IMPLEMENTATION OF A RAPID RESPONSE FEVER PROTOCOL FOR IMMUNOCOMPROMISED PATIENTS WITH HEMATOLOGICAL MALIGNANCIES

A Quality Improvement Initiative at the University of Colorado Hospital

Glen J. Peterson, RN, DNP, ACNP
Clinical Director, APP Education & Quality
Blood Cancer/Blood and Marrow Transplant
University of Colorado Hospital
University of Colorado Health
OBJECTIVES

• To discuss risk factors associated with fever and infection in the immunocompromised host
• To describe the significance of fever and infection in oncology patients
• To discuss initial strategies for fever management in oncology patients
• To discuss Rapid Response Fever Protocol implementation in immunocompromised patients
WHY DO WE CARE ABOUT FEVER???

- 80% of patients with a heme malignancy will develop FEVER
- 10-40% of solid tumor oncology patients will develop FEVER
- FEVER is a sign of INFECTION
- FEVER is a sign of SEPSIS
- FEVER may be the ONLY sign of INFECTION and impending SEPSIS
- SEPSIS may progress to SHOCK and DEATH
WHY DO WE CARE ABOUT SEPSIS???

- Sepsis is the 10th leading cause of death in the United States
- Mortality rate nearly 30% and >50% in cancer patients
- Leading cause of non-relapse mortality in patients with cancer
- 1 out of 10 admitted with neutropenic fever will die of SEPSIS
- FEVER may be the only sign of SEPSIS in oncology patients
- Serious infections cause delays in cancer treatment
- Serious infections impact quality of life, survival and cost
WHO IS AT RISK FOR SEPSIS???

- Immunocompromised patients
  - Innate
  - Adaptive/acquired
- Neutropenia
  - Chemotherapy
  - Medications
  - Bone marrow failure
- Immunosuppression
  - Chemotherapy
  - Targeted therapies/monoclonal antibodies
  - GVHD treatment
RISK FOR SEPSIS Cont’d…

- The very young (<1 yr)
- The old (>65 yr)
- Those with comorbidities
  - Diabetes
  - Lung disease
  - CHF
  - Psychological instability
  - Recent surgery/invasive/dental procedure
  - Lines and devices
  - Immobility/wounds
DISEASE AND TREATMENT CONSEQUENCES

- Breakdown of mucocutaneous barrier
  - Tumor invasion
  - Surgical intervention
  - Chemotherapy
  - TBI/localized XRT
  - Lines/tubes
  - GVHD
- Cellular destruction
  - Phagocytes
  - B/T-cells/Asplenia
  - Disease
- Neurologic/functional/nutritional impairment
CAUSES OF FEVER

• Variety of infections
• Medications
  • Antibiotics
  • Chemotherapy
  • Monoclonal Abs
  • ATG
• Malignancy
• Inflammatory conditions
  • GVHD
  • Connective tissue disorders
• Endocrine disorders
• Vaccines/blood products
INFECTION

Viral

Bacterial

Fungal

Viral
INFECTIOUS CAUSES OF FEVER/SEPSIS

- **Gram negative bacteria**
  - Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, etc.
  - Account for 40-50% of septic shock
  - Typically more pathogenic
- **Gram positive bacteria**
  - Streptococcus pneumoniae, Staphlococcus aureus, enterococcus
  - Account for 5-10% of septic shock
  - Typically less pathogenic
- **Yeast/Fungal organisms**
  - Candida, Aspergillus, Zygomycetes
- **Viral**
- In 20% of septic shock, organism not identified
SIGN AND SYMPTOMS OF INFECTION

- Physical Exam/ROS
  - **Vital Signs** - HR, RR, BP, O2
  - **General** - *ill* appearance, *fever*, *chills*
  - **CNS** - *lethargy*, headache, disorientation, somnolence
  - **HEENT** - sinus, *oral lesions*, *thrush*, esophogitis
  - **Abdomen** - *tenderness*, *distension*, hypoactive BS, N/V/D
  - **GU** - urgency, freq, burning, hematuria, flank pain, dark urine, N/V, *decreased urinary output*
  - **Skin** - *rash*, *wounds*, erythema, drainage, IV’s, foleys, lines, etc.
FEBRILE NEUTROPENIA (FN)

- **Definition**
  - FEVER $\geq 38^\circ C$ (oral) on 2 occasions 1 hour apart OR a single temperature of $\geq 38.3^\circ C$
  - **AND**
    - ANC of $<500\text{cells/mm}^3$ or an ANC expected to decrease to $<500\text{cells/mm}^3$ during next 48 hrs.

