LOCAL OPERATING PROCEDURE

**CLINICAL POLICIES, PROCEDURES & GUIDELINES**

Approved by Quality & Patient Safety Committee
21 August 2014

# SEPSIS INTRAVENOUS ANTIBIOTIC GUIDELINE ADULT – INPATIENT

Clinical Excellence Commission Guideline attached

**REVISION & APPROVAL HISTORY**
Endorsed Gynaecology Services Division Management Committee 10/7/14

**FOR REVIEW :** by Clinical Excellence Commission

# SEPSIS INTRAVENOUS ANTIBIOTIC GUIDELINE ADULT - INPATIENT

The Clinical Excellence Commission (CEC) Adult Inpatient Sepsis Intravenous Antibiotic Guideline aims to guide the prescription and timely administration of antibiotics for **adult inpatients** that have a diagnosis of sepsis, severe sepsis or septic shock and have been admitted to hospital for 48 hours or more.

The guideline is based on the recommendations in *Therapeutic Guidelines: Antibiotic* version 14, 2010[1]. It is intended to provide an accessible resource, which can be adapted to suit individual facility preferences in liaison with the antimicrobial stewardship team and local antimicrobial susceptibility patterns. Antimicrobial stewardship teams may wish to refer to their latest hospital cumulative antibiogram, if available, when modifying the guideline.

**Prompt administration of antibiotics and resuscitation fluids is vital in the management of the patient with sepsis. The goal is to commence antibiotic therapy within the first hour of the recognition and diagnosis of severe sepsis.**

The selection of appropriate antimicrobial therapy is complex and this guideline is not intended to cover all possible scenarios.

Clinicians must review antimicrobial therapy within 24 hours of commencement, and change or cease antibiotics as required once microbiology results are available.

This guideline is not intended for:

- patients with FEBRILE NEUTROPENIA who should be managed using local febrile neutropenia guidelines
- small hospitals and multi-purpose services where it would be more appropriate to use the Sepsis Adult FIRST DOSE Empirical Intravenous Antibiotic Guideline – Emergency Department
- patients who are deemed to have had incubating or unrecognised community acquired sepsis on admission. Use the Sepsis Adult FIRST DOSE Empirical Intravenous Antibiotic Guideline – Emergency Department

Obtain **at least two sets of blood cultures from separate venepuncture sites** before antibiotic administration.

Obtain other clinical specimens as appropriate **but do not delay administration of antibiotics** or wait for results of investigations.

The antimicrobial treatment indication and plan should be documented in the patient record.

