

Symptom Management Guidelines: FEVER AND NEUTROPENIA

Definition	
<ul style="list-style-type: none"> • Fever: A single oral temperature of $\geq 38.3^{\circ}\text{C}$ (101°F) OR a temperature $\geq 38^{\circ}\text{C}$ (100.4°F) which lasts more than 1h • Neutropenia: An abnormally low number of neutrophils in the blood ($\text{ANC} < 1.0 \times 10^9/\text{L}$). The lower the neutrophil count, the greater the risk of infection • Febrile neutropenia: Fever and Neutropenia 	
Contributing Factors of Neutropenia	
Cancer Related & Cancer Treatment Related	<ul style="list-style-type: none"> • Chemotherapy agents • Monoclonal antibodies (e.g. alemtuzumab) • Extensive radiation to bone marrow (e.g. pelvis, legs, and sternum) • Stem cell transplants - at risk for severe, prolonged neutropenia • Cancers that affect bone marrow (e.g. lymphoma, leukemia or myeloma) • Solid tumors • Febrile neutropenia in previous course of therapy • Immunotherapy – Checkpoint inhibitors
Medications that induce neutropenia	<ul style="list-style-type: none"> • Antibiotics, antifungals, antimalarials • Anticonvulsants, anti-inflammatories, antithyroid • Cardiovascular agents, diuretics • Gastrointestinal agents, immunosuppressants • Phenothiazines, psychotropic drugs
Co-morbidities	<ul style="list-style-type: none"> • Autoimmune diseases • AIDS • Hypersplenism • Aplastic anemia • Congestive heart failure • Diabetes • Cerebrovascular disease • Tuberculosis
Other	<ul style="list-style-type: none"> • Age ≥ 65 years • Ethnic groups known to have a slightly lower ANC (e.g. African Americans, Yemenite Jews, Ethiopians and certain Arabs) • Pre-existing infections (e.g. bacterial, viral, fungal, rickettsial, protozoal) • Vitamin deficiencies (e.g. vitamin B₁₂, folate, copper); albumin level < 35 g/L; dehydration • Hemodialysis, hypotension • Recent exposures: travel, blood product administration
Causative Factors of Infection in Patients with Neutropenia	
Factors Related to Infection	<ul style="list-style-type: none"> • Immunosuppression. Herpes Simplex Virus (HSV) reactivation in immunocompromised patients may be as high as 75% • Prior infection and /or antibiotic use in last 90 days • Chemotherapy- induced mucositis • Presence of open wounds, catheters or drains • Obstruction of the lymphatic system, biliary tract, bronchial, gastrointestinal or urinary systems by tumours or secondary to surgical procedures • Graft versus host disease - may be at higher risk of developing fungal infections up to 6 months after transplant • Potential exposure to pathogens during hospital stay
Consequences	
<ul style="list-style-type: none"> • Febrile neutropenia is considered an ONCOLOGICAL EMERGENCY which if left untreated, can quickly lead to sepsis, acute respiratory distress syndrome and/or septic shock See Appendix A • Severe or prolonged neutropenia increases patient risk of infection (moderate risk: 7-10 days; high risk: >10days) • Chemotherapy dose delays, reductions, or discontinuation of treatment 	