- **Oncologic EMERGENCY**

- An analysis of $>40,000$ patients admitted with FN (1995-2000)
  - Mortality rate is nearly 10% among all cancer patients hospitalized with FN
  - Highest mortality 14.3% in leukemia
  - Mortality 21% in patients with $>1$ comorbidities
  - Average length of FN hospital stay (LOS) was 11.5 days
  - Average length of FN LOS for leukemia was 19.7 days

IDSA, 2010; Kuderer, et al.
FEBRILE NEUTROPENIA COST/LOS

• Kuderer analysis (n=55,276 encounters)-mean cost-$19,110 ($1,661/day)
  ✓ Mean leukemia FN cost $38,583 ($1,958/day)

• Caggiano analysis (n=22,060)-mean heme malignancy cost-$20,400 ($1,594/day)
  ✓ Mean leukemia FN cost-$28,200 ($1,669/day)

• Shilling analysis (n=3,814)-mean hospitalization cost-$18,042-$27,587 ($2,004-$2,189/day)
  ✓ Mean cost for hematologic malignancies-$52,579 ($2,590/day)

Kuderer, et al., 2006; Shilling, Parks, Deeter, 2011; Caggiano, et al., 2005
HOW DO WE PREVENT INFECTION???

- Minimize exposure
  - Hand hygiene (patients, caregivers, staff)
  - Masks
  - Avoid crowds and ill contacts
  - Food restrictions
  - HEPA filtration
  - Positive pressure
  - Environmental exposures (plants, flowers, soil, dust, etc.)
- Prophylactic/Empiric antibiotics
- Myeloid growth factors
The PROBLEM:
- HUGE antibiotic delays
- HUGE delays in supportive care
- HUGE delays in order entry procedures

WHERE?
- EVERYWHERE!!
  - ED
  - Clinics
  - Infusion Centers
  - Express Admit Units
  - Inpatient Units
SYSTEM STRATEGIES FOR TIMELY INTERVENTIONS

- #1 Rapidly *identify* patients at risk for sepsis
- #2 Rapidly *triage* patients at risk for sepsis
- #3 Rapidly *treat* patients at risk for sepsis

Rapid Response Treatment Protocols
DOES TIMELINESS REALLY MATTER???

- Timeliness of interventions makes a difference!!
  - reduces morbidity
  - reduces mortality
  - reduces hospital LOS
  - reduces ICU interventions
  - reduces healthcare cost
EVIDENCE SUMMARY
“EARLY INTERVENTION”

• Rivers et al. Landmark Study (2001)
  • Lower 28 and 60 day mortality rates
  • Reduced hospital LOS
  • Lower healthcare associated costs
  
  Early goal-directed anti-sepsis interventions reduce mortality and associated cost

• Kumar, et al. (2006)
  • 7.6% decrease in survival for each hour delay in antibiotics
  • 82.7% survival when antibiotics within 30 minutes
  • 77.2% survival when given within 1 hour
  • 42% survival when delayed for >6 hours

Timeliness of antibiotics improves survival

Rivers et al. (2001); Kumar, et al.
EVIDENCE SUMMARY
“ANTIBIOTIC APPROPRIATENESS”

• Gaieski, et al. (2010)
  • Improved survival when appropriate antibiotics given within 1 hour vs. >1hr (mortality 19.5% vs. 33.2%, p=.02)
  • Improved survival when given within 1 hour of qualification for EGDT vs. >1hr from EGDT qualification (25% vs. 38.5%, p=.03)

**Timeliness and appropriateness of antibiotics improves survival**

• Kumar, et al. (2009)
  • Appropriate antibiotic therapy in 80.1% of cases
  • Overall survival 43.7%
  • Survival after appropriate and inappropriate initial antibiotic therapy 52% vs. 10.3%, p<.0001.

