Neutropenic Fever Clinical Pathway

Updated: October 2021

Outcomes/Goals	**1.** Rapid identification/treatment of pediatric patients' w/fever at risk for neutropenia. **2.** Create an efficient team-oriented approach in conjunction with Peds Hem/Onc (PHO service) **3.** **Antibiotic administration within 60 minutes of arrival** **4.** Ensure stability of patient after antibiotic administration prior to admission to the floor.
Inclusion Criteria	Patients aged <20 years with temp >38.3, temp 38 for > 1 hour, or temp 38 x 2 in a 12-hour period and : 1) New diagnosis of malignancy or undergoing antineoplastic chemotherapy ***OR*** 2) BMT patients < 100 days from transplant ***OR*** 3) BMT patients > 100 days but on > 0.5mg/kg of prednisone daily
Exclusion Criteria	Patients with history of malignancy, now > 3 months in remission **and** no longer have a central line. Patient's s/p BMT who did not meet inclusion criteria defined above.
NURSE Documentation	Vital signs, evidence of shock/decompensation, neuro status w/ attention to alertness. Onset of fever. Presence of central line, last access to port, history of line infections or problems with port. Chief complaint with associated symptoms. If BMT patient, number days since BMT. Medications, allergies, vital signs, weight per standard of care and triage guidelines. General appearance. Monitor vital signs throughout antibiotic infusion and post infusion.
INTERVENTIONS Initiate on arrival	ESI Triage level II. RN/MD Don mask, gloves, gown, and eye protection. Mask patient and place immediately in room. LMX to Port (if not done prior to arrival) – Do not delay access if unstable Bedside vitals and weight. No rectal temps. Central line access and maintenance per CLABSI prevention Bundle (# HC-NSG-259-POL and HC-NSG-260-PRO) ***Port-a-cath access should occur within 15-30 minutes or 2 attempts. After 2 attempts, place an IP Consult to VAT for port access **AND** place a PIV and continue pathway. **** Cardiac/respiratory monitoring with minimum Q30 minutes vitals during and immediately after antibiotic infusion or more frequently as patient condition warrants. Fluid bolus 20 mg/kg NS– initiate ***with*** antibiotic infusion
DIAGNOSTICS	Consider bedside CBG. Draw Blood Cultures (central draw – each lumen, peripheral only w/specific order), CBC with Manual Diff, CMP (Hold/Send if indicated/LIP order), and Type and cross (Hold in anticipation of blood, platelets or FFP) UA/Mandatory culture – Do Not Cath for specimen – Do not delay antibiotics for urine collection Cough, congestion, rhinorrhea—consider Flu/RSV/COVID-19 testing Chest x-ray if indicated (URI s/s, abnormal lung exam, hypoxia, tachypnea) Localized signs of infection may be appropriate for culture
PHYSICIAN (LIP)	
Documentation	Onset of fever, date and type of most recent chemo, last blood counts, days since BMT (if applicable)
Fluids	Normal Saline bolus 20 ml/kg if indicated for hypotension or poor perfusion May repeat as indicated by abnormal vitals/poor perfusion
Antipyretics	Acetaminophen 12.5 mg/kg PO (No Ibuprofen)
Antibiotics	**Administer within 60 minutes of arrival:** Cefepime 50 mg/kg IVPB (LIP to order upon taking referral call or if no referral call ordered within 13 minutes from arrival) ***If High risk (ill appearing, history of MRSA, hypotension):*** Add Vancomycin 10-15 mg/kg/dose IV
ADMISSION	Call Peds Hem/Onc Fellow with results and develop follow-up/admission plan ANC < 500 BMT criteria for admission (*regardless of ANC)*: -BMT patients < 100 days from transplant -BMT patients > 100 days but on > 0.5mg/kg of prednisone daily Prepare family/patient for admission as appropriate Ensure stability of vital signs prior to admission to floor
*High Risk versus Low Risk Considerations	Factors that favor **low risk** for severe infection: 1. ANC > 500 2. Nearly normal results of hepatic and renal function tests 3. Resolution of Neutropenia expected in <10 days 4. No intravenous catheter site infection 5. Early evidence of bone marrow recovery 6. Non-toxic presentation

Clinical Pathway Decision Making Process
Neutropenic Fever

Temp >38.3, or Temp 38 and ANC ≤500

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Port-a-cath access should occur within 15-30 minutes or 2 attempts. After 2 attempts, place an IP Consult to VAT for port access ***AND* place a PIV and continue with labs, Cx, and antibiotic administration.

Immediate Action

1. Mask patient and place immediately in room
2. Bedside triage/registration—RN in full PPE
3. Central line access**
4. Blood cultures
5. CBC with manual diff
6. Draw/hold CMS
7. UA/mandatory cx (do not delay antibiotics for UA)
8. COVID testing
9. Order Cefepime/Verify Cefepime has already been ordered

Administer Cefepime 50 mg/kg IV. Do not wait for lab results before antibiotic administration
NS Bolus 20 mg/kg

Toxic Appearance?