Focused Health Assessment

GENERAL ASSESSMENT	SYMPTOM ASSESSMENT	PHYSICAL ASSESSMENT
<p>Contact & General Information</p> <ul style="list-style-type: none"> Physician name – oncologist, family physician Pharmacy Home health care Other health care providers Allergies <p>Consider Causative Factors</p> <ul style="list-style-type: none"> Cancer diagnosis and treatment(s) – note type and date of last treatment Post BMT Medical history <ul style="list-style-type: none"> Recent infections, antibiotic therapy Recent reports of diarrhea, constipation, vomiting, dysphagia, urinary symptoms Medication profile <ul style="list-style-type: none"> Review recent lab, diagnostic reports 	<p>Normal</p> <ul style="list-style-type: none"> Refer to pretreatment nursing or oncology assessment <p>Onset</p> <ul style="list-style-type: none"> When did symptoms begin? <p>Provoking / Palliating</p> <ul style="list-style-type: none"> What makes it better? Worse? <p>Quality (in last 24 hours)</p> <ul style="list-style-type: none"> Can you describe your symptoms? What is your temperature? For how long? <p>Region / Radiation</p> <ul style="list-style-type: none"> Where are your symptoms? 	<p>Vital Signs</p> <ul style="list-style-type: none"> Frequency – as clinically indicated. If severe neutropenia, presence of fever or infection then every 4 hours and prn
<p>* Special Consideration*</p> <p>High Risk Indicators Requiring Medical Attention such as:</p> <ul style="list-style-type: none"> Recent chemotherapy/radiation regimen of high risk for febrile neutropenia Prior febrile neutropenia Post BMT Fever, chills, rigors Recent or current infection Poor performance status Change in mental status Diarrhea, cough, dyspnea, chest or abdominal pain, headache, stiff neck, rash Age > 65 Potential for infection (Central vascular devices, IV lines, drains and catheters, prosthetic devices (e.g. cardiac valves)) 	<p>Severity / Other Symptoms</p> <ul style="list-style-type: none"> Have you been experiencing any other symptoms such as: <ul style="list-style-type: none"> Chills, sweating Shortness of breath Cough, with sputum (colour?) Fatigue or feeling unwell Mouth sores or sore throat Urination (Burning, urgency, frequency) Vaginal discharge, itching Constipation/diarrhea? Any areas of redness/swelling/pain? Recent blood transfusion Recent travel or exposure to sick individuals <p>Treatment</p> <ul style="list-style-type: none"> Using any antipyretics? If so, what type? Any other medications or treatments? (e.g. anti-diarrheas, granulocyte colony-stimulating factors) <p>Understanding / Impact on You</p> <ul style="list-style-type: none"> How much are you eating or drinking? What do you believe is causing these symptoms? How is this affecting you? 	<p>Systems Assessment</p> <ul style="list-style-type: none"> Presence of shaking (rigors), chills, diaphoresis level of consciousness and orientation skin and oral mucosa for signs of infection <ul style="list-style-type: none"> Note any areas of redness, swelling, pain, warmth, impaired skin integrity, exudate Respiratory tract: <ul style="list-style-type: none"> Respiration – note ease, presence of adventitious sounds Cough – note quality of phlegm, duration of cough or phlegm Sinuses –congestion, tenderness, unilateral eye tearing or facial swelling, bleeding, periorbital cellulitis Nares –ulcerations, drainage Drains and catheters (e.g. central vascular device, bladder catheters) for function and signs of infection

FEBRILE NEUTROPENIA GRADING SCALE*

NCI Common Terminology Criteria for Adverse Events (Version 4.03)

GRADE 1 (Mild)	GRADE 2 (Moderate)	GRADE 3 (Severe)	GRADE 4 (Life threatening)	GRADE 5
—	—	ANC <1000/mm ³ with a single temperature of >38.3 degrees C OR A sustained temperature of >=38 degrees C for more than one hour	Life-threatening consequences; urgent intervention indicated	Death

*A semi-colon indicates 'or' within the description of the grade and a single dash (-) indicates a grade is not available

***Step-Up Approach to Symptom Management:
Interventions Should Be Based On Current Grade Level and Include Lower Level Grade Interventions As Appropriate**

GRADE 1 AND GRADE 2



NON – URGENT:

