacin	Age <5 years: 10 mg/kg/dose PO twice daily for 7 days Age ≥5 years: 10 mg/kg/dose PO once daily for 7 days <b>MAX</b> daily dose: 750 mg
<b>Inpatient Low Risk Management</b>	Ceftriaxone	50 mg/kg/dose IV every 24 hours <b>MAX:</b> 2 grams/dose
<b>Inpatient High Risk Management</b>	Vancomycin	Weight <70 kg: 15 mg/kg/dose IV every 8 hours Weight ≥70 kg: 1000 mg/dose IV every 12 hours <b>MAX:</b> 1 gram/dose
	Cefepime	50 mg/kg/dose IV every 8 hours <b>MAX:</b> 2 grams/dose
	<u>Suspected Intra-abdominal Process</u> Add MeTRONidazole	7.5 mg/kg/dose IV every 6 hours <b>MAX:</b> 500 mg/dose

**TCH Evidence-Based Outcomes Center**  
**Clinical Algorithm for Fever and Neutropenia in Children Receiving Cancer Treatment or With Blood Disorders**  
**EC Algorithm**



**TCH Evidence-Based Outcomes Center**  
**Clinical Algorithm for Fever and Neutropenia in Children Receiving Cancer Treatment or With Blood Disorders**  
 Inpatient Algorithm



**<sup>‡</sup>Discharge Considerations**

- Afebrile for ≥ 24 hrs
- Negative BC for 48 h
- No signs of localized infection
- Evidence of a rising ANC
- 24 h caregiver available at home, able to take temperature, lives within 1 h from accessible medical care, phone and transportation access

**Preserving/Removing the Central Line <sup>^</sup>**

Prompt removal of the central line should be considered when any of the following conditions and/or organisms exists:

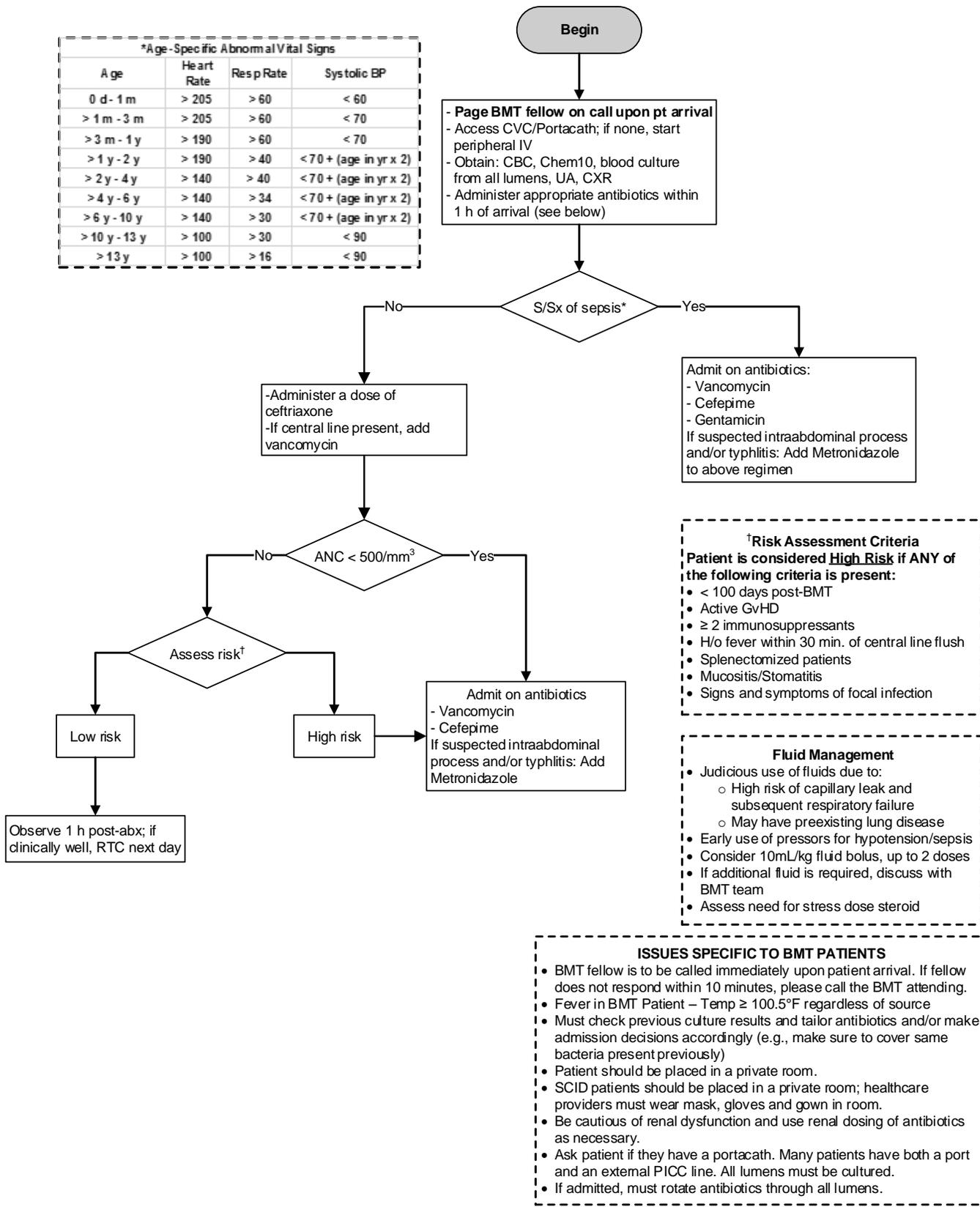
- Severe sepsis
- Endocarditis
- Bloodstream infection that continues despite > 72 h of antimicrobial therapy to which the infecting microbes are susceptible
- Infections due to *S. aureus*, gram-negative bacilli including *P. aeruginosa*, *Bacillus* species, and/or enterococci