**Inappropriate antibiotic therapy in sepsis adversely affects survival**

Kumar, et al. (2009); Gaieski, et al. (2010)
EVIDENCE SUMMARY
“CLINICAL PRACTICE GUIDELINES”

- Surviving Sepsis Campaign
- National Comprehensive Cancer Network (NCCN) Guidelines
- Infectious Disease Society of America (IDSA) Guidelines
- American Society of Clinical Oncology (ASCO)
- National Collaborating Centre for Cancer (NCC-C; NICE)

*CPG’s recommend prompt interventions to reduce morbidity and mortality related to infection*

NCCN (2012); Flowers, et al. (2013); Freifeld, et al. (2010); Dellinger, et al. (2013); NICE, (2012)
RAPID RESPONSE FEVER PROTOCOL (RRFP)
INTERVENTIONS
RAPID PATIENT IDENTIFICATION

What To Do If You Have A Fever

**If you feel cold or have chills or shaking**
- Take your temperature right away
- Take it again in 30 minutes
- Take it again 1 hour after your symptoms start

**If you get a fever higher than or equal to 100.4 °F (38°C) for 1 hour or any fever higher than or equal to 101 °F (38.3°C) during weekdays from 8AM-5PM**, please call the BIC at 720-848-2206 (2207 or 2208).

**If no answer, call back in 5 minutes. If still no answer, DO NOT leave a message. Call 720-848-0000 and ask for the BMT NP.**
- Please DO NOT take any medicine to lower your fever (acetaminophen, aspirin or ibuprofen) until you speak with a medical provider.

**For fever on weekends or after hours (5PM-8AM)**, call 720-848-0000. Ask for the After Hours BMT NP.

**Other signs of infection to report are:**
- Change in cough or a new cough
- Redness, soreness, or swelling in any area, including surgical wounds and ports
- Stiff neck or bad headache
- Unusual vaginal discharge or irritation
- Uncontrolled diarrhea
- Pain in the abdomen or rectum
- Sore throat or new mouth sores
- Nasal or sinus congestion
- Burning, painful, bleeding or increased urination
- Shortness of breath
- Uncontrolled vomiting
- Any new pain

**Call 911 if you have:**
- Chest pain
- Trouble breathing
- Uncontrolled bleeding
- Sudden and severe belly pain
- Feelings of passing out or blacking out

**When coming to the hospital**
- Wear a mask
- Stay away from sick people
- Wash your hands often

**When coming through the Emergency Department**
- Show your Patient ID card at check in
- Tell the nurses “I am a Heme/BMT patient with FEVER and a poor immune system”

© 2012, University of Colorado Hospital, Aurora November 2012
I am an immunosuppressed patient. I am getting treatment for a blood cancer at the University of Colorado Hospital.

My diagnosis is______________________________________________________

I had a Stem Cell Transplant on________________________________________

I am at high risk for infection and complications of infection

I need immediate treatment to prevent complications

My allergies are________________________________________________________

My doctor's name is____________________________________________________

My doctor’s phone number is 720-848-0300
Hematology/BMT Pathway

Patient identified as Heme/BMT patient by physician (i.e. any patient with history of active or latent Blood Cancer)

Discuss patient with Heme/BMT NP/PA (Pager # 303-266-4162) on arrival REGARDLESS OF COMPLAINT

Is Heme/BMT specific complication identified?
1. New diagnosis of a Heme/Malignancy (eg. suspected leukemia, lymphoma, multiple myeloma, etc.)
2. Relapse or progression of Heme Malignancy
3. Complications of Graft vs Host Disease (non-solid tumor)

