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24/7 REGIONAL ONCOLOGY ON-CALL

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Topics covered today

- Febrile neutropenia
- Malignant spinal cord compression
- Hypercalcaemia of malignancy

Definition

- Any acute, potentially life-threatening or life-altering event directly or indirectly related to a patient's tumour or it's treatment.
- Prevention & early detection requires a high degree of suspicion
- Early presentation & recognition of symptoms & signs reduces morbidity and mortality.

Febrile neutropenia

Definition:

- temperature of 38.3°C or (38°C greater sustained over 1 hour), and neutrophil count of less than 0.5 x 10^9 cells/L, or less than 1.0 x 10^9 cells/L and predicted to fall to lower than 0.5 x 10^9cells/L.
- Patients with neutropenic sepsis may present with haemodynamic compromise without fever (e.g. if elderly, or on steroids).
- Neutropenic sepsis with or without fever is a medical emergency.
- All clinical signs indicating sepsis need to be acted upon immediately.
- The administration of empiric antibiotics should **not** be delayed in order to perform blood cultures.

Clinical suspicion / likelihood of febrile neutropenia (See Box A)

Patient shows signs of shock
(low BP, O_2 sats, organ dysfunction, confusion, raised serum lactate)

YES

- Urgent review by Medical Officer / Resus Team within 30 minutes (See Box B)
- IV access, fluid resuscitation, urgent bloods taken
- Commence empirical antibiotic therapy within 30 minutes.
- Consider ICU admission or urgent MedStar retrieval (see Box C)
- Commence fluid balance chart &15 minute observations.

NO

Patient has a Febrile Neutropenia Emergency Letter

YES

Follow instructions in Febrile Neutropenia Emergency Letter

NO

1. Urgent investigation (see Box B)
   AND
2. Commence empirical antibiotic therapy **within30 minutes**

Box A: Probable Febrile Neutropenia

Consider febrile neutropenia if:

- Up to 3 months post stem cell or bone marrow transplant; **OR**
- Prescribed long term steroids for Graft vs. Host Disease; **OR**
- Presents with a 'febrile neutropenia emergency letter' (see Appendix 1); **OR**
- Has had recent chemotherapy e.g. last 4 weeks; **OR**
- Is known to be neutropenic: neutrophils <1.0 x10^9/L; **AND**
- Has recorded temperature ≥ 38°C (or is not febrile but shows signs of shock – consider sepsis without fever)

TO AVOID SEPTIC SHOCK, IV ANTIBIOTICS NEED TO BE ADMINISTERED WITHIN 30 MINUTES. DO NOT WAIT FOR BLOOD RESULTS

Box B: Investigations

Urgent Investigations:

Complete the following within 30 minutes:

Septic Screen:

- Blood cultures from peripheral vein and CVC / PICC (if present) prior to antibiotics IF ABLE
- MBA20
- Lactate (if available)
- Lactate (if available)
- MBA20

Non Urgent Investigations:

Complete within 1-2 hours:

- Chest x-ray
- Respiratory viral PCR if indicated clinically
- Sputum and urine specimen for MC&S
- Other swabs (for culture / viral PCRs) as clinically indicated e.g. mouth, wounds, or lesion(s)

Box C: Considerations for ICU admission or urgent MedStar retrieval

Not responding to resuscitation

- Altered conscious state
- Hypoxia not corrected by oxygen therapy
- Clinical deterioration in any other form
- Lactate remains > 2mmol/L despite intervention

The Multinational Association for Supportive Care in Cancer risk index MASCC: A multinational scoring system for identifying low-risk febrile neutropenic cancer patients

Characteristic	Point score
Burden of illness •No or mild symptoms •Moderate symptoms	 5 3
No hypotension	5
No chronic obstructive pulmonary disease	4
Solid tumour or no previous fungal infection	4
Outpatient status	3
No dehydration	3
Aged < 60 years	2

The maximum value in this system is 26.
A score of ≥ 21 predicts a ≤ 6% risk for severe complications and a very low mortality (< 1 %) in neutropenic febrile patients.

(including death, intensive care unit admission, confusion, cardiac complications, respiratory failure, renal failure, hypotension, bleeding, and other serious medical complications

Table 1 Typical Pathogens During Bacterial Sepsis in Cancer Patients

Origin	**Frequent pathogens**
Unknown	Coagulase-negative staphylococci, *Escherichia coli, Enterococcus* species
Lung	*Pseudomonas aeruginosa,* Pneumococci, Alpha-haemolytic streptococci, *Acinetobacter* species
Abdomen	*Escherichia coli, Pseudomonas aeruginosa, Clostridium* species, *Enterococcus* species, *Klebsiella* species
Urogenital	*Escherichia coli, Klebsiella* species, *Pseudomonas aeruginosa*
Soft tissue	*Staphylococcus aureus*, Alpha-haemolytic streptococci
Central venous catheter	Coagulase-negative staphylococci, *Corynebacteriae, Propionibacterium* species, *Candida Albicans, Candida tropicalis*

Diagnosis and Evaluation

Meticulous physical assessment of common sites of infection

- mouth, pharynx,
- respiratory tract,
- skin and soft tissue,
- perineal area,
- Urinary and gastrointestinal tract
- exit sites of peripheral or venous catheter
- Potentially infected foreign bodies (e.g. vascular access devices) should be removed when possible and sent for culture, and abscesses should undergo percutaneous or surgical drainage.