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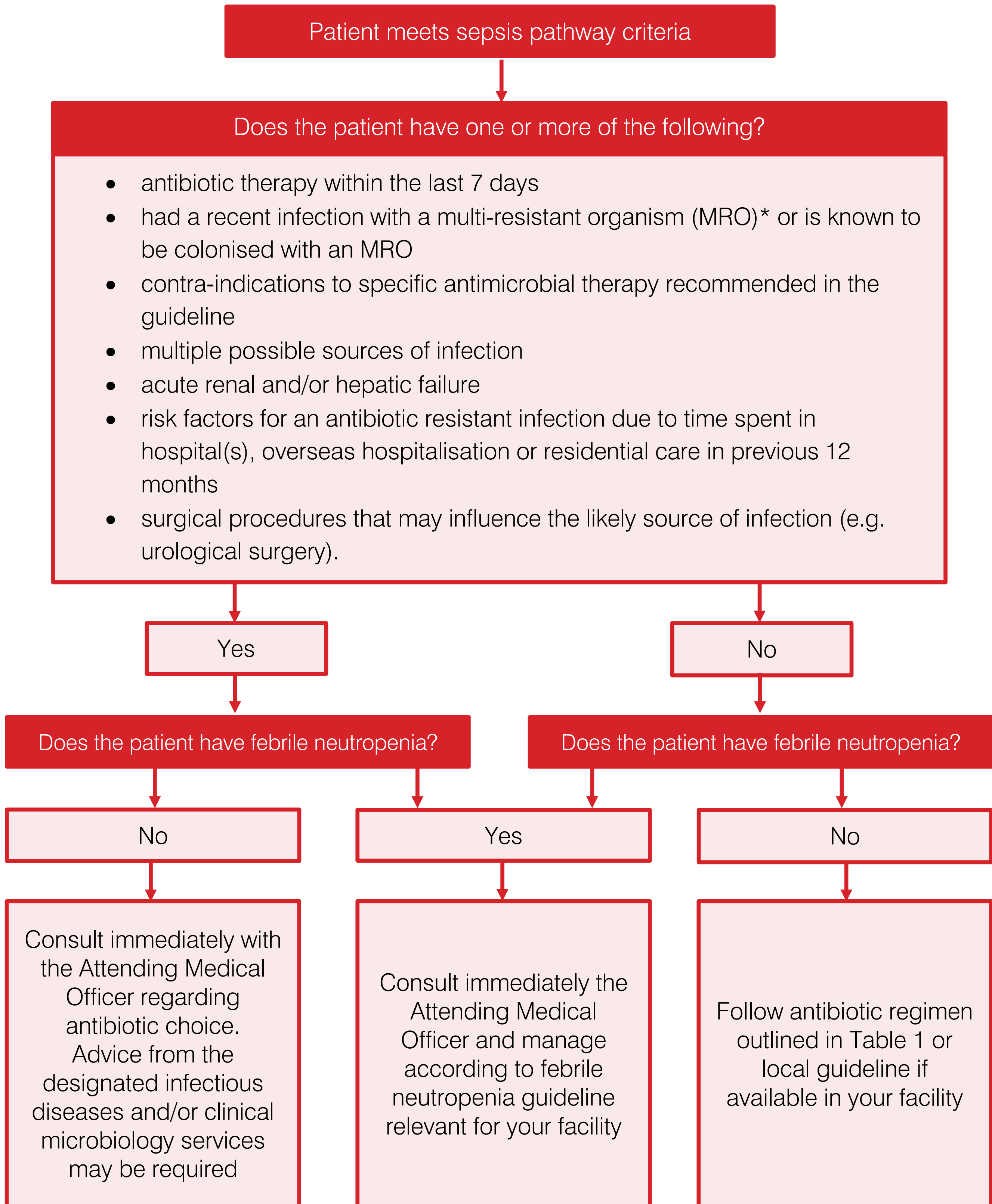


*Examples of MROs include methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant enterococci (VRE), extended-spectrum beta-lactamase (ESBL) producing organisms and carbapenem-resistant Gram negative organisms*

| TABLE 1: ANTIBIOTIC PRESCRIBING (review after 24 hours) | | | |
|---|---|---|---|
| Apparent source of sepsis | Sepsis antibiotic regimen | Penicillin allergic <u>not immediate</u> hypersensitivity | Penicillin or cephalosporin allergic <u>Immediate</u> hypersensitivity or severe prior reaction |
| Sepsis secondary to hospital acquired pneumonia, *low risk of MRO*<br><br>*(generally patient who has been in hospital < 5 days who does not have risk factors for MRO)* | ceftriaxone 1 g IV, daily | ceftriaxone 1 g IV, daily | moxifloxacin<br>400 mg IV, daily |
| | OR | OR | |
| | benzylpenicillin 1.2 g IV, 6-hourly<br>PLUS<br>gentamicin 4 to 6 mg/kg IV, for 1 dose<br>(severe sepsis 7 mg/kg) | cefotaxime 1 g IV, 8-hourly | |
| | OR | | |
| | cefotaxime 1 g IV, 8-hourly | | |
| | OR | | |
| | piperacillin+tazobactam<br>4+0.5 g IV, 8-hourly | | |
| | OR | | |
| | ticarcillin+clavulanate<br>3+0.1 g IV, 6-hourly | | |
| Sepsis secondary to hospital acquired pneumonia, *high risk of MRO* | piperacillin+tazobactam<br>4+0.5 g IV, 6-hourly | cefepime 2 g IV, 8-hourly | Seek expert advice |
| | OR | *If the patient is ventilated*<br>ADD<br>gentamicin 4 to 6 mg/kg IV, for 1 dose (severe sepsis: 7 mg/kg) | |
| | ticarcillin+clavulanate<br>3+0.1 g IV, 6-hourly | | |
| | OR | | |
| | cefepime 2 g IV, 8-hourly | | |
| | *If the patient is ventilated*<br>ADD<br>gentamicin 4 to 6 mg/kg IV, for 1 dose<br>(severe sepsis: 7 mg/kg) | | |
| | *If MRSA prevalent in your hospital*<br>*ADD*<br>vancomycin 1.5g IV, 12-hourly | *If MRSA prevalent in your hospital*<br>ADD<br>vancomycin 1.5g IV, 12-hourly | |

