Neutropenic sepsis is a potentially life threatening condition which must be considered in the differential diagnosis of any haematology or oncology patient who is unwell, particularly if they have had recent chemotherapy (within 6 weeks). These patients will be immune suppressed as a result of their disease and/or treatment and those who are neutropenic (absolute neutrophil count (ANC) <1x10^9 /L) in case of illness require urgent medical assessment as septic shock in immunocompromised or neutropenic patients is life threatening. It needs to be recognised as a Time Dependent Condition, with early therapeutic intervention required to reduce morbidity and mortality.

- The ‘First 60 Minutes’ component of the NIcaN guideline should be implemented in the ED and Acute Receiving Units to achieve a maximum “door to needle” time for IV antibiotics of 60 minutes.
- The ‘First 48 Hours’ component should be used by clinicians managing patients in hospital neutropenic sepsis beds.

Management: Follow flow charts and complete care pathway:

- Monitor vital signs → follow ‘MEWS chart’ protocol, temp, pulse, BP, RR, O₂ sats, AVPU. Temperature is tympanic measurement.

- Establish IV access with urgent bloods: FBC, U&E, CRP, LFTs, venous lactate.

- Blood cultures (peripheral first then central if relevant).

- If sepsis is suspected (any of: temp >38 or <36°C, pulse >90bpm, RR>20/min) proceed with first dose of antibiotics before blood results available; check most recent U&E. See flow chart for antibiotics.
o Severe sepsis indicated by altered mental state or hypoxia (O₂ sats <94%) or shock (SBP <90mmHg). See flow chart for antibiotics.

o Ensure a full history and examination (inspect mouth, skin, central line exit site, perianal area if symptoms related, ENT, CVS, chest, abdomen and neurological examination).

o Investigations: urinalysis, cultures/swabs from sputum/faeces/throat/skin lesions and CXR if clinically appropriate.

o Check - any recent bacterial culture & susceptibility results and blood group

o GCSF should not be used for the treatment of uncomplicated febrile neutropenia or in cases where pegfilgrastim has already been given as part of the patient’s chemotherapy regimen.

Contact consultant haematologist / acute oncology team (or oncology registrar on call, BCH) for advice regarding GCSF. It may be considered under the following circumstances:
- Profound neutropenia (ANC<0.1 x 10⁹/L) with expectation of prolonged neutropenia
- Persistent fever >48 hrs despite appropriate antibiotics and/or antifungals
- Invasive fungal infection
- Pneumonia
- Unwell patients particularly in the presence of sepsis syndrome (hypotension and multi-organ dysfunction)
- Uncontrolled primary disease.

o When GSCF is appropriate, standard (non-pegylated) filgrastim 30 million units once daily subcutaneously should be prescribed until neutrophils >1.0 x 10⁹/L for two consecutive days.

o Inform Consultant Haematologist / acute oncology team of patient’s admission.

**Indications for Change in Management**

- **Temperature:** If temperature persists beyond 48 hrs or condition deteriorates, discuss antibiotic regimen and management with Consultant Microbiologist.

- **Pulse/BP and Fluid balance:** Use volume expander (crystalloid fluids) to treat hypotension. Insert catheter and monitor output. If despite fluid challenge hypotension persists for 45 minutes or recurs seek senior advice urgently as per MEWS protocol

- **Systemic complications:** Observe for evidence of bacterial endocarditis, thrombocytopenia, DIC. If anaemic or thrombocytopenic or DIC develops discuss transfusion support with a Consultant Haematologist.
Patients who have received prophylaxis with a quinolone are at a higher risk of being infected with more resistant organisms. Please consider a lower threshold for escalation for adding gentamicin in such patients.

**NICaN Neutropenic Sepsis Guideline (First 60 minutes)**

**Triage Assessment**
- Identify: All haematology/oncology patients within 6/52 SACT (consider potential for neutropenia in all haem patients)
- Assume: Neutropenic sepsis until proven otherwise
- Observations: Temp, pulse, BP, RR, O₂ sats, APVU
- Commence: Early Warning Score chart
- IV access: Blood rapidly to Lab
- Blood cultures (peripheral & if relevant central), FBC, U&E, CRP, LFTs, venous lactate
- Treatment: Offer first line antibiotics immediately, consider need for supplemental O₂ and IV fluids
- Commence Neutropenic Sepsis Care Pathway

**Resuscitation Management**
- Triage red
- Resuscitation room
- Optimise haemodynamics & O₂ delivery
- Add gentamicin
- ECG

**Severe Sepsis?**
- Altered mental state or
- Hypoxia (O₂ sats <94%) or
- Shock (sys BP <90mmHg)

**Medical Assessment**
- History & Examination: Identify potential sources of infection, presenting complaint/co-morbidity
- Investigations: Urinalysis, cultures/swabs from sputum/urine/faeces/throat/skin lesions & CXR if clinically appropriate

**Admit**
- Differentiate between neutropenic & non-neutropenic sepsis
- Ensure supportive measures in place
- Ensure appropriately monitored bed

**Discharge**
- Only if physiologically stable
- When co-morbidity treated
- Neutropenic Sepsis advice re-iterated
- Inform helpline re discharge & arrange early follow-up call
- Consider early review

**First Line Antibiotics in Neutropenic Sepsis**

- **Preferred Regimen:**
  - Piperacillin 4g / Tazobactam 500mg IV qid
  - Gentamicin 5mg/kg slow IV od after line flush

- **In severe sepsis add**
  - Gentamicin 5mg/kg slow IV od after line flush

- **Penicillin Allergy Regimen:**
  - Ciprofloxacin 600mg slow IV bd (see notes)
  - Gentamicin 5mg/kg slow IV od after line flush
  - Teicoplanin 10mg/kg slow IV (bd for 3 doses then od)

- **Penicillin Allergy Regimen for patients who have received prophylactic ciprofloxacin:**
  - Aztreonam 2g IV tid
  - Gentamicin 5mg/kg slow IV od after line flush
  - Teicoplanin 10mg/kg slow IV (bd for 3 doses then od)
### References

- NICAN Guidelines for the management of oncology/haematology adult patients with neutropenic sepsis August 2013.