Prevention, Support, teaching & follow-up care as required

Patient Care and Assessment	<ul style="list-style-type: none"> Review cancer treatment and potential for neutropenia Refer to specific chemotherapy protocol for direction: http://www.bccancer.bc.ca/health-professionals/professional-resources/chemotherapy-protocols Not all patients with neutropenia exhibit a fever in the presence of an infection (e.g. elderly, patients on corticosteroids)- assess for other signs of clinical deterioration (e.g. hypothermia, hypotension, confusion)
Recommendations for Prevention of Infection	<ul style="list-style-type: none"> Maintaining adequate hydration and nutrition incorporating protein, vitamin B and C during treatment assists with maintaining skin integrity. Use an electric shaver rather than a razor for shaving. Have a flu shot and other immunizations as indicated Vaccination should be at least 2 weeks before receiving chemotherapy or immunosuppressive therapy. Patients having chemotherapy or radiation therapy should not receive live attenuated vaccines unless instructed by physician. Inform dentist of current treatment prior to dental treatment and to limit treatment, if possible, to periods when counts will be higher (within a couple of days of chemotherapy treatment). Use a water-soluble lubricant during intercourse. If unsure of partner disease status, use lubricated condoms to protect against sexually transmitted diseases. If severely neutropenic, check with health care team to determine if intercourse should be avoided during this time. Avoid handling pet feces, including fish tanks, bird cages and cat litter boxes Avoid large crowds or anyone with signs of infection (e.g. chicken pox, measles, cold, flu, and shingles) especially during nadir (typically 7 to 14 days). Avoid constipation and straining to prevent trauma to rectal tissue. Do not use suppositories and/or enemas when neutrophil count low unless advised by physician.
Hygiene	<ul style="list-style-type: none"> Bathe daily using warm water, pat skin dry Hand hygiene: Soap and warm water or antiseptic hand sanitizer Wash hands: prior to handling foods, before and after eating, after using the washroom, coughing or sneezing in hands Avoid touching face and mucous membranes as much as possible Keep mouth clean by brushing with a soft toothbrush at least twice daily. If there is an alteration in skin integrity, a dressing and/or topical agents may be indicated.

Safe Food Handling	<ul style="list-style-type: none"> • Maintain appropriate temperatures for foods (cold and hot) • Wash all fresh fruits and vegetables thoroughly • During periods of severe neutropenia avoid: raw or rare cooked meats, seafood, eggs; unpasteurized juices or cheese.
Pharmacological Management	<ul style="list-style-type: none"> • Antibiotic prophylaxis may be considered in patients with expected duration of neutropenia (ANC <1.0 X 10⁹/L) for > 7 days or for patients receiving immunosuppressive regimens (e.g. systemic corticosteroids). • Antifungal prophylaxis may be recommended for high risk patients (e.g. those with acute leukemia and stem cell transplantation). • Granulocyte colony stimulating factor (GCSF- e.g. filgrastim, pegfilgrastim) may be prescribed prophylactically following previous episodes of chemotherapy induced neutropenia.
Patient Education and Follow-Up	<ul style="list-style-type: none"> • Demonstrate how to perform regular temperature checks and advise patient to keep a record at home • Provide contact information and access to resources. • Teach patients signs and symptoms of infection and to notify doctor and/or nurse immediately if: <ul style="list-style-type: none"> - Oral temperature ≥ 38.0° C. (Do not take acetaminophen, ibuprofen, or acetylsalicylic acid for fever unless advised by physician). - Cough with or without sputum - Sore throat or sores in mouth - Any areas of redness or swelling - Headache, stiff neck, or rash - Loose or liquid stools or constipation - Increased frequency or burning with urination - Vaginal drainage or itching - Flu-like symptoms - body aches, general fatigue - Chills, sweating, shortness of breath, changes in mental status

GRADE 3- GRADE 4



EMERGENCY: Requires IMMEDIATE medical attention	
Patient Assessment and Care	<ul style="list-style-type: none"> • Have patient go to nearest emergency department or ambulatory setting immediately for further assessment (Low risk, reliable patients may be able to be treated as an outpatient with close follow-up). Notify oncologist of assessment and facilitate arrangements as necessary. • If on active treatment, will require chemotherapy dosage reductions, delays or discontinuation of treatment. Refer to specific chemotherapy protocols for specific direction: http://www.bccancer.bc.ca/health-professionals/professional-resources/chemotherapy-protocols • If patient on Immunotherapy, remind patient to present Immunotherapy alert card • Lab and diagnostic testing: <ul style="list-style-type: none"> - Review most recent lab reports. - Lab or diagnostic tests that may be ordered: complete blood count, leukocyte differential, blood cultures (two sets), creatinine, C-reactive protein, electrolytes, BUN, blood glucose, serum lactate, and liver function tests, stool or urine cultures, throat or skin swabs, chest x-ray. - Assess for drug toxicities from support medications (e.g. antibiotics). • Frequent nursing assessments including; <ul style="list-style-type: none"> - Vital signs (every four hours and as clinically indicated) - Assess for signs and symptoms of infection: culture any suspected areas, assess CVC and/or IV sites If there is an alteration in skin integrity, a dressing and/or topical agents may be indicated. • High efficiency particulate air (HEPA) filtration is recommended for allogeneic stem cell transplant patients and patients with prolonged neutropenia (if available).