Prompt removal of the catheter is necessary in cases of:

- Infections due to mycobacteria and/or fungi
- Tunnel site infection (e.g., redness, inflammation along catheter line, purulent drainage)
- Suppurative thrombophlebitis

**TCH Evidence-Based Outcomes Center  
Clinical Algorithm for Management of BMT Patient with Fever**

*Age-Specific Abnormal Vital Signs			
Age	Heart Rate	Res p Rate	Systolic BP
0 d - 1 m	> 205	> 60	< 60
> 1 m - 3 m	> 205	> 60	< 70
> 3 m - 1 y	> 190	> 60	< 70
> 1 y - 2 y	> 190	> 40	< 70 + (age in yr x 2)
> 2 y - 4 y	> 140	> 40	< 70 + (age in yr x 2)
> 4 y - 6 y	> 140	> 34	< 70 + (age in yr x 2)
> 6 y - 10 y	> 140	> 30	< 70 + (age in yr x 2)
> 10 y - 13 y	> 100	> 30	< 90
> 13 y	> 100	> 16	< 90



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### Related Documents

- Low Risk Fever and Neutropenia Discharge Instructions - English
- Low Risk Fever and Neutropenia Discharge Instructions - Spanish

### Clinical Standards Preparation

This clinical standard was prepared by the Evidence-Based Outcomes Center (EBOC) team in collaboration with content experts at Texas Children's Hospital. Development of this clinical standard supports the TCH Quality and Patient Safety Program initiative to promote clinical standards and outcomes that build a culture of quality and safety within the organization.

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No relevant financial or intellectual conflicts to report.

### Development Process

This clinical standard was developed using the process outlined in the EBOC Manual. The literature appraisal documents the following steps:

- Review Preparation
  - PICO questions established
  - Evidence search confirmed with content experts
- Review of Existing External Guidelines
  - TCH Fever and Neutropenia in Children Receiving Cancer Treatment (April 2010), Guideline for the Management of Fever and Neutropenia in Children With Cancer and/or Undergoing Hematopoietic Stem-Cell Transplantation (Dec 2012), Infectious Disease Society of America Clinical Practice Guideline for the Use of Antimicrobial Agents in Neutropenic Patients with Cancer (2010), Prevention and Treatment of Cancer Related Infections National Comprehensive Cancer Network (2012), Neutropenic Sepsis: Prevention and Management of Neutropenic Sepsis in Cancer Patients (2012)
- Literature Review of Relevant Evidence
  - Searched: PubMed, Cochrane, CINAHL, Google Scholar
- Critically Analyze the Evidence
  - 12 meta-analyses, 3 randomized studies, 19 non-randomized studies

### 5. Summarize the Evidence

- Materials used in the development of the guideline, evidence summary, and order sets are maintained in a Fever and Neutropenia in Children Receiving Cancer Treatment or with Blood Disorders Clinical Guideline evidence-based review manual within EBOC.

### Evaluating the Quality of the Evidence

Published clinical guidelines were evaluated for this review using the **AGREE II** criteria. The summary of these guidelines are included in the literature appraisal. AGREE II criteria evaluate Guideline Scope and Purpose, Stakeholder Involvement, Rigor of Development, Clarity and Presentation, Applicability, and Editorial Independence using a 4-point Likert scale. The higher the score, the more comprehensive the guideline.

This clinical standard specifically summarizes the evidence *in support of* or *against* specific interventions and identifies where evidence is *lacking/inconclusive*. The following categories describe how research findings provide support for treatment interventions.

**"Evidence Supports"** provides evidence to support an intervention

**"Evidence Against"** provides evidence against an intervention.

**"Evidence Lacking/Inconclusive"** indicates there is insufficient evidence to support or refute an intervention and no conclusion can be drawn *from the evidence*.

The **GRADE** criteria were utilized to evaluate the body of evidence used to make practice recommendations. The table below defines how the quality of the evidence is rated and how a strong versus weak recommendation is established. The literature appraisal reflects the critical points of evidence.

Recommendation	
<b>STRONG</b>	Desirable effects clearly outweigh undesirable effects or vice versa
<b>WEAK</b>	Desirable effects closely balanced with undesirable effects
Quality	Type of Evidence
<b>High</b>	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies
<b>Moderate</b>	Evidence from RCTs with important limitations (e.g., inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies
<b>Low</b>	Evidence for at least 1 critical outcome from observational studies, RCTs with serious flaws or indirect evidence
<b>Very Low</b>	Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence

### Recommendations

Practice recommendations were directed by the existing evidence and consensus amongst the content experts. Patient and family preferences were included when possible. The Content Expert Team and EBOC team remain aware of the controversies in the diagnosis/management of Fever and Neutropenia in Children Receiving Cancer Treatment or with Blood Disorders Clinical Guideline in children. When evidence is lacking, options in care are provided in the clinical standard and the accompanying order sets (if applicable).

### Approval Process

Clinical standards are reviewed and approved by hospital committees as deemed appropriate for its intended use. Clinical standards are reviewed as necessary within EBOC at Texas Children's Hospital. Content Expert Teams are involved with every review and update.

**Disclaimer**

Practice recommendations are based upon the evidence available at the time the clinical standard was developed. Clinical standards (guidelines, summaries, or pathways) do not set out the standard of care and are not intended to be used to dictate a course of care. Each physician/practitioner must use his or her independent judgment in the management of any specific patient and is responsible, in consultation with the patient and/or the patient's family, to make the ultimate judgment regarding care.

**Version History**

Action	Date
Originally completed	June 2010
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