| TABLE 1: ANTIBIOTIC PRESCRIBING (review after 24 hours) | | | |
|---|---|---|---|
| Apparent source of sepsis | Sepsis antibiotic regimen | Penicillin allergic <u>not immediate</u> hypersensitivity | Penicillin or cephalosporin allergic <u>Immediate</u> hypersensitivity or severe prior reaction |
| Severe sepsis with an apparent urinary tract source | gentamicin 4-7 mg/kg IV, for 1 dose<br>PLUS<br>ampicillin 2 g IV, 6-hourly | gentamicin 4-7 mg/kg IV, for 1 dose<br>OR<br>ceftriaxone 1 g IV, daily *if gentamicin is contraindicated*<br>OR<br>cefotaxime 1 g IV, 8-hourly *if gentamicin is contraindicated* | gentamicin 4-7 mg/kg IV, for 1 dose |
| Severe sepsis with an apparent biliary or gastrointestinal tract source | ampicillin 1 g IV, 6-hourly<br>PLUS<br>gentamicin 4 to 7 mg/kg IV, for 1 dose<br>PLUS<br>metronidazole 500 mg IV, 12-hourly | metronidazole 500 mg IV, 12-hourly<br>PLUS<br>ceftriaxone 1 g IV, daily<br>OR<br>metronidazole 500 mg IV, 12-hourly<br>PLUS<br>cefotaxime 1 g IV, 8-hourly | gentamicin 4 to 7 mg/kg IV, for 1 dose<br>AND<br>seek expert advice |
| Severe sepsis resulting from a skin infection (including cellulitis) or surgical site infection | flucloxacillin 2 g IV, 6-hourly<br>*If MRSA prevalent in your hospital*<br>ADD<br>vancomycin 1.5g IV, 12-hourly | cephazolin 2 g IV, 8-hourly<br>*If MRSA prevalent in your hospital*<br>ADD<br>vancomycin 1.5g IV, 12-hourly | clindamycin 450 mg IV, 8-hourly<br>OR<br>vancomycin 1.5 g IV, 12-hourly |
| Maternal sepsis (peri or post-partum) if source unclear | piperacillin+tazobactam 4+0.5 g IV, 8-hourly<br>*If patient meets criteria for toxic shock*<br>ADD<br>clindamycin 600mg IV, 8-hourly<br>*If likely to be MRSA colonized*<br>ADD<br>vancomycin 1.5g IV, 12-hourly | ceftriaxone 1g IV, 24-hourly<br>PLUS<br>metronidazole 500mg IV 12-hourly<br>*If patient meets criteria for toxic shock*<br>ceftriaxone 1g IV, 24-hourly<br>PLUS<br>clindamycin 600mg IV, 8-hourly<br>*in place of above regimen* | Seek expert advice |

| TABLE 1: ANTIBIOTIC PRESCRIBING (review after 24 hours) | | | |
|---|---|---|---|
| Apparent source of sepsis | Sepsis antibiotic regimen | Penicillin allergic not immediate hypersensitivity | Penicillin or cephalosporin allergic Immediate hypersensitivity or severe prior reaction |
| Maternal sepsis likely to be due to Group A streptococcal infection | benzylpenicillin 2.4g IV, 4-hourly<br>PLUS<br>clindamycin 600mg iv 8-hourly | cephazolin 2 g IV, 6-hourly<br>PLUS<br>clindamycin 600mg iv 8-hourly | Seek expert advice |
| | OR | OR | |
| | benzylpenicillin 2.4g IV, 4-hourly<br>PLUS<br>lincomycin 600 mg IV 8-hourly | cephazolin 2 g IV, 6-hourly<br>PLUS<br>lincomycin 600 mg IV 8-hourly | |
| Severe sepsis, unknown source or focus, including possible IV line-associated sepsis<br>**Removal of the infected IV device is usually required** | flucloxacillin 2 g IV, 6-hourly<br>PLUS<br>gentamicin 4-7 mg/kg IV, for 1 dose | cephazolin 2 g IV, 8-hourly<br>PLUS<br>gentamicin 4-7 mg/kg IV, for 1 dose | vancomycin 1.5 g IV, 12-hourly<br>PLUS<br>gentamicin 4-7 mg/kg IV, for 1 dose |
| | *If MRSA prevalent in your hospital*<br>ADD<br>vancomycin 1.5g 12-hourly | *If MRSA prevalent in your hospital*<br>ADD<br>vancomycin 1.5g 12-hourly | |