Does patient have any of the following?
1. Cardiac dysrhythmia/condition requiring Cardiology or CCU support
   a. Acute MI requiring cardiac intervention and monitoring
   b. Any unstable dysrhythmia
   c. Any dysrhythmia requiring continuous IV medications
   d. Acute cardiac problem or exacerbation of chronic cardiac problem requiring hospital admission
2. Acute or impending surgical condition requiring Surgical Service support
   a. Acute/unstable orthopedic condition
   b. Surgical abdomen
   c. Neurosurgical condition
3. Pulmonary decompensation requiring Pulmonary Medicine/ICU support
4. Neurologic condition requiring Neurology support
   a. Stroke
   b. Status epileptics/uncontrolled seizure activity
5. Other medical problem requiring specialty management that cannot be appropriately provided on oncology patient until by oncology nursing staff

Admit to other Specialty Service (not Heme/BMT)

Heme/BMT Rapid Response Fever Protocol

NOTE: Please also reference “Presumed Severe Sepsis Pathway”

Use EPIC “ED Heme/BMT Order Set”
1. Obtain VS every 15 minutes x 4*
   a. Then every 30 minutes x 2
   b. Then every hour once normalized
   *Note: if patient unstable (SBP < 90, HR > 120, dizziness, altered mental status) -- start IV Fluid Bolus (NS 1000 cc wide open) immediately
2. Obtain blood cultures: 2 from central line and 1 from peripheral stick
3. Place lab orders for CBC with differential, CMP, Mg, Phos, LDH, Lactate, Uric Acid
4. Order Abs:
   a. 1st choice: Cefepime IV- 2 g infused over 30 minutes every 8 hours
   b. For hemodynamic instability, pneumonia, suspected line infection, skin/soft tissue infection, documented gram positive infection suspected, history of MRSA OR mucositis -- add Vancomycin 15mg/kg
   NOTE: Ideally this should be completed within 60 min of patient arrival to ED, no need to wait for laboratory testing
5. Order diagnostic testing as determined by suspected source of infection (eg. CXR, CT, UA, C&S, etc.)
6. Admit to ICU if showing signs of septic shock

Approved: EDCQI 4/2014
Heme/BMT (Peterson) 4/2014

Pathway- Heme/BMT v14_5-23-14-FINAL
RAPID PATIENT TRIAGE

EMERGENCY DEPARTMENT/DIRECT HOSPITAL ADMISSION FEVER Triage Guidelines

TELEPHONE TRIAGE GUIDELINES for determining FEVER RISK in OUTPATIENTS

Please Note: At any time (during or after business hours), patients with reported SIGNS OF ACUTE DISTRESS such as syncope/near-syncope (significant dizziness, feeling faint, significant mental status changes), moderate to severe SOB, chest pain/pressure/palpitations, severe bleeding or severe abdominal pain should be sent to the ED or instructed to call “911”

Patients meeting the below criteria who call AFTER HOURS should be Directly Admitted to the Hospital OR sent to the ED if SIGNS OF ACUTE DISTRESS or if Inpatient Bed unavailable. All others WITHOUT SIGNS OF ACUTE DISTRESS DURING BUSINESS HOURS should be triaged by the Outpatient NP

High Risk FEVER Outpatients Requiring ED/Direct Hospital Admission after Tele-Triage

- Patients with neutropenia or impending neutropenia (within 48hrs) or functional neutropenia with a hematological malignancy
- Non-neutropenic allogeneic HSCT on therapeutic immunosuppression (tacrolimus, cyclosporine, sirolimus, prednisone, monoclonal antibodies, etc.)
- Autologous HSCT patients recently discharged from transplant admission
- Life threatening comorbidity (significant bleeding, uncontrolled diabetes, uncontrolled hematologic malignancy, recent surgery or dental procedure, psychological instability, recent hospital admission for fever or serious infection, progressive immobility)
High-Risk NEUTROPENIC FEVER Patients Requiring Hospital Admission

