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°C (101°F) or a temperature ≥ 38.0 °C (100.4°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/ mm³), moderate (ANC ≥ 200-500/ mm³) or severe (ANC < 200/ mm³). (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 ≥ 500) and fever (< 7 days) respond better than those with moderate to severe neutropenia (ANC < 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)

Guideline Eligibility Criteria
Child with fever and neutropenia receiving therapy for cancer
Child with fever after BMT see page 4 & BMT algorithm

Guideline Exclusion Criteria
Septic Shock

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>
<thead>
<tr>
<th>Table 1. Vital Sign Changes of Sepsis (45)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chills</strong></td>
</tr>
<tr>
<td><strong>Age</strong></td>
</tr>
<tr>
<td>1wk-1m</td>
</tr>
<tr>
<td>1m – 1yr</td>
</tr>
<tr>
<td>1yr -5 yr</td>
</tr>
<tr>
<td>5yr -12 yr</td>
</tr>
<tr>
<td>12yr -&lt;18 yr</td>
</tr>
</tbody>
</table>

History: Assess
- 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, Hx MRSA, recent CVL 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 perirectal areas
- Central line-note any redness or drainage along tunnel or at exit site
- Mental status and changes in sensorium

Laboratory Studies: Assess
- Complete CBC, Chem 7, urinalysis (bagged or clean catch only), blood culture (CVL-all lumens)
- Optional studies to consider: C-reactive protein (CRP), stool cultures for Hx 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

### Table 2. Signs and Symptoms of Shock

<table>
<thead>
<tr>
<th>Early</th>
<th>Intermediate</th>
<th>Late</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin warm, pink, dry</td>
<td>Skin cool, mottled</td>
<td>Trunk cool, mottled</td>
</tr>
<tr>
<td>Beginning ↓ perfusion</td>
<td>Clamy extremities</td>
<td>Cold extremities</td>
</tr>
<tr>
<td>Chills and fever</td>
<td>↑ thirst, ↓ urine output</td>
<td>No urine output</td>
</tr>
<tr>
<td>Normal RR, HR, BP</td>
<td>Increasing HR, BP, ↑ RR</td>
<td>↓ BP &amp; cardiac output</td>
</tr>
<tr>
<td>Early signs of confusion</td>
<td>↑ hypoxia and mental confusion</td>
<td>Delirium progressing to coma</td>
</tr>
<tr>
<td>Slight ↓ PO₂</td>
<td>Pulmonary congestion</td>
<td>Metabolic, lactic acidosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hemorrhagic lesions</td>
</tr>
</tbody>
</table>
## CRITICAL POINTS OF EVIDENCE

<table>
<thead>
<tr>
<th>Evidence Supports</th>
<th>Evidence Inconclusive</th>
<th>Evidence Against</th>
</tr>
</thead>
<tbody>
<tr>
<td>-Fever and neutropenia risk factor assessment: recent chemotherapy, prolonged hospitalization, prolonged granulocytopenia, broad spectrum abx use, relapse, indwelling catheters, damaged mucosa, recent steroids, hyperalimentation, increased CRP, decreased platelets (1-16)</td>
<td>- Surveillance BC in the presence of neutropenia (32)</td>
<td>- Cefepime as an abx agent (22, 23-24 systematic reviews)</td>
</tr>
<tr>
<td>-Definition of low risk patients: No comorbidity, no signs of bacterial infection, AMC &gt; 100, CRP ≤ 0.90 mg/mL (17-19)</td>
<td>- Repeated blood cultures after starting abx (1-2)</td>
<td>- Empiric use of carbapenems as first line agents (22, 23-24 systematic reviews)</td>
</tr>
<tr>
<td>-Ceftazidime, piperacillin/tazobactam, imipenem/cilastatin and meropenem as suitable agents for monotherapy (9, 20-24)</td>
<td>- IL6, IL8, Procalcitonin as part of initial work up (2, 7-8)</td>
<td>- HSV as a common infection in children with cancer with febrile neutropenia (31)</td>
</tr>
<tr>
<td>-GCSF leads to earlier recovery but does not influence mortality (25-29)</td>
<td>- abx impregnated catheters (33)</td>
<td>- CXR in absence of respiratory symptoms (41-44)</td>
</tr>
<tr>
<td>-Removal of central venous catheter in presence of specific pathogens such as: <em>P aeruginosa</em>, <em>Bacillus</em> species, vancomycin-resistant enterococci, <em>Stenotrophomonas maltophilia</em>, <em>C jeikeium</em>, <em>Acinetobacter</em> species, polymicrobial organisms, atypical mycobacteria, multidrug resistant organism or fungemia due to <em>Candida</em> (2, 28-30)</td>
<td>- GCSF routine use (25-26)</td>
<td>- Lumbar puncture (1-2)</td>
</tr>
<tr>
<td>-HSV prolongs mucositis (31)</td>
<td>- Benefit versus toxicity of granulocytes (1-2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Rotating abx through central catheter lumens (1-2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Peripheral blood cultures in patients with a CVL (28, 34-36)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Minimum blood volume for cultures (2 mL) (37)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Pipercillin-tazobactam as safe alternative in pts &lt; 25 months (21)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Early discharge and daily outpatient therapy at 72 hours of therapy for neutropenic cancer patients who are afebrile for minimum 24 hours, negative initial blood culture or two negative repeat cultures, absence of localized infection, performance scale score of ≥ 80, ANC ≥ 100, not in or after first induction therapy for AML, reside within 1 hour of hospital (38)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Oral treatment as an acceptable alternative to IV antibiotic (abx) treatment in low risk febrile neutropenic cancer patients (excluding patients with acute leukemia) in continuation therapy who are hemodynamically stable, without organ failure, not having pneumonia, infection of a central line or a severe soft tissue infection (39-40; same study sample)</td>
<td></td>
</tr>
</tbody>
</table>
## PRINCIPLES OF CLINICAL MANAGEMENT FOR CHILDREN RECEIVING CANCER TREATMENT