## NOTES FOR TABLE 1

| | |
|---|---|
| Definitions of penicillin hypersensitivity | **Immediate hypersensitivity** involves the development of urticaria, angioedema, bronchospasm or anaphylaxis within one to two hours of drug administration.<br><br>**Severe prior reaction** involves a history of drug rash eosinophilia and systemic symptoms (DRESS) or Stevens-Johnson Syndrome following administration of a penicillin or cephalosporin.<br><br>All penicillin and cephalosporin class antibiotics are contraindicated in patients with history of drug rash eosinophilia and systemic symptoms (DRESS), Stevens-Johnson Syndrome or IgE-mediated immediate penicillin or cephalosporin allergy.<br><br>Refer to *Therapeutic Guidelines: Antibiotic* for more information<br>http://etg.hcn.com.au/desktop/tgc/abg/1315.htm |
| Definitions of low risk and high risk of MRO | Refer to *Therapeutic Guidelines: Antibiotic* for more information<br>http://etg.hcn.com.au/desktop/tgc/abg/5313.htm |
| Doses for renal impairment<br>(creatinine clearance ≤ 60mL/min) | **Consult AMO (who may request referral to ID/Microbiology) in conjunction with guidance provided in *Therapeutic Guidelines: Antibiotic***<br>http://etg.hcn.com.au/desktop/tgc/abg/8571.htm |

| | |
|---|---|
| Gentamicin and vancomycin dosing and frequency | Refer to *Therapeutic Guidelines: Antibiotic* for more information<br>http://etg.hcn.com.au/desktop/tgc/abg/7823.htm<br>http://etg.hcn.com.au/desktop/tgc/abg/7971.htm |
| Criteria for toxic shock | Refer to *Therapeutic Guidelines: Antibiotic* for more information<br>http://etg.hcn.com.au/desktop/tgc/abg/6225.htm |
| Notes for gentamicin | One dose of gentamicin is recommended; for subsequent doses, assess renal function and adjust frequency accordingly<br><br>Use for a maximum of 48 hours as empirical therapy pending outcome of investigations; monitoring of plasma concentrations NOT required if gentamicin is not used beyond 48 hours<br><br>Directed therapy (beyond 48 hours, based on microbiology results) should be used on the advice of infectious diseases physician or clinical microbiologist only<br><br>Dose should be based on ideal body weight or actual body weight – whichever of the two is lower<br><br>The maximum dose of gentamicin in severe sepsis is 640 mg<br>For other indications, the maximum dose is lower. Refer to Table 2.24 in *Therapeutic guidelines: Antibiotic*, version 14, 2010.<br><br>Contraindications:<br>Previous vestibular or auditory toxicity due to an aminoglycoside<br>Serious hypersensitivity reaction to an aminoglycoside<br><br>Precautions:<br>Pre-existing significant hearing problems<br>Pre-existing vestibular problems<br>Neuromuscular disorders, including myasthenia gravis<br>Chronic liver disease or severe cholestasis (bilirubin above 90 micromol/L)<br>Chronic renal failure or deteriorating renal function – consult AMO |

## TABLE 2: ANTIBIOTIC ADMINISTRATION [2,3]

- Reconstitute antibiotics with sterile water for injection (WFI) unless stated otherwise.
- If further dilution is required for IV injection or infusion, use sterile sodium chloride 0.9% or sterile glucose 5% unless stated otherwise.
- Where possible use separate dedicated lines for resuscitation fluid and for medications. When injecting antibiotics directly into an IV injection port which has resuscitation fluid running:
    - clamp the infusion fluid line and flush with 20 mL sterile sodium chloride 0.9% solution
    - administer antibiotic over the required time
    - flush the line with 20 mL sterile sodium chloride 0.9% solution and recommence resuscitation fluid.