- MASCC score <21 (see MASCC Risk Index)
- Expected or actual prolonged and profound neutropenia (chronically neutropenic patients or those undergoing AML induction or consolidation)
- Neutropenic autologous and allogeneic HSCT patients
- Hemodynamic/cardiovascular instability (SBP<90, HR>120, RR>24, new hypoxia/SOB/or pneumonia, exacerbation of COPD/asthma, CHF, new dysrhythmia, chest pain)
- Gastrointestinal symptoms such as abdominal pain, moderate to severe nausea, vomiting or diarrhea, significant oral or gastrointestinal mucositis.
- Other life threatening comorbidity (significant bleeding, uncontrolled diabetes, uncontrolled hematologic malignancy, recent surgery or dental procedure, psychological instability, recent hospital admission for fever or serious infection, progressive immobility)
- New neurologic or mental status changes
- New hepatic insufficiency (ALT/AST 5X normal)
- New renal insufficiency (creatinine clearance <30ml/min)
- Central line infection
- Fever developing while on standard antibiotic prophylaxis
- Patients who lack social support, reliable caregiver, or adequate means for urgent transportation to the hospital
RAPID PATIENT TRIAGE

High-Risk NON-NEUTROPENIC FEVER Patients Requiring Hospital Admission

- MASCC score <21 in non-neutropenic allogeneic HSCT on therapeutic immunosuppression (tacrolimus, cyclosporine, sirolimus, prednisone, monoclonal antibodies, etc.) (see MASCC Risk Index)
- Hemodynamic/cardiovascular instability (SBP<90, HR>120, RR>24, new hypoxia/SOB/or pneumonia, exacerbation of COPD/asthma, CHF, new dysrhythmia, chest pain)
- Autologous HSCT patients recently discharged from transplant admission
- Functional neutropenia with a hematological malignancy
- Other life threatening comorbidity (significant bleeding, uncontrolled diabetes, uncontrolled hematologic malignancy, recent surgery or dental procedure, psychological instability, recent hospital admission for fever or serious infection, progressive immobility)
- New neurologic or mental status changes
- New hepatic insufficiency (ALT/AST 5X normal)
- New renal insufficiency (creatinine clearance <30ml/min)

Low Risk FEVER Outpatients Potentially NOT Requiring ED/Direct Hospital Admission after Tele-Triage

- Non-neutropenic patients without symptoms of hemodynamic/cardiovascular instability, life threatening comorbidity, recent organ dysfunction or neurologic/mental status changes (described above). These patients should receive close follow-up (either telephone or physical visit-preferred) frequently until fever resolves and further infectious work-up is complete.
- No High Risk Criteria as described above
- PLEASE NOTE: the majority of patients who call After Hours with FEVER or other signs of infection should be evaluated by the NP/PA either on the Inpatient Unit or in the ED as appropriate
RAPID PATIENT TRIAGE

MASCC Risk Index

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burden of illness: no or mild symptoms</td>
<td>5</td>
</tr>
<tr>
<td>Burden of illness: moderate symptoms</td>
<td>3</td>
</tr>
<tr>
<td>Burden of illness: severe symptoms</td>
<td>0</td>
</tr>
<tr>
<td>The above are not cumulative (only score 1)</td>
<td></td>
</tr>
<tr>
<td>No hypotension (sys&gt;90)</td>
<td>5</td>
</tr>
<tr>
<td>No chronic obstructive pulmonary disease</td>
<td>4</td>
</tr>
<tr>
<td>Solid tumor or hematologic malignancy with no previous fungal infection</td>
<td>4</td>
</tr>
<tr>
<td>No dehydration requiring IV fluids</td>
<td>3</td>
</tr>
<tr>
<td>Outpatient status at time of fever</td>
<td>3</td>
</tr>
<tr>
<td>Age &lt;60</td>
<td>2</td>
</tr>
</tbody>
</table>

**MASCC score ≥21 = low-risk patient**

**MASCC score <21 = high-risk patient**

MASCC analysis:

- Low risk (MASCC ≥21) (n-551)-6% serious complications, 1% death
- High risk (MASCC <21) (n-205)-39% serious complications, 14% death

Klastersky, et al., 2000
HEME/BMT RAPID RESPONSE FEVER PROTOCOL (RRFP)

Patient Qualifies for RAPID RESPONSE FEVER PROTOCOL
Hospital Admission

Please note: This pathway is NOT an order set. This is a guideline for nurses for the INITIAL (first hour) management of Heme/BMT patients who are directly admitted with FEVER. This pathway will be accompanied by an order set.

