

# STAFF INFORMATION – NEUTROPENIC FEVER SYNDROME

## Definitions

**Systemic infection in neutropenic patients is potentially life-threatening.** Therefore, a neutropenic fever or sepsis syndrome is considered a time-dependent condition in which early recognition of the cancer patient's potential to have neutropenic sepsis is critical to successful management.<sup>1</sup>

**FEVER** – Single oral temperature (T) greater than 38.3°C (101°F), **OR** greater than 38°C (100.4°F), lasting at least one hour, **OR** greater than or equal to 38°C (100.4°F), documented at least twice over a 12-hour period

**SEVERE NEUTROPENIA** – Absolute Neutrophil Count (ANC) less than  $0.5 \times 10^9/L$  **OR** ANC less than  $1.0 \times 10^9/L$  with a predicted decline of the ANC to less than  $0.5 \times 10^9/L$  over the next 48 hours

### RISK FACTORS

- Pre-existing neutropenia
- History of a neutropenic fever syndrome
- Bone marrow failure secondary to:
  - Prior cytotoxic chemotherapy
  - Prior radiation therapy
- Open wounds or active tissue infection
- Impaired immune function associated with an absolute lymphocyte count (ALC) less than  $0.5 \times 10^9/L$

Cancer patients with neutropenic sepsis syndromes may present with body temperatures of less than 38°C.

Patients presenting with hypothermia (body temperature less than 36°C) have a higher likelihood of bacteremic events.

## Telephone Triage

### ASK:

- Name of chemotherapy drugs the patient has been prescribed. Treatment schedule patient is on; particularly ask the date of the first dose of the current cycle of chemo–radiotherapy in order to identify the treatment day
- Date of last CBC
- Current medications, including antimicrobial therapy
- Adverse drug reaction history. ALLERGIES
- If patient has taken acetaminophen/Tylenol®
- Presence of fever, chills (fever may not be present if patient is taking corticosteroids or acetaminophen)
- If patient is receiving hematopoietic growth factors (e.g. Neupogen®, filgrastim)

### If severe symptoms and/or change in mental status:

Decide whether to direct patient to Emergency Department (E.D.) or to manage patient at Cancer Centre

**Medical assessment is required within 15 minutes of presentation to facility**

**Notify as appropriate:** Physician (Oncologist, Hematologist, FPO); Non-Physician Provider (Clinical Assistant, Physician Assistant); Nurse Practitioner; E.D. Staff

## Assessment and Workup

Look for subtle changes in respiration, mucous membranes, urinary tract symptoms and nervous system:

### Assessment

- Full vital signs (temperature, pulse, respiration, blood pressure, O<sub>2</sub> saturation)
- Focal pain referable to:
  - eyes (e.g. conjunctivitis, periorbital cellulitis)
  - ears (e.g. otitis externa or media)
  - nose (e.g. sinusitis)
  - mouth (e.g. stomatitis and oral ulcers)
  - throat (e.g. oral mucositis, gingivitis, pharyngitis, parapharyngeal space infection)
- Symptoms that may suggest a lower respiratory focus:
  - rapid or deep breathing (e.g. dyspnea)
  - chest pain (e.g. pleuritic inflammation)
  - cough or wheezing
- Focal abdominal pain and diarrhea may suggest an intra-abdominal sepsis syndrome
- Presence of central venous access device (CVAD), or peripheral venous catheter
- Focal skin or soft tissue swelling, tenderness, and erythema, especially anatomically related to a CVAD may suggest a cellulitis or CVL-related infection

Use **MASCC Risk Index Score**

### Work up

- Before antibiotic administration: blood cultures from at least two (2) separate anatomical sites (note that a multilumen CVAD represents a single site)
- CBC and leukocyte differential to establish the state and degree of neutropenia
- Chemistry including serum electrolytes (sodium, potassium, chloride, and total CO<sub>2</sub>); serum glucose, urea, creatinine, lactate
- INR, prothrombin time, AST, ALT, LDH, GGT, ALP, total bilirubin
- Venous blood gases
- **Consider**
  - Chest x-ray posterior-anterior and lateral views
  - ECG
  - CSF sample
  - Mid-stream urine for microbiological culture and for urinalysis
  - Stool sample (i.e. if diarrhea is present) for *Clostridium difficile* toxin testing, or where appropriate enteric pathogens (*Salmonella* spp., *Shigella* spp., *E. coli* 0H157, and *Campylobacter* spp.)
  - Foci of skin/soft tissue inflammation (e.g. wound swabs)

### Decision Regarding

- Prescription of oral versus intravenous antibiotics
- Need for hospitalization vs. the safety of outpatient management
- Need for reverse isolation, respiratory precautions, or enteric precautions

## Algorithm

Neutropenic Fever - Initial Assessment, Workup and Treatment, Adults with Cancer – Ambulatory Setting (**SEE OVER**)

### References

1. Scullin, P., Coyle, V., Kettle, P. et al. 2013. Guidelines for the management of oncology/haematology adult patients (>18) with neutropenic sepsis. Northern Ireland Cancer Network. Retrieved from <http://www.cancerni.net/>

# NURSING ALGORITHM - NEUTROPENIC FEVER

INITIAL ASSESSMENT, WORKUP AND TREATMENT  
ADULTS WITH CANCER – AMBULATORY SETTING

## ANTIBIOTICS WITHIN ONE HOUR

PATIENT PRESENTS



PATIENT PHONES

... with a single oral temperature 38.3°C or higher, or greater than 38°C lasting at least one hour, or greater than 38°C documented at least twice over a 12 hour period; or feels “unwell”; and has had cytotoxic chemotherapy within the past 6 weeks.