### Risk Factors for Life-Threatening Infection

<table>
<thead>
<tr>
<th>Risk Assessment at presentation of F&amp;N (High Risk if + for any of these factors)</th>
<th>Discharge Criteria (All below must be present)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Signs and symptoms of sepsis</td>
<td>1. Afebrile ≥ 24 hr</td>
</tr>
<tr>
<td>2. Focal infection (examples include: mucositis, abdominal pain, cellulitis, pneumonia, perianal tenderness)</td>
<td>2. Negative BC for 48 hrs</td>
</tr>
<tr>
<td>3. ANC &lt; 100/mm³</td>
<td>3. No signs of focal infection</td>
</tr>
<tr>
<td>4. &lt; 7 days since receiving intensive chemotherapy including- dexamethasone as cancer treatment</td>
<td>4. ANC &gt; 100/mm³ and climbing</td>
</tr>
<tr>
<td>5. Infant ALL, ALL/Lymphoma during any phase other than maintenance, AML, relapse</td>
<td>5. Performance scale score at baseline</td>
</tr>
</tbody>
</table>

### Early Assessment and Diagnostic Work-up

- Careful, detailed history and thorough physical exam
- Initiate Life Threatening Lab System – CBC, BUN, Cr
- Draw other labs: Lyses, LFTs, urinalysis, blood culture from all CVL lumens/ports, site specific cultures as clinically indicated
- Diagnostic Imaging – CXR if signs/symptoms including chest pain, tachypnea, decreased pulse oximetry

### Expeditious Treatment

- Be prepared to start IV or access CVL and draw blood
- Initiate abx ASAP (preferably within ONE HOUR of arrival)
- Normal saline bolus for hypotension
- Blood product support if needed

### Correct initial ABX choices for inpatient treatment

**Low Risk:** Cefazidime as monotherapy

**High Risk:** Vancomycin, Piperacillin/tazobactam, Gentamicin

All antibiotics should be rotated among the different CVL 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.

Patients with history of renal dysfunction calculate antibiotic dosing with creatinine clearance method below

| If patient continues with fever > 48 hrs and on monotherapy: add Vancomycin |
| If patients continues fever > 48 hrs and on triple abx consider changing/adding abx |

**If fever continues on ABX for > 5 days begin antifungal agents, pursue further evaluation of infection source and consider ID consult**

### Careful Ongoing Assessment

- Careful monitoring should continue as long as the child is neutropenic
- Daily evaluate
  - Central venous catheter site(s)
  - Surgical incisions, other breaks in skin
  - Oral mucosa
  - Peri-rectal area
- Daily blood culture while patient is febrile
- With continued fever repeat urine, stool, and tissue cultures, obtain diagnostic imaging as clinically indicated