| Antibiotic | Presentation (adult) | Reconstitution fluid/volume | Final volume | Minimum administration time | Notes |
|---|---|---|---|---|---|
| ampicillin | Vial 1 g | 10 mL WFI | 10 - 20 mL | 3 – 5 minutes | Penicillin class antibiotic |
| benzylpenicillin | Vial 600 mg | 2 mL WFI | 10 mL | 3 – 5 minutes | Penicillin class antibiotic<br><br>**Doses $\geq$ 1.2 g must be administered over 30 minutes** |
| | Vial 1.2 g | 4 mL WFI | | | |
| cefepime | Vial 1 g | 10 mL NS | 10 mL | 3 - 5 minutes | Cephalosporin class antibiotic<br><br>**Doses $\geq$ 2 g must be administered over 20 minutes** |
| ceftriaxone | Vial 1 g | 10 mL WFI | 10 mL | 2 – 4 minutes | Cephalosporin class antibiotic incompatible with calcium containing solutions, flush thoroughly before and after with sodium chloride 0.9% |
| cefotaxime | Vial 1 g | 10mL WFI | 10 mL | 3 – 5 minutes | Cephalosporin class antibiotic |
| cephazolin | Vial 1 g | 10 mL WFI | 10 mL | 3 – 5 minutes | Cephalosporin class antibiotic |
| clindamycin | Ampoules<br>300 mg/2 mL<br>600 mg/4 mL | N/A | 600 mg in 50 mL | 20 minutes | Check product is clear of any crystals prior to administration |
| | | | 900 mg in 100 mL | 30 minutes | |

| Antibiotic | Presentation (adult) | Reconstitution fluid/volume | Final volume | Minimum administration time | Notes |
|---|---|---|---|---|---|
| flucloxacillin | Vial 1 g | 5 mL WFI | 10 mL | 3 - 5 minutes (1 g) | Penicillin class antibiotic<br>Repeated doses of 2 g via a peripheral line should be further diluted and infused over 20 – 30 minutes |
| | | | 20 mL | 10 minutes (2 g) | |
| gentamicin | Ampoule 80 mg/2 mL | N/A | 10- 20 mL | (240mg or less) 3 – 5 minutes | Refer to notes for gentamicin |
| | | | 50 mL or 100 mL | (more than 240mg) 30 minutes | |
| lincomycin | Vial 600mg/2mL | N/A | 100mL | 60 minutes | |
| metronidazole | Infusion bag 500 mg / 100 mL | N/A | See presentation column | 20 minutes | |
| moxifloxacin | Infusion bag 400 mg / 250 mL | N/A | See presentation column | 60 minutes | May prolong QT interval and lead to ventricular arrhythmias. May induce seizures in epileptics |
| piperacillin with tazobactam | Vial 4 g/0.5 g | 20 mL WFI | 50 mL | 30 minutes | Penicillin class antibiotic |
| ticarcillin with clavulanic acid | Vial 3 g/0.1 g | 13 mL WFI | 50 mL | 30 minutes | Penicillin class antibiotic |
| vancomycin | Vial 500 mg | 10 mL WFI | Dilute to maximum concentration of 5mg/mL for peripheral line | Maximum of 10 mg/minute | Infusion related effects are common, decrease infusion rate and monitor closely if these occur |
| | Vial 1 g | 20 mL WFI | | | |

## FURTHER MANAGEMENT

The patient should be reviewed by the Attending Medical Officer within 24 hours of commencing the sepsis pathway and antibiotic therapy, with referral to the infectious diseases and/or clinical microbiology services for specific advice.

Microbiology results are generally available within 48-72 hours, and should be used to guide further management of the patient. This may include de-escalating or ceasing antimicrobial therapy.

Clinicians that are experiencing difficulty in assessing positive or negative microbiology results when rationalising antibiotic therapy at 48-72 hours should contact the designated infectious diseases and/or clinical microbiology services.

*Check local instructions regarding referral*

References


1. Antibiotic Expert Group. *Therapeutic Guidelines: Antibiotic. Version 14*. Melbourne: Therapeutic Guidelines Limited; 2010. Accessed through *eTG complete* (via CIAP).
2. Burridge N (ed). *Australian Injectable* Drugs Handbook (4th ed). The Society of Hospital Pharmacists Australia; 2008.
3. Rossi S (ed). *Australian Medicines Handbook.* Chapter 5. Adelaide: Australian Medicines Handbook

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