↓

Vital Signs

↓

Labs
(CBC/diff, CMP, Mg, Phos, LDH, Uric acid, Lactate)

↓

Blood cultures
(2 sets from Central Line and 1 simultaneous peripheral set)
If difficult peripheral stick, complete Central Line cultures only OR 2 set peripherally if no Central Line

↓

IV Fluid Bolus
(NS 1000cc wide open)
If patient unstable (SBP<90, HR>120, dizziness, altered mental status), start IV Fluid Bolus immediately after Vital Signs and notify NP/MD immediately

↓

ANTIBIOTICS
Per NP/MD order

Above interventions to be completed within 30 min. of patient admission

↓

Diagnostic Testing/Source ID
CXR, CT, UA C&S, etc.
Do NOT delay antibiotics waiting for CXR or UA!

↓

11th Floor Inpatient Management OR ED/ICU Transfer if Unstable
RAPID PATIENT TREATMENT

Recommended Antibiotic Management for High-Risk Patients

Cefepime 2gm IV every 8 hours (use in all patients without severe allergy to penicillin or cephalosporins)
OR
Meropenem 1000mg IV every 8 hours (if concern of anaerobic or ESBL infection)
OR
Zosyn 3.375gm IV every 8 hours or 4.5gm IV every 6 hours (if concern of anaerobic infection)
PLUS
Vancomycin (use only if: hemodynamic instability, pneumonia, suspected line infection, skin or soft-tissue infection, documented gram + infection, suspected or h/o MRSA infection, severe mucositis)

If Allergy: (review antibiotic tolerance history)
Moderate-severe (severe rash (excluding Red Man's), anaphylaxis)

Penicillins, cephalosporins or carbapenems
May use alternative below:
Aztroenam 2gm IV Q 8 hours
PLUS
Vancomycin (per weight based dosing)
AND Consider
Tobramycin 7mg/kg IV QD (if clinically unstable)

Vancomycin
May use alternative below:
Daptomycin 6mg/kg IV QD (if suspected or h/o VRE infection)
OR
Linezolid 600mg IV Q 12 hours (consider if lung penetration required; may cause bone marrow suppression and SSRI interactions)

Recommended Antibiotic Management for Low-Risk Patients
Levofloxacin 500-750mg po daily
OR
Moxifloxacin 400mg po daily (if concern over anaerobic or skin type infection; no urinary tract penetration)
OR
Ciprofloxacin 500mg po BID PLUS Augmentin 875mg po BID
OR
Ceftriaxone 1-2gm IV daily (if concern over malabsorption, ie cGVHD)
OR
Ertapenem 1gm IV daily (if concern over malabsorption, ie cGVHD)

An outpatient approach to fever management requires diligent monitoring. If fever is persistent or recurrent after initiating oral antibiotics, new signs of infection develop, or the patient exhibits High-Risk signs/symptoms, hospital admission is indicated.
ED RAPID PATIENT TREATMENT

**ED Order Entry and Notification Process**

- If sending patient to the ED, call 8-9111 to notify ED CTA of pending patient and ask CTA to create “ED Expected” encounter
- Ask CTA to transfer call to ED Provider to discuss the case and inform Provider that NP will be placing orders on the RRFP
- Go to “Patient Station” and enter patient name or MRN
- Go to “Encounter” field and double-click on “ED Encounter” or “ED Admission” for today’s date and time
- Click on “Pre-admit Orders” and enter appropriate orders using the RRFP Order Set (Type “FEVER” in “Order Set” section). Order CXR, blood cultures X2-3, UA C&S, IVF’s, antibiotics as appropriate
- Click “sign and hold for admission”
- Click “Rounding” tab in far left hand column
- Click “orders” in left hand column
- Click “signed and held orders” in upper left hand corner of screen
- Click to highlight all orders then click “release orders” then EXIT
PURPOSE: To promote the timeliness of antibiotic administration and supportive care in immunocompromised patients who develop fever or signs of serious infection.

LOCATION: For use in the Inpatient and Emergency Department settings.