YES → Resuscitate as appropriate
Broad-spectrum abx
Notify Hem/Onc fellow and PICU
*Admission

NO

Hypoxemia? Severe respiratory symptoms?

YES → Flu/RSV testing
Oxygen
Obtain chest x-ray as part of initial evaluation
*Admission

NO

Monitor vital signs during and post antibiotic infusion for hypotension (Minimum q 30 minutes)

Determine **High** Risk vs **Low** Risk (Consult PHO)

High Risk (ANC <500; -BMT patients < 100 days from transplant; BMT patients > 100 days but on > 0.5mg/kg of prednisone daily)

→ *Admission
Consider Vancomycin
Consult with hem/onc

*NOTE FOR ADMISSION: **Please COVID test prior to all admissions.***

Low Risk
(ANC > 500, non-toxic, and not BMT patient)

→ Home with Follow-up

Neutropenic Fever Rationale and Data

Goals of Clinical Pathway

1. Rapid identification and treatment of the pediatric patient with neutropenia and fever
2. Create a team-oriented approach to efficient and timely evaluation and work-up in conjunction with Peds Hem/Onc
3. Antibiotic administration within 60 minutes of arrival

Data Considerations	Interventions	Rationale
Neutropenia	Documented ANC level	The absolute neutrophil count (ANC) number defines Neutropenia. The ANC is calculated by multiplying the percentage of bands and neutrophils (segmented neutrophils or granulocytes) on a CBC differential times the total white WBC count. The risk of bacterial infection is related to both the severity and duration of neutropenia. In prolonged severe neutropenia, life-threatening gastrointestinal and pulmonary infections occur, as does sepsis. Patients with neutropenia do not appear to be at increased risk for parasitic and viral infections.
Urine collection	Urine specimen collection	Urine analysis and culture indicated if no focal point for infection. Due to compromised immune response urine should not be obtained via catheterization.
Bacteremia rates	Blood culture collection	Bacteremia rates for children with neutropenic fever range between 2-20%. Gram positive infections are more common than gram negative ones, though gram negative bacteremia tends to present in a more fulminant fashion and is associated with higher mortality. The majority of patients with fever and bacteremia rapidly respond to antibiotics, however, a minority will develop toxic shock-like syndrome with fever, hypotension, diffuse rash with subsequent desquamation and ARDS with mortality rates of 6-30%. Careful and frequent monitoring after antibiotic administration is therefore mandatory.
Time to antibiotic (TTA) administration	Administer antibiotics ASAP within 60 minutes	Data suggest that minimizing time to antibiotic administration may result in decreased adverse outcomes, including need for resuscitation, intensive care unit admission, and death. Additionally, US News and World Report has been tracking TTA as a Quality of Care measure since 2010; in 2012, a survey of pediatric oncology centers revealed that 45% of respondents were using TTA as a quality measure, with over 90% using a standard of <30 or 60 minutes of time from presentation to administration.

Risk Stratification

- For children who are clinically stable, intravenous monotherapy consisting of an antipseudomonal beta-lactam agent should be administered. Cefepime is standardly used at Doernbecher Children's Hospital. For clinically stable children, routine use of combination therapy has not been shown to be of benefit. For patients with hemodynamic instability, focal soft tissue infections, or a history of previous infection with MRSA, Vancomycin should be added to the regimen. Antifungal agents are generally considered if fever persists > 96 hours or if patient has a known fungal infection or history of fungemia.

Low Risk Criteria

- Several institutions have adopted criteria to identify low-risk patients with febrile neutropenia who can be treated safely with outpatient antibiotics. However, there is no widely accepted standard to guide this practice and robust data are lacking. Given this, current practice at DCH dictates that all patients with ANC < 500 be admitted for intravenous antibiotic therapy.

Bacterial Pathogen Consideration

Gram-positive cocci and bacilli (account for 60-70% of isolates in most studies)
- Staphylococcus, Streptococcus, Enterococcus, Corynebacterium

Gram-negative cocci and bacilli
- Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa

Anaerobes
- Bacteroides, Clostridium, Fusobacterium, Peptococcus/peptostreptococcus, Veilonella

Citations:

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Burns B, Hartenstein M, Lin A, et al. Optimizing Time to Antibiotic Administration in Children with Possible Febrile Neutropenia through Quality Improvement Methodologies. Pediatr Qual Saf. 2019;4(6):e236.

Rivas-Ruiz R, Villasis-Keever M, Miranda-Novales G, Castelán-Martínez OD, Rivas-Contreras S. Outpatient treatment for people with cancer who develop a low-risk febrile neutropaenic event. Cochrane Database Syst Rev. 2019 Mar 19;3(3):CD009031.

Beyar-Katz O, Dickstein Y, Borok S, Vidal L, Leibovici L, Paul M. Empirical antibiotics targeting gram-positive bacteria for the treatment of febrile neutropenic patients with cancer. Cochrane Database Syst Rev. 2017 Jun 3;6(6):CD003914.