### Monitor Toxicities

- Complete blood count with differential daily until afebrile, then every other day
- Serum chemistries at least every 3 days - monitor for electrolyte depletion, hepatic & renal toxicity
- Monitor creatinine daily if rises over baseline
- Urine samples – monitor for glucosuria, 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 3rd to 5th dose

| *Creatinine Clearance estimation method:* |
| children (6 months – 20 years) = k x length (cm) |
| serum creatinine (mg/dL) |
| k = 0.33 in preterm infants; 0.45 in full term infants; 0.55 in children and adolescent girls; 0.7 in adolescent boys |
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 °C (100.5°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/mm³), moderate (ANC $\geq$ 200-500/mm³) or severe (ANC < 200/mm³). (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. (3-5)

**Rationale:** Because of the high-risk of infection post BMT (whether 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. (6)

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

<table>
<thead>
<tr>
<th>Gram positive</th>
<th>Gram negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus</td>
<td>E. coli</td>
</tr>
<tr>
<td>Streptococcus</td>
<td>Enterobacter</td>
</tr>
<tr>
<td>Enterococcus</td>
<td>Klebsiella</td>
</tr>
<tr>
<td></td>
<td>Pseudomonas</td>
</tr>
</tbody>
</table>

**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
- Tachycardia
- Hypotension
- Pulse oximetry < 95%
- Decreased urine output
- Early - warm, flushed, dry skin
- Late - cool, clammy skin

**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 (see Tables 1 and 2, page 1)
- 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

**Laboratory Studies: Assess**
- Complete CBC, Chem 10, LFTs
- Blood culture (CVL-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
### Antibiotic Therapy

<table>
<thead>
<tr>
<th>ANC &gt; 500 - Emergency Center or TXCCC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dose and Frequency</strong></td>
</tr>
<tr>
<td>Ceftriaxone</td>
</tr>
<tr>
<td>50mg/kg/dose IV x 1 dose; MAX: 2000mg/dose</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ANC &lt; 500 – Admit on Low Risk Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dose and Frequency</strong></td>
</tr>
<tr>
<td>Ceftazidime</td>
</tr>
<tr>
<td>50mg/kg/dose IV every 8 hours; MAX: 2000mg/dose</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ANC &lt; 500 – Admit on High Risk Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dose and Frequency</strong></td>
</tr>
<tr>
<td>Vancomycin</td>
</tr>
<tr>
<td>Children &lt; 70 kg: 15mg/kg/dose IV every 8 hours</td>
</tr>
<tr>
<td>Children &gt; 70 kg: 1000mg/dose IV every 12 hours; MAX: 1000mg/dose</td>
</tr>
</tbody>
</table>

| Piperacillin/tazobactam                |
| Infants 2 – 8 months: 80mg/kg/dose piperacillin component IV every 8 hours |
| Infants > 9 months and Children < 40kg: 100mg/kg/dose piperacillin component IV every 8 hours; MAX 18gm/day piperacillin |
| Children > 40kg and Adults: 3.375gms IV every 6 hours or 4.5gms every 6-8 hours; MAX: 18gm/day piperacillin |

| Gentamicin                             |
| Infants and children: 2.5mg/kg/dose IV every 8 hours |
| Adults: 1.7mg/kg/dose IV every 8 hours; MAX: 120mg/dose |

### Discharge Criteria

1. Afebrile ≥ 24 hr
2. Negative BC for 48 hrs
3. No signs of focal infection (examples include: mucositis, abdominal pain, cellulitis, pneumonia)
4. ANC > 100/mm³ and climbing***
5. Performance scale score at baseline
6. 24 hr caregiver available at home, able to take temperature, live within 1 hr of accessible medical care, phone and transportation access

*** or as suggested by patient’s cancer therapy protocol

### Outcome Measures

- Readmission through EC or TXCCC triage for fever and neutropenia
- Patients transferred to PICU within 72 hours of admission
- Antibiotics administration initiated within one hour of patient arrival to ER or TXCCC triage
- Patients admitted for monotherapy who were changed to triple antibiotics
- Admission due to positive blood culture after discharge from EC or TXCCC triage
TCH Evidence-Based Clinical Decision Support Center
Clinical Algorithm for Fever and Neutropenia in Children Receiving Cancer Treatment

- Assess for v/s sepsis and serious infection
- No signs of sepsis or serious infection give IV ceftriaxone
- Observe 1 hr post abx discharge if clinically well
- Return to clinic or EC next day if remains febrile or new symptoms

