Local Guideline

Short Course Antibiotics for Intra-abdominal Sepsis - Adult

Sites where guideline applies: John Hunter Hospital

Target audience: Acute Surgical Unit, Gastroenterology, General Surgery, Medical Service, Medical officers, and Pharmacists

Description This document consists of expert recommendations for short course antibiotic use for intra-abdominal infection at the John Hunter Hospital

This local guideline applies to:
1. Adults Yes
2. Children up to 16 years No
3. Neonates – less than 29 days No

National Standard: 4

Keywords: JHH, medication, antimicrobial stewardship, AMS

Replaces Existing Guideline / Procedure: No

Registration Number(s) and/or name and of Superseded Documents:

Relevant or related Documents, Australian Standards, Guidelines etc:
- NSW Health Policy Directive PD2007_036 Infection Control Policy
- NSW Health Policy Directive 2013_043 Medication Handling in NSW Public Health Facilities
- NSW Health Policy Directive 2013_049 Recognition and management of Patients who are Clinically Deteriorating
- HNE LHD Policy Compliance Procedure Recognition and Management of Patients who are Clinically Deteriorating PD2013_049:PCP 1
- HNE LHD PD2013_049 PCP2 Vital Sign Observations 16 years and over
- Therapeutic Guidelines: Antibiotic, Therapeutic Guidelines®, Melbourne, Victoria 2014

Note: Over time some links in this document may cease working. Where this occurs please source the document in the PPG Directory at: http://ppg.hne.health.nsw.gov.au/

Prerequisites: Nil

Local guideline note : This document reflects what is currently regarded as safe and appropriate practice. However in any clinical situation there may be many factors that cannot be covered by a single document and therefore does not replace the need for the application of clinical judgment in respect to each individual patient. If this document needs to be utilised outside JHH liaise with the patient’s medical officer to ensure the appropriateness of the information contained within the guideline.

Date initial authorisation: April 2017

Authorised by: JHH Quality Use of Medicines Committee
This local guideline contains advice on therapeutics

Approval gained from JHH Quality Use of Medicines Committee on 13/4/17

Contact Person: Clinical Pharmacist
Contact Details: Lisa Harris, 13635
Date Reviewed: 
Review due date: April 2019
Responsible for review: Director Infectious Diseases JHH
Version: 1.1 22 June 2017

RISK STATEMENT
Intra-abdominal sepsis is a life-threatening condition which requires adjunctive antimicrobial therapy. However, only the minimum effective dose and duration should be used to reduce the risk of Clostridium difficile infection and superinfection with antimicrobial resistant microorganisms and/or fungal pathogens. Reducing antimicrobial exposure also has a positive impact on drivers of bacterial resistance.

OUTCOMES

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<table>
<thead>
<tr>
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<tbody>
<tr>
<td>1</td>
<td>Clinically appropriate short course antibiotic use for intra-abdominal infection</td>
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<tr>
<td>2</td>
<td>Minimise the risk of antibiotic resistance</td>
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ABBREVIATIONS & GLOSSARY

<table>
<thead>
<tr>
<th>Abbreviation/Word</th>
<th>Definition</th>
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<tbody>
<tr>
<td>E. coli</td>
<td>Escherichia coli</td>
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<tr>
<td>TDM</td>
<td>Therapeutic drug monitoring</td>
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</table>

Hospital / Service Manager Responsibility
- Ensure that the principles and requirements of this guideline are applied, achieved and sustained

Line management responsibility
- Ensure that all staff are made aware of their obligations regarding this guideline through staff education

Employee responsibility
Clinical staff must:
- comply with the requirements of this guideline

GUIDELINE
This guideline does not replace the need for the application of clinical judgment in respect to each individual patient.
The scope of this guideline is intra-abdominal infections including diverticulitis, appendicitis, cholangitis, cholecystitis and peritonitis due to perforated viscus.
Management of intra-abdominal infections involves resuscitation where necessary, control of the source of contamination, removal of any infected or necrotic material and administration of antimicrobial agents to decrease the pathogen burden (Appendix 1).