PATIENT CRITERIA: Hematologic malignancy / Bone Marrow Transplant / Neutropenic / Immunocompromised patients presenting with or developing fever or signs of serious infection.

CALL Heme / BMT staff at 720-355-4791 upon patient presentation.

GOAL: Initiate first dose of IV antibiotics within one hour of patient presentation or initial fever.

**General**

- **Vital Signs**
  - Obtain vital signs every 15 minutes x 4, then every 30 minutes x 2, then every 1 hour x 2, then every 4 hours.
  - Notify MD of sepsis symptoms:
    - Shaking chills
    - Temperature GREATER than OR EQUAL to 38 degrees C
    - Heart Rate GREATER than 120
    - SBP LESS than 90 mmHg
    - RR GREATER than 24
    - O2 LESS than 90%
    - Urine Output LESS than 50 ml/h
    - Altered Mental Status

- **Isolation**
  - Contact isolation status
  - Droplet isolation status
  - Airborne isolation status
  - Contact and airborne isolation status
  - Contact and droplet isolation status

- **Nursing Assessments**
  - INITIATE FIRST DOSE OF ANTIBIOTIC WITHIN ONE HOUR of patient presentation or fever development. THIS PATIENT IS ON THE HEME/BMT/ONC RAPID RESPONSE PROTOCOL. Fever in the immunocompromised patient is a medical emergency. Administration of IV antibiotics and supportive care is critical in this patient population. DO NOT DELAY antibiotics for chest x-ray or any cultures OTHER THAN blood cultures. Obtain blood cultures STAT prior to the administration of antibiotics in all patients.
  - STAT, UNTIL DISCONTINUED starting Today at 1221 Until Specified

- **Nursing Interventions**
  - Intake and output: Routine, EVERY 4 HOURS First occurrence Today at 1600 Until Specified
  - Initiate neutropenic precautions
  - Place patient in positive-pressure isolation room if available

- **Labs**
  - **Rapid Response Fever Protocol Labs - Blood Cultures**
    - Blood culture orders for patient WITH central line:
    - Blood culture orders for patient WITHOUT central line:
  - **Rapid Response Fever Protocol Labs - Cultures**
    - Notify NP / MD immediately if UNABLE to obtain peripheral blood culture after 2 attempts
    - Respiratory culture
    - Multiplex respiratory PCR
    - Respiratory FA - adult
    - Respiratory FA - pediatric
    - Urinalysis reflex microscopic
    - Urine culture
Rapid Response Fever Protocol Labs

- CBC with auto diff
- Manual diff if auto fails
- Magnesium serum
- Phosphorus, serum/plasma
- Lactate dehydrogenase
- Lactate whole blood venous
- Comprehensive metabolic panel
- Uric acid serum
- Prothrombin time
- PTT
- Fibrinogen

Imaging

- Chest
  - XR CHEST 2 VIEW (PALAT)
  - XR CHEST SINGLE (AP)

IV Fluids

- IV Fluids
  - NS bolus
    - 500 mL, Intravenous, for 2 Hours
  - NS infusion

Medications

- Antibacterials
  - VANCOMycin nomogram
    - cefepIME (MAXIPIME) IV
      - 2 g, Intravenous, EVERY 8 HOURS, Starting 11/18/13
    - meropenem (MERREM) IV for suspected or confirmed ESBL infection
      - Starting 11/18/13
    - piperacillin-tazobactam (ZOSYN) IV for suspected anaerobic infection
      - 3,375 g, Intravenous, EVERY 6 HOURS, Starting 11/18/13
    - VANCO: hemodynamic instability, pneumonia, suspected line infxn, skin/soft tissue infxn, severe mucositis, documented Gram + infxn, suspected or MRSA
    - adreOMycin + VANCOMycin for penicillin allergy
    - DAPTOmycin (CUBICIN) IV for VRE or VANCOMycin allergy (NOT requiring lung penetration)
    - linezolid (Zyvox) IV for VRE or VANCOMycin allergy (REQUIRING lung penetration)
      - Intravenous, Starting 11/18/13
    - TOBRAmycin IV for use with adreOMycin (penicillin allergy) in patients with hemodynamic instability