ANC <500/mm³

NO

Low risk

Initiate IV abx within 1 hr of arrival
- Cefazidime

Admit

YES

High risk

Initiate IV abx within 1 hr of arrival
- Vancomycin
- Piperacillin/tazobactam
- Gentamicin

Admit

Reassess at 48 hrs

Pathogen found in culture

NO

YES

Meets discharge criteria

Discharge on abx to complete total abx course

 Persistent fever

NO

YES

Meets discharge criteria

NO

Persistent fever

NO

YES

END

Risk Assessment Criteria
- Patient is considered high risk if ANY of the following criteria is present
- Signs and symptoms of sepsis
- ANC <100/mm³
- Focal infection (examples include mucositis, abdominal pain, cellulitis, pneumonia, perianal tenderness)
- >7 days since receiving intensive chemotherapy + dexamethasone as cancer treatment
- Infant ALL, ALL, lymphoma during any phase other than maintenance, AML, relapse

Signs and symptoms of sepsis
- Chills
- Age-specific vital signs

<table>
<thead>
<tr>
<th>Age</th>
<th>Heart rate/min</th>
<th>Systolic BP</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 wk</td>
<td>&gt;180 or &lt; 100</td>
<td>&lt;79</td>
</tr>
<tr>
<td>1 wk - 1m</td>
<td>&gt;180 or &lt; 90</td>
<td>&lt;75</td>
</tr>
<tr>
<td>1m - 1yr</td>
<td>&gt;140</td>
<td>&lt;74</td>
</tr>
<tr>
<td>1 yr - 5 yr</td>
<td>&gt;130</td>
<td>&lt;83</td>
</tr>
<tr>
<td>5 yr - 12yr</td>
<td>&gt;110</td>
<td>&lt;90</td>
</tr>
</tbody>
</table>


Discharge Criteria
- Afebrile for ≥24 hrs
- Negative BC for 48 hrs
- No signs of localized infection
- Performance scale score to baseline
- ANC >100/mm³ and climbing
- 24 hr caregiver available at home, able to take temperature, live within 1 hr from accessible medical care, phone and transportation access

Discharge with scheduled follow up

Persistent fever

NO

YES

Consider change/additional abx
- Add vancomycin if receiving cefazidime monotherapy
- Persistent fever for 5 days begin antifungal therapy
- Consult Infectious Disease
- Examine antibiotic drug levels
- Evaluate for fungal, mycobacterial and viral infections

YES

Continuous tailored abx coverage
- Discharge when meets criteria on abx to complete total abx course

YES

Discharge on abx to complete total abx course
TCH Evidence-Based Clinical Decision Support Center
Clinical Algorithm for Management of BMT Patient with Suspected Infection

- Page BMT Fellow on call upon patient arrival
- Assess risk
- Obtain: CBC, chem10, blood culture from all lumens, UA, CXR
- VBG and lactate level if ill-appearing

Initiate IV abx within 1 hr of arrival
- No signs s/s sepsis
  - Vancomycin
  - Ceftazidime
- Signs s/s sepsis
  - Vancomycin
  - Piperacillin/tazobactam
  - Gentamicin

ANC <500/mm³

Risk Assessment Criteria
- Patient is considered **High Risk** if ANY of the following criteria is present
  - Signs and symptoms of sepsis
  - < 100 days post BMT
  - Active GVHD
  - ≥2 immunosuppressants
  - INR fever within 30 mins of central line flush
  - Splenectomized patients
  - Mucositis/stomatitis
  - Signs and symptoms of focal infection

Low risk

Central Line

High risk

Initiate IV abx within 1 hr of arrival
- Vancomycin
- Ceftaxone
Observe 1 hr post abx if clinically well, RTC next day

Fluid Management
- Judicious use of fluids
- High risk of capillary leak and subsequent respiratory failure
- May have pre-existing lung disease
- Early use of pressors for hypotension/episodes

Initiate IV abx within 1 hr of arrival
- No signs s/s sepsis
  - Vancomycin
  - Ceftazidime
- Signs s/s sepsis
  - Vancomycin
  - Piperacillin/tazobactam
  - Gentamicin

