Initial Management of **Neutropenic Sepsis** in **ADULTS**

NHS Greater Glasgow and Clyde

DEFINITIONS

SEPSIS
Pyrexial temperature >38°C or hypothermic (<36°C) on 2 occasions, at least 30 minutes apart, OR

Clinically unwell even if apyrexial.

Symptoms may include fever, sweats, chills, rigors, malaise, respiratory rate >20/minute, tachycardia >90 bpm, hypotension. Note that patients may appear to be well perfused despite hypotension.

SEVERE SEPSIS
Sepsis with signs of at least one acute organ dysfunction e.g. hypotension, confusion, oliguria, raised serum lactate

SEPTIC SHOCK
Sepsis induced hypotension requiring inotropic support or hypotension that is unresponsive (within 1 hr) to adequate fluid resuscitation i.e. systolic BP < 90 mmHg or a reduction of > 40 mmHg from baseline.

NEUTROPENIC SEPSIS
Sepsis (as defined previously) AND

Neutropenia (Neutrophil count < 0.5, OR < 1 if recent chemotherapy within 3 weeks)

OTHER PATIENT GROUPS INCLUDED:
Clinically septic with normal neutrophil count, no identified source of sepsis but known to be immunocompromised due to previous transplant (solid organ or bone marrow), high dose steroids (e.g. prednisolone > 15 mg /day for > 2 weeks), taking other immunosuppressive agents (e.g. anti – TNF agents, cyclophosphamide etc) or primary immunodeficiency.

IMMEDIATE CLINICAL MANAGEMENT

Neutropenic sepsis is a life-threatening medical emergency. Patients who exhibit signs of haemodynamic compromise should not remain untreated whilst awaiting confirmation of neutropenia. **Patients should be assessed by experienced clinical staff within 15 minutes of presentation. ALL patients should have the following initiated immediately and within one hour of presentation (Sepsis 6 care bundle);**

- Deliver high flow oxygen
- IV fluids Resuscitation
- Blood cultures prior to antibiotics
- Intravenous antibiotics as per risk category (see below)
- Measure serum lactate with Full Blood Count
- Measure urine output & consider catheter

Once clinically stable, the patient's oncology / haematology / specialist team should be contacted as soon as possible (via on-call medical staff if necessary)

EMPIRICAL ANTIBIOTICS

Is patient a stem cell transplant / solid organ transplant recipient or are they receiving chemotherapy for acute leukemia

NO → Does patient have severe sepsis, septic shock or NEWS ≥5?

- **NO** → **STANDARD RISK**
- **YES** → **HIGH RISK**

YES → Does patient have severe sepsis, septic shock or NEWS ≥5?

- **NO** → **HIGH RISK**
- **YES** → **CRITICAL RISK**

STANDARD RISK

IV Piperacillin / Tazobactam 4.5 g 6 hourly

If history of penicillin allergy (NOT anaphylaxis)
IV Aztreonam 2g 6 hourly
AND IV Vancomycin***

If history of penicillin allergy (anaphylaxis)
IV Gentamicin**
AND IV Vancomycin***

HIGH RISK

IV Piperacillin / Tazobactam 4.5g 6 hourly
AND IV Gentamicin**

If history of penicillin allergy (NOT anaphylaxis)
IV Aztreonam 2g 6 hourly
AND IV Gentamicin**
AND IV Vancomycin***

If history of penicillin allergy (anaphylaxis)
IV Gentamicin**
AND IV Vancomycin***
AND IV Ciprofloxacin 400mg 12 hourly

CRITICAL RISK

First line including penicillin allergy (NOT anaphylaxis)
IV Meropenem 1g 8 hourly
AND IV Amikacin*

If history of penicillin allergy (anaphylaxis)
IV Amikacin*
AND IV Ciprofloxacin 400mg 12 hourly
AND IV Vancomycin***

Additional antibiotics for specific infection risks
Known MRSA positive or any suspected line infection (e.g. rigors, pyrexia with line use) – ADD IV vancomycin***

Suspected atypical pneumonia – ADD IV/PO Clarithromycin 500mg 12 hourly (check for drug interactions)