Empirical Antibiotic therapy for Febrile Neutropenia

- patients with features of systemic compromise (such as hypotension, hypoxia, confusion, major organ dysfunction) should receive antibiotics within 30 minutes of presentation.
- Where possible, blood culture samples should be taken before administering antibiotics
- clinically stable patients should receive antibiotics within 1 hour of presentation after appropriate cultures have been taken
- administration of antibiotics should not be delayed by the conduct of laboratory or radiological investigations

Perform septic workup

- 1 set blood cultures (aerobic and anaerobic bottles) from each lumen of central venous access device (CVAD) (if in situ)
- 1 set blood cultures from peripheral blood
- blood tests: FBC (with differentials), EUC, CMP, LFTs, serum lactate
- mid-stream urine/catheter specimen urine
- sputum sample (if clinically indicated)
- respiratory swabs (if clinically indicated)
- stool sample (if clinically indicated)
- swab of CVAD exit site (only if clinically indicated)
- swab of any other wounds/focal lesions
- arterial blood gas (if clinically indicated).

Empirical antibiotic therapy for Febrile Neutropenia [1-4]

<table>
<tr><th>No Penicillin / Cephalosporin Allergy</th><th>Moderate risk penicillin allergy
History suggestive of moderate/low risk (delayed rash which is NOT urticarial or DRESS/SJS/TEN)*</th></tr>
<tr><td rowspan="4">> Piperacillin/tazobactam 4.5g IV every six hours

Note: Continue piperacillin/tazobactam as mono-therapy in stable patients

See additional information below for patients with known or suspected MRSA colonisation/infection</td><td>> Cefepime 2g IV every eight hours
Note: Continue cefepime as mono-therapy in stable patients
See additional information below for patients with known or suspected MRSA infection/colonisation</td></tr>
<tr><td>High risk penicillin / cephalosporin allergy
History suggestive of high risk (e.g. anaphylaxis, angioedema, bronchospasm, urticarial, DRESS/SJS/TEN)</td></tr>
<tr><td>> Vancomycin 25mg/kg IV (Actual Body Weight) up to a maximum of 3g for initial dose
(See Table 2 in the Statewide Vancomycin Dosing Guidelines for subsequent doses)
PLUS
> Ciprofloxacin 400mg IV every twelve hours
Note: Continue vancomycin and ciprofloxacin as dual-therapy in stable patients.</td></tr>
<tr><td>ADD
> Metronidazole 500mg IV every twelve hours in patients with features of intraabdominal infection (e.g. diverticulitis/typhlitis or perineal abscess/collection</td></tr>
<tr><td colspan="2">NOTE: Unless specifically stated antibiotic doses in this guideline reflect recommendations for patients with NORMAL RENAL FUNCTION. Refer to Therapeutic Guidelines or AMH for dose adjustments in patients with renal impairment.</td></tr>
</table>

Additional considerations:

Gentamicin:

If the following apply:

- severe sepsis or shock SBP < 90 mmHg or lactate > 2mmol/L *OR*
- onset of sepsis 48 hours after admission to hospital *OR*
- previous resistant gram negative isolates,

THEN ADD

Gentamicin 7mg/kg (CrCl > 60ml/min) or 5mg/kg (CrCl < 60ml/min) ideal body weight IV for initial dose. If CrCl< 40ml/min, contact consultant to consider alternative treatment

REFER TO **STATEWIDE AMINOGLYCOSIDE GUIDELINES** FOR FURTHER DOSING if required

Vancomycin

If the patient is not already on vancomycin *AND*:

- has severe sepsis or septic shock or skin/soft tissue/catheter related infection or clinical deterioration (whilst receiving 1st line ß-lactam therapy); *OR*
- is known or suspected to be colonised with methicillin-resistant Staphylococcus aureus (MRSA); *OR*
- is not responding to 1st line ß-lactam therapy with central venous access PLUS culture negative PLUS low index of suspicion for fungal infection; ***THEN***

ADD vancomycin to empiric regimen: **Vancomycin[#] 25mg/kg (Actual Body Weight) up to a max of 3g** for initial dose (see table 1 in Appendix 2).

For subsequent doses refer to table 2 in the Statewide Vancomycin Dosing Guidelines and cease after 3 days if no evidence of gram positive infection.

[#] *If allergic to vancomycin CONTACT Infectious Diseases/Microbiology Specialist for advice*

Review therapy if culture positive or no improvement after 48 hours

***Moderate risk cephalosporin allergy: History suggestive of moderate/low risk (delayed rash which is not urticarial or DRESS/SJS/TEN) → consult ID/micro for advice**

"DRESS/SJS/TEN are systemic drug reactions with skin involvement (DRESS - Drug Rash With Eosinophilia and Systemic Symptoms, SJC- Stevens-Johnson syndrome, TEN -toxic epidermal necrolysis)"

Summary

- Cancer patients on chemotherapy presenting with fevers or symptoms/signs suggesting infection needs urgent assessment.
- Examination and investigation.
- All patients should receive antibiotics as soon as possible; within 30 minutes of presentation for patients in septic shock, and within 1 hour for all other patients.
- Beta-lactam monotherapy, such as piperacillin-tazobactam (Tazocin®) or cefepime, is the empiric therapy of choice for all clinically stable patients with neutropenic fever.
- An antipseudomonal beta-lactam antibiotic plus gentamicin is recommended for patients with systemic compromise
- Vancomycin is not recommended as routine initial empiric therapy, and should be reserved for patients with specific indication as outlined above.