Pharmacological Management	<ul style="list-style-type: none"> Prompt initiation of antibacterial therapy impacts patient outcomes May require new or change in prescription for anti-infective agents (oral, IV), analgesics, granulocyte colony stimulating factor (G-CSF- e.g. filgrastim, pegfilgrastim). Administer medications as prescribed. See BCCA Antibiotic Guidelines for Febrile Neutropenia: http://www.bccancer.bc.ca/nursing-site/Documents/FebrileNeutropeniaGuidelines2008Nov1.pdf
Follow-up	<ul style="list-style-type: none"> Follow-up is recommended for any positive cultures, persistent fever lasting 3 to 5 days, subsequent infection, adverse events, or if unable to continue prescribed antibiotic regimen

RESOURCES & REFERRALS	
Referrals	<ul style="list-style-type: none"> Patient Support Centre Telephone Care for follow – up Home Health Nursing Oncologist Infectious Disease Physician
Cancer Management Guidelines	Febrile Neutropenia – Solid Tumour/Lymphoma: <ul style="list-style-type: none"> Patient Assessment for Hospital Admission - http://www.bccancer.bc.ca/nursing-site/Documents/PatientAssessment2.pdf Antibiotic Guidelines: http://www.bccancer.bc.ca/nursing-site/Documents/FebrileNeutropeniaGuidelines2008Nov1.pdf
Patient Education	<ul style="list-style-type: none"> Neutropenia – What is it? http://www.bccancer.bc.ca/health-info/coping-with-cancer/managing-symptoms-side-effects/neutropenia
Immunotherapy	<ul style="list-style-type: none"> Immunotherapy Alert Card Please refer to protocol specific algorithms to guide management of immune mediated side effects.
Related Online Resources	<ul style="list-style-type: none"> E.g. Fair Pharmacare; BC Palliative Benefits. Can be found in “Other Sources of Drug Funding Section” http://www.bccancer.bc.ca/health-professionals/professional-resources/pharmacy/drug-funding
Bibliography List	<ul style="list-style-type: none"> http://www.bccancer.bc.ca/health-professionals/professional-resources/nursing/symptom-management

Appendix A: Septic Shock

SEPTIC SHOCK	
EMERGENT: Requires IMMEDIATE medical attention	
<ul style="list-style-type: none"> Sepsis: a systemic inflammatory response to infection in the blood. Septic Shock: a condition caused by sepsis that leads to severe hypotension which results inadequate blood flow, impaired tissue perfusion and organ dysfunction. This is a MEDICAL EMERGENCY that can have a fatal outcome. 	
Early Signs of Septic Shock	<ul style="list-style-type: none"> Dry, warm, flushed skin Fever, chills Hypotension Tachypnea, tachycardia, widening pulse pressure Anxiety, apprehension Restlessness, confusion, disorientation, reduced mental alertness Decreased urinary output Decreased breath sounds and crackles Hyperglycemia
Late Signs of Septic Shock	<ul style="list-style-type: none"> Cold, pale, clammy skin Temperature > 38°C or <36°C Hypotension

- Tachycardia, narrowing pulse pressure
- Disorientation
- Dyspnea, shortness of breath, cyanosis
- Oliguria, anuria
- Lethargy, obtundation
- Decreased breath sounds, crackles, wheezes
- Hyperglycemia or hypoglycemia

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Contributing Authors:

Revised by: Jagbir Kohli, RN MN; Lindsay Schwartz, RN MSc(A)

Created by: Colleen Sherriff, RN; Vanessa Buduhan, RN MN; Rosemary Cashman, RN MSc(A), MA (ACNP);

Elizabeth Cooper, RN BScN, CON(c); Karen Levy, RN MSN; Ann Syme RN PhD(C)

Reviewed by: Shirin Abadi, Pharm