Consider possibility of opportunistic infection such as PCP or reactivation of previous infection e.g. CMV, VZV. Discuss with appropriate specialist / Microbiologist / Infectious Disease physician

Discuss all patients with a diagnosis of myeloma with appropriate specialist/ Microbiologist/ Infectious Disease physician

INFORMATION ON ANTIBIOTIC DOSES (see above for choice of antibiotic)

The recommended antibiotic doses above are for patients with normal renal function:

To calculate the initial doses of Amikacin*, Gentamicin** and Vancomycin*** please see below. Review all antibiotic prescriptions daily and rationalise as soon as microbiology results are available.

Amikacin*

- Record the exact times of all doses and concentration measurements on the monitoring form
- If creatinine is known calculate creatinine clearance(CrCl, see Therapeutics Handbook) and dose as below:

Creatinine clearance	Dose (24 hourly)
20–29 ml/min	5.5 mg/kg
30–49 ml/min	6 mg/kg
50–70 ml/min	12 mg/kg
>70 ml/min	15 mg/kg

- If Creatinine is not known, give 7.5 mg/kg (max 600 mg)
- Check peaks (1 hour post dose) and troughs (end of dosage interval) within the first 48 hours of therapy and every 2 – 3 days thereafter. See Therapeutics Handbook for interpretation.

Gentamicin**

- Do not prescribe in patients with myeloma unless discussed with relevant haematologist.
- Use the gentamicin prescribing, administration and monitoring chart to prescribe and record all doses and concentration measurements
- If creatinine is known calculate the gentamicin dose/ frequency using the online calculator on StaffNet
- If creatinine is not known give an initial dose of 5 mg/kg. If patient was previously known to have chronic renal impairment (ie. CKD 5 or CrCl < 21 ml/minute) give an initial dose of 2.5 mg/kg (max 180 mg)
- If CrCl is ≥ 21 ml/minute check a level 6 – 14 hours after the start of the first gentamicin infusion. If CrCl is < 21 ml/minute check a level 24 hours after the start of the first gentamicin infusion. See Therapeutics Handbook for interpretation.

Vancomycin***

- Use the vancomycin prescribing, administration and monitoring chart to prescribe and record all doses and concentration measurements
- If creatinine is known calculate the vancomycin dose/ frequency using the online calculator on StaffNet
- If creatinine is not known calculate the single loading infusion dose as below. Calculate the maintenance dose once creatinine is available.
- Check a trough level within 48 hours of starting therapy. See Therapeutics Handbook for interpretation.

Actual body weight	Dose
< 40 kg	750 mg
40–59 kg	1000 mg
60-90 kg	1500 mg
> 90 kg	2000 mg

INVESTIGATIONS

Radiology	CXR; Other tests as indicated
Haematology	FBC; WCC-Total and Differential; Clotting screen
Biochemistry	U+Es; LFTs, CRP, Bicarbonate, Lactate
Microbiology	Blood Cultures (2 sets taken from different sites). (N.B. If central line in situ blood cultures should be taken from each lumen and another from a peripheral venepuncture); MSSU; Sputum; Urine for 'Legionella Antigen' if legionella suspected; MRSA screen (according to policy); Swabs for C+S from potential sources of sepsis (e.g. Throat, Hickman Line, Wound Swabs); stool if gastroenteritis; CSF if meningitis etc.

VIROLOGY

- Send 10 ml EDTA plasma sample for CMV/EBV/ Adenovirus PCR testing (For specific patients after discussion with haematologist).
- If respiratory symptoms; send a sputum sample or a throat gargle (20ml water) or a non charcoal flocked nasal swab and throat swab in viral PCR sample solution (VPSS).
- If rash send a plasma and throat swab (in VPSS) and a stool sample in an ordinary universal container.
- If vesicular rash send lesion swab/aspirate in VPSS.
- If diarrhoea send a stool sample in an ordinary universal container or a non-charcoal flocked rectal swab in VPSS.
- **All of the above samples must be marked "for virology".**
- If viral infection strongly suspected contact duty Virologist.

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