Initial Management of Sepsis in Neutropenic/ Immunocompromised Adults

NHS Greater Glasgow and Clyde

DEFINITIONS

FEVER: Pyrexia temperature > 38˚C or Hypothermia (< 36˚C) OR > 37.5 ˚C on 2 occasions 30 minutes apart.

SIRS (Systemic Inflammatory Response Syndrome): symptoms include sweats, chills, rigors, malaise, tachypnoea RR > 20/ minute, tachycardia HR > 90 bpm, hypotension (Patients may appear well perfused despite hypotension)

SEPSIS: Evidence of infection (including SIRS) PLUS Organ dysfunction i.e. ≥ 2 of hypotension, confusion or tachypnoea (RR ≥ 22/ minute)

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

NEUTROPENIC SEPSIS or FEBRILE NEUTROPENIA

Neutrophil count < 0.5 or < 1 x 10^9/L if recent chemotherapy (usually within 10 days but can persist for up to 21 days)
PLUS Fever/ Hypothermia or SIRS or Sepsis/ Septic shock.

OTHER Immunocompromised Patient Groups Including:

Patients who are clinically unwell with undifferentiated infection with normal neutrophil count but known to be immunocompromised e.g. previous transplant (solid organ or stem cell), high dose corticosteroid therapy (e.g. prednisolone > 15 mg/ day for > 2 weeks), taking other immunosuppresive 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. ALL patients should be assessed by experienced clinical staff within 15 minutes of presentation to hospital and resuscitation should be commenced following the Sepsis 6 care bundle:

1. Blood cultures (& any other relevant samples)
2. Antibiotic administration
3. Oxygen to maintain target Saturation
4. Measure lactate and haemoglobin
5. IV fluids
6. Monitor urine output

The patient's oncology/ haematology/ specialist team must be contacted as soon as possible (via on-call medical staff if necessary).
If patient is clinically deteriorating seek urgent senior review.

EMPIRICAL ANTIBIOTICS

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

NO

Does patient have sepsis, septic shock or NEWS ≥ 7

NO

STANDARD RISK

IV Piperacillin/ Tazobactam 4.5g 6 hrly
+/- IV Vancomycin$^{\Delta}$**

If true penicillin/ beta-lactam (Anaphylaxis)
IV Gentamicin**
AND IV Vancomycin**

YES

HIGH RISK

IV Piperacillin/ Tazobactam 4.5g 6 hrly
AND IV Gentamicin**
AND IV Vancomycin**

If true penicillin/ beta-lactam (Anaphylaxis)
IV Gentamicin**
AND IV Vancomycin**
AND IV Ciprofloxacin 400mg 8 hrly

YES

Does patient have sepsis, septic shock or NEWS ≥ 7

NO

HIGH RISK

IV Piperacillin/ Tazobactam 4.5g 6 hrly
AND IV Gentamicin**
AND IV Vancomycin**

If true penicillin/ beta-lactam (Anaphylaxis)
IV Gentamicin**
AND IV Vancomycin**
AND IV Ciprofloxacin 400mg 8 hrly

YES

CRITICAL RISK

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

If true penicillin/ beta-lactam (Anaphylaxis)
IV Amikacin**
AND IV Vancomycin**
AND IV Ciprofloxacin 400 mg 8 hrly

****IV Amikacin, Gentamicin and Vancomycin dosing as per Therapeutics handbook. Discuss with an infection specialist (ID or microbiology) if an aminoglycoside is to be used for > 4 days.**
All antibiotic doses are based on normal renal/ hepatic function. See BNF for dose adjustments.

REMEMBER TO REVIEW IV THERAPY DAILY: consider IVOST (or stopping if infection excluded)

ADDITIONAL antimicrobials and advice for specific infection risks:

- $^{\Delta}$IV Vancomycin if recent infection with MRSA, MRSA colonised (current or previous), suspected central line infection or signs of skin/ soft tissue infection.
- IV Clarithromycin 500 mg 12 hourly if Community Acquired Pneumonia suspected and atypical cover required (check drug interactions)
- IV Metronidazole 500 mg 8 hourly in patients with history of true penicillin/ beta-lactam allergy with suspected intra-abdominal sepsis.
- Previous ESBL infection or known ESBL carrier use a carbapenem in place of piperacillin/ tazobactam. Check previous microbiology results for resistance.
- 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.

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). (NB 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 (20 ml 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.

Approved by NHSGGC Antimicrobial Utilisation Committee; Feb 2019, Expires Feb 2022