For patients with complicated intra-abdominal infections\(^1\) who have adequate source control\(^2\), a 4 day course of antibiotic therapy after source control has been shown to be as effective as a course of up to 10 days and shortening therapy did not appear to increase the risk for adverse outcomes\(^3\). Moreover, shorter courses of antibiotics lower the rates of adverse effects, reduce opportunities for bacteria to develop resistance and may reduce costs.

A majority of bacteraemic intra-abdominal infections are associated with sepsis due to Enterobacteriaceae. Across HNELHD, 2015/16 blood isolate antibiograms for 1,651 unique patient isolates of Gram negative Enterobacteriaceae (\textit{E. coli}, \textit{Klebsiella}, \textit{Enterobacter} species and other) showed 65% to be susceptible to amoxicillin/clavulanate and 97% susceptibility to the combination of amoxicillin/clavulanate with gentamicin. See Table 1 for single antibiotic susceptibility rates.

### Table 1: Single agent antibiograms, HNELHD 2015–2016 blood isolates

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<table>
<thead>
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<tbody>
<tr>
<td>All unique patient Enterobacteriaceae isolates</td>
<td>1,651</td>
<td>100%</td>
</tr>
<tr>
<td>Amoxicillin/clavulanate % susceptible</td>
<td>72%</td>
<td></td>
</tr>
<tr>
<td>Cefazolin % susceptible</td>
<td>66%</td>
<td></td>
</tr>
<tr>
<td>Ceftriaxone % susceptible</td>
<td>93%</td>
<td></td>
</tr>
<tr>
<td>Gentamicin % susceptible</td>
<td>94%</td>
<td></td>
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</table>

**Patients with severe sepsis or septic shock**

(as per [Adult Sepsis Pathway](#), September 2016, Clinical Excellence Commission)

Patients who potentially have an acute intra-abdominal infection in association with systemic sepsis, satisfying either the Red zone or Yellow zone criteria above require addition of gentamicin IV to their antibiotic regimen.

In this setting, short course gentamicin (see appendix 2) is preferred because:

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\(^1\) The term ‘Complicated’ refers to patients with established peritonitis or intra-abdominal abscess or a perforated viscus where more than 12 hours have elapsed (closed or open traumatic perforation) or more than 24 hours in non-traumatic perforation cases.

\(^2\) Procedures that eliminate infectious foci, control factors that promote ongoing infection and correct or control anatomical derangements to restore normal physiological function.

\(^3\) Trial of Short-Course Antimicrobial Therapy for Intraabdominal Infection New England Journal of Medicine 372;21 2015.
• most Enterobacteriaceae\(^4\) are gentamicin susceptible across HNELHD (see Table 1 above)
• aminoglycosides are the most rapidly bactericidal agents, potentially achieving faster control of the bacteraemic infection associated with severe sepsis and mortality
• in contrast to broad spectrum penicillins and cephalosporins, gentamicin is less likely to contribute to the development of *Clostridium difficile* infection and the selection of antibiotic-resistant organisms

**Aminoglycosides should NOT be used in patients with:** A history of vestibular or auditory toxicity caused by an aminoglycoside, a history of serious hypersensitivity reaction to an aminoglycoside (rare), myasthenia gravis.

**Unless the infection is life-threatening, aminoglycosides should generally be avoided in patients with:** Pre-existing significant auditory impairment (hearing loss or tinnitus), pre-existing vestibular condition (dizziness, vertigo or balance problems), a family history (first-degree relative) of auditory toxicity caused by an aminoglycoside, chronic renal impairment (creatinine clearance less than 40 mL/min) or rapidly deteriorating renal function, advanced age (e.g. 80 years or older, depending on calculated renal function)

**Monitoring**
- Regular Surgical and Guidance registration audits will assess correct agent and correct dose. Reports will be tabled at the Antimicrobial Stewardship Working Party and at the JHH Quality Use of Medicines Committee.
- Use of piperacillin + tazobactam General Surgery will be monitored monthly and results fed back to clinicians

**APPENDICES**
Appendix 1: Empirical treatment of intra-abdominal infections
Appendix 2: Gentamicin dosing—not to be used beyond 48 hours without Infectious Diseases approval

**REFERENCES**
Nil

\(^4\) *E. coli, Klebsiella Enterobacter* species and other species. For recent cumulative antibiograms, see [Pathology North antibiograms](#).
N.B. In the presence of any red zone criterion or two or more yellow zone criteria, gentamicin IV is to be added to the first- or second-line regimen (unless already part of the regimen). For dosing of gentamicin, see Table 3.