- Analgesics
  - acetaminophen (Tylenol) tablet
    - 650 mg, Oral, EVERY 6 HOURS PRN, Fever
  - mephenidine (Demerol) injection
    - 50 mg, Intramuscular, As Needed, Fever, Pain
RAPID RESPONSE FEVER PROTOCOL RESULTS

So far...
OVERALL INTERVENTION TIMELINESS

- Time to first antibiotic: p<.001
- Time to fluid resuscitation: p=.001
- Time to provider order entry: p<.001
• Mean ED time to antibiotics and order entry reduced-\(p=0.001; <.001\)

• Mean 11\textsuperscript{th} floor time to antibiotics, fluids and order entry reduced-\(p<0.001; <.001; 0.001\)

• Mean BIC time to antibiotics, fluids and order entry reduced-\(p<0.001; 0.034; <0.001\)
OUTCOMES - LENGTH OF STAY

- Overall Hospital LOS - mean reduction of 2.3 days (p=.026)
- ICU LOS - mean reduction of 1.77 days (p=.385)
- Neutropenic Hospital LOS - mean reduction of 2.65 days (p=.160)
- Non-neutropenic Hospital LOS - mean reduction of 1.89 days (p=.107)
- "Non-septic" Hospital LOS - mean reduction of 4.09 days (p=.001)
• Hospital LOS-mean reduction of 2.6 days (p=.01)

• Hospital mortality-8 deaths overall, 7 with antibx delays (p=.39)
SIGNIFICANCE OF INTERVENTION FINDINGS

- Significant improvement in timeliness of antibiotics and support
- RRFP implementation improves outcomes
- Significant LOS reduction and cost savings
- Mortality higher in non-intervention encounters (6 vs. 2)
- Mortality higher in patients having antibiotic delays (7 vs. 1)
- MASCC validation
**Purpose:** To improve the timeliness of antibiotics and supportive care interventions in patients with hematological malignancies presenting with fever or signs of serious infection requiring hospitalization for intravenous antibiotic therapy.

**Methods:** A quality improvement study utilizing a pretest/posttest design analyzed data 12 months prior to intervention and 15 months after intervention. A Rapid Response Fever Protocol and order set was implemented in common patient care locations with staff, patient and provider education. Primary outcomes were time to provider order entry, volume resuscitation and antibiotic administration. Secondary outcomes of mortality, length of hospital stay (LOS), use of ICU resources and healthcare cost were evaluated.

**Results:** A total of 192 encounters were included, 73 pre-intervention and 119 post-intervention. The overall time to antibiotics, volume resuscitation and order entry improved from 174, 87 and 127 minutes respectively to 59, 56 and 25 minutes respectively and improved significantly in all locations (p=.000, .001, .000) in patients who received the intervention. Post-intervention analysis displayed a significant reduction in hospital LOS (8.06 days vs 5.76 days, p=.026) and ICU days were reduced in the intervention group (4.77 vs 3 days). Associated healthcare cost reduction was estimated at $5,957 per encounter (N=63) totaling $375,291 in approximate savings over a 15-month period. Eight patients died during the analysis, 7 of which had significant delays in antibiotics.

**Conclusion:** Implementation of a Rapid Response Fever Protocol with staff, provider and patient education improves timeliness of antibiotics and supportive care interventions in immunocompromised patients with hematological malignancies and reduces hospital LOS, mortality and associated healthcare cost.
CONCLUSIONS

• Fever in the immunocompromised host is a common medical condition requiring prompt evaluation and treatment

• Rapid Response Protocols and processes improve the timeliness of interventions and supportive care in oncology patients

• Rapid Response Protocols and processes improve outcomes in patients with cancer

• Rapid Response Protocols and processes reduce healthcare associated cost in patients with cancer
QUESTIONS
REFERENCES


REFERENCES


REFERENCES


Glen J. Peterson RN, DNP, ACNP
Blood Cancer and Bone Marrow Transplant Program
University of Colorado Hospital
University of Colorado Health
glen.peterson@ucdenver.edu
Pager-303-266-1189
Cell-773-636-2638