Admit

ISSUES SPECIFIC TO BMT PATIENTS
- BMT fellow is to be called immediately upon patient arrival. If fellow does not respond within 10 minutes, please call the BMT attending
- Fever in BMT Patient – Temp ≥ 100.5 regardless of source
- Must check previous culture results and tailor antibiotics and/or make admission decisions accordingly (i.e., make sure to cover same bacteria present previously)
- Patients should be placed in a private room
- SCID patients should be placed in a private room. Healthcare providers must wear mask, gloves and gown in room
- Be cautious of renal dysfunction and use renal dosing of abx as necessary
- Ask patient if they have a port/cath. Many patients have both, a port and an external PICC line. All lumens must be cultured
- If admitted, must rotate abx though all lumens

References

Chills
Age-specific vital signs
- Heart rate min
- Systolic BP
- 1wk-Im
  - >180 or <100
  - <79
- 1m-yr
  - >180 or <90
  - <75
- 1 yr - 5 yr
  - >140
  - <74
- 5 yr - 12 yr
  - >130
  - <83
- 12 yr - 13 yr
  - >110
  - <90


Guideline Preparation

This guideline was prepared by the Evidence-Based (EB) Clinical Decision Support Team in collaboration with content experts at Texas Children’s Hospital and the Texas Children’s Pediatric Associates. Development of this guideline supports the TCH Quality and Patient Safety Program initiative to promote clinical guidelines and outcomes that build a culture of quality and safety within the organization.

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Development Process

This guideline was developed using the process outlined in the EB Clinical Decision Support Manual (2007). The review summary documents the following steps:

1. Review Preparation
   - PICO questions established
   - Evidence search terms confirmed with content experts

2. Review of Existing Internal and External Guidelines
   - TCCC Guidelines for Empiric Antibiotic Coverage (3/9/2006) and TCCC Guidelines for Approach to Neutropenic Disorders in Childhood (19/22/2006); Six external guidelines reviewed

3. Search for Relevant Evidence
   - Searched: Embase, PubMed, Cochrane, AHRQ, CINAHL, Trip, Best BETS, AAP, PedsCCM, U of Mich, Google Scholar

4. Critically Analyze the Evidence
   1. Systematic Review 5 metaanalysis, 5 RCTs, 22 Non randomized studies, 4 reviews, 2 abstracts

5. Summarize the Evidence by preparing the guideline, order sets and interdisciplinary plan of care
   - Materials used in the development of the guidelines, review summaries and content expert team meeting minutes are maintained in a fever & neutropenia EB review manual within the Center for Quality.

Evaluating the Quality of the Evidence

The Critical Appraisal Skills Program (CASP) criteria were used to evaluate the quality of articles reviewed. Application of the CASP criteria are completed by rating each reviewed study or review as:

Strong study/systematic review - well designed, well conducted, adequate sample size, reliable measures, valid results, appropriate analysis, and clinically applicable/relevant.

Study/systematic review with minor limitations - specifically lacking in one of the above criteria

Study/systematic review with major limitations - specifically lacking in several of the above criteria.

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

“Evidence that supports” the guideline (p.1) provides clear evidence from more than one well-done randomized controlled trial (RCT) (based on CASP criteria) that the benefits of the intervention exceed harm.

“Evidence against” (p.1) provides clear evidence from more than one well-done RCT (based on CASP criteria) that the intervention is likely to be ineffective or that it is harmful.

“Evidence lacking” (p.1) indicates there is currently insufficient data or inadequate data to recommend for or against specific intervention.

Recommendations

Recommendations for the guidelines were developed by a consensus process directed by the existing evidence, content experts and patient and family preference when possible. The Content Expert Team and EB Clinical Decision Support Team remain aware of the controversies in the management of fever and neutropenia in pediatric oncology patients. When evidence is lacking, options in care are provided in the guideline and the order sets that accompany the guideline.

Approval Process

Guidelines are reviewed and approved by the Content Expert Team, EB Clinical Decision Support Team, EB Executive Steering Team, Pharmacy and Therapeutics Committee and other appropriate hospital committees as deemed appropriate for the guideline’s intended use.

Guidelines are reviewed and updated as necessary every 2 years within the EB Clinical Decision Support Team at Texas Children’s Hospital. Content Expert Teams will be involved with every review and update.

Disclaimer

Guideline recommendations are made from the best evidence, expert opinions and consideration for the patients and families cared for within TCH/TCPA. The guideline is NOT intended to impose standards of care preventing selective variation in practice that are necessary to meet the unique needs of individual patients. The physician must consider each patient’s circumstance to make the ultimate judgment regarding best care.

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