<table>
<thead>
<tr>
<th>Condition</th>
<th>First-line IV therapy</th>
<th>Non-immediate penicillin allergic IV therapy</th>
<th>Immediate allergy to penicillin</th>
<th>Treatment duration</th>
<th>Oral treatment if applicable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute appendicitis 6</td>
<td>amoxicillin/clavulanate 1.2 g IV 8-hourly until surgery (if performed)</td>
<td>cefazolin 2 g IV 8-hourly PLUS metronidazole IV 500 mg 12-hourly until surgery (if performed)</td>
<td>gentamicin IV PLUS clindamycin 600 mg IV 8-hourly until surgery (if performed)</td>
<td>Non-perforated - no post-operative doses required. Perforated/abscess- 4 (four) days total post-surgery - treatment choice guided by positive culture results if available</td>
<td>amoxicillin/clavulanate orally 875+125 mg 12-hourly OR in penicillin allergic patient, trimethoprim/sulfamethoxazole orally 160+800 mg 12-hourly</td>
</tr>
<tr>
<td>Acute uncomplicated cholecystitis 8</td>
<td>amoxicillin/clavulanate 1.2 g IV 8-hourly until surgery (if performed)</td>
<td>ceftriaxone 1 g IV daily until surgery (if performed)</td>
<td>gentamicin IV until surgery (if performed)</td>
<td>No post-operative doses required - otherwise 5–7 days total for non-operative cases - treatment choice guided by positive culture results if available</td>
<td>amoxicillin/clavulanate orally 875+125 mg 12-hourly OR in penicillin allergic patient, trimethoprim/sulfamethoxazole orally 160+800 mg 12-hourly</td>
</tr>
<tr>
<td>Ascending cholangitis</td>
<td>amoxicillin/clavulanate 1.2 g IV 8-hourly</td>
<td>ceftriaxone 1 g IV, daily (ADD metronidazole 500 mg IV 12-hourly in chronic biliary obstruction)</td>
<td>gentamicin IV (ADD metronidazole 500 mg IV 12-hourly in chronic biliary obstruction)</td>
<td>Cease antibiotic therapy when signs &amp; symptoms of inflammation have resolved (usually 4–7 days - treatment choice guided by positive culture results if available).</td>
<td>amoxicillin/clavulanate 875+125 mg 12-hourly OR in penicillin allergic patient, trimethoprim/sulfamethoxazole 160+800 mg 12-hourly</td>
</tr>
</tbody>
</table>

5 Oral switch can take place early provided patient clinically improving, normotensive (> 48 hours), afebrile (T < 38°C for 24 hours) and gut working. Microbiological culture and susceptibility should be considered in the decision. Seek Infectious Diseases or Clinical Microbiology advice if multiply resistant pathogens are isolated.

6 Antibiotic therapy can be successful in selected patients with uncomplicated appendicitis who wish to avoid surgery and accept up to a 25% recurrence risk. A majority of patients with appendicitis do not have severe sepsis and/or culture-proven bloodstream infection. It is therefore safe to rely on amoxicillin/clavulanate (includes Gram negative anaerobe cover) or cefazolin with metronidazole for primary therapy.

7 Amoxicillin/clavulanate IV was recently registered in Australia and is available on formulary.

<table>
<thead>
<tr>
<th>Condition</th>
<th>First-line IV therapy</th>
<th>Non-immediate penicillin allergic IV therapy</th>
<th>Immediate allergy to penicillin</th>
<th>Treatment duration</th>
<th>Oral treatment if applicable^5</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute diverticulitis</strong></td>
<td>For uncomplicated cases, antibiotics are not required