Patients with neutropenic sepsis may present with temperature less than 38°C

**0** MINUTES

**TRIAGE**  
ASSUME NEUTROPENIC  
FEVER SYNDROME

**Assess Symptoms:** fever, chills, cough, shortness of breath, muscle aches, joint pains, rapid heart rate, dizziness or light-headedness, decreased urine output, abdominal pain, nausea/vomiting  
**Vital Signs:** TPR, BP, O<sub>2</sub> sat

**Start Immediately:**

**Supplemental O<sub>2</sub> as needed**  
**IV Access (as needed):** CVAD, or peripheral line, 18G plus 0.9% saline  
**Blood Tests:** CBC with leukocyte differential (to confirm neutropenia), Na, K, Cl, TCO<sub>2</sub>, lactate, glucose, urea, creatinine, INR, PT, AST, ALT, LDH, GGT, ALP, total bilirubin, venous blood gases  
**Blood Cultures before antibiotic administration:** 1 aerobic and 1 anaerobic bottle from 2 separate peripheral sites OR if CVAD 1 aerobic bottle from each lumen plus 1 aerobic and 1 anaerobic bottle from a peripheral site  
**Notify (as appropriate):** Physician or Non-Physician Provider, Nurse Practitioner, E.D. Staff

**SEVERE SYMPTOMS AND/OR CHANGE IN MENTAL STATUS**  
**DECIDE**  
Direct Patient to E.D.  
OR  
Manage Patient at Cancer Centre

**15** MINUTES

**MEDICAL ASSESSMENT**  
WITHIN 15 MINUTES OF TRIAGE

Notify E.D.  
Verbal Communication:  
Nurse-to-Nurse/Physician-to-Physician  
Complete Patient Transfer Form(s)  
Document in Patient Record (i.e. ARIA)

**Medical Assessment to Include:**

**History:** date of last chemotherapy, status of cancer, recent blood transfusions, travel, close contact with sick people, previous documented infection, presence of advanced care plan (ACP), ECOG status

**Medications:** including antimicrobials, ALLERGIES, adverse reactions

**Further testing:** sites of infection including upper and lower respiratory tract, skin and wounds, GI, urine specimens, CNS (cerebrospinal fluid)

**Consider:** CXR (PA and Lateral), ECG, skin biopsy, wound swabs, CVAD, stool cultures, MSU

**Assess Risk of Medical Complications using MASCC.** . . . . .

**MASCC Score**

Burden of febrile neutropenia with no or mild symptoms.....	5
No Hypotension (systolic BP > 90 mm Hg).....	5
No chronic obstructive pulmonary disease.....	4
Solid tumor or hematological malignancy with no previous fungal infection.....	4
No dehydration requiring parenteral fluids.....	3
Burden of febrile neutropenia with moderate symptoms.....	3
Outpatient status.....	3
Age < 60 years.....	2

**LOW RISK**

**MASCC Score 21 or greater,**  
ANC less than 0.5 anticipated duration less than 7 days AND no acute co-morbidities, ECOG status 0 – 1, clinically stable, no hepatic and/or renal dysfunction, resides 1 hour or less from clinic/hospital, telephone access and in-home support, no history of non-compliance

**HIGH RISK**

**MASCC Score less than 21,**  
ANC less than 0.5 anticipated duration 7 or more days, co-morbidities, clinical instability, hepatic and/or renal dysfunction, progressing cancer, pneumonia OR lack of social support, history of non-compliance

**60** MINUTES

**EMPIRIC ANTI-BACTERIAL THERAPY**  
WITHIN ONE HOUR OF TRIAGE

**Outpatient Therapy\***  
**Administer first dose of antibiotics at Cancer Centre**  
**Consider Route: IV → PO or PO**

- ciprofloxacin 750 milligrams by mouth every 12 hours OR levofloxacin 750 milligrams by mouth every 24 hours
- PLUS EITHER** amoxicillin/clavulanate 500/125 milligrams by mouth every 8 hours OR amoxicillin/clavulanate 875/125 milligrams by mouth every 12 hours

**Inpatient Therapy\***  
**Administer first dose of antibiotics while arranging transfer to E.D.**

- piperacillin/tazobactam 4.5 grams IV every 8 hours

**For penicillin hypersensitivity (immediate and delayed type) and other clinical considerations See CCMB Neutropenia Protocol\* for alternative oral and IV antibiotic therapies. Note: Use of some drugs may require consult with Infectious Diseases Services.**

- Observe for 4 hours after first dose within facility
- Agreement from primary care physician or oncologist with outpatient management
- Prescription should be written for 7 or 14 days
- Complete documentation in patient record (i.e. ARIA®)

Follow up within 24 hours by telephone and clinical assessment within 48 to 72 hours  
Follow up on test results/blood cultures

- Ensure appropriate notification occurs – nurse-to-nurse verbal communication; physician-to-physician verbal communication
- Complete transfer form(s) prior to patient transfer
- Complete documentation in patient record (i.e. ARIA®)

**TRANSFER PATIENT TO E.D.**

\* Full Details: CCMB Neutropenia Protocol No. 12.500 – Identification and Management of Neutropenic Fever Syndromes

**References:**

- Flowers CR, Seidenfeld J, Bow EJ, et al. Antimicrobial prophylaxis and outpatient management of fever and neutropenia in adults treated for malignancy: American Society of Clinical Oncology Clinical Practice Guideline. J Clin Oncol 2013; 31(6): 794-810.
- Freifeld AG, Bow EJ, Sepkowitz KA, et al. Clinical Practice Guidelines for the use of Antimicrobial Agents in Neutropenic Patients with Cancer: 2010 Update by the Infectious Diseases Society of America. Clin Infect Dis 2011;52(4):e56-e93.
- MASCC FN Risk Index Score, [www.mascc.org](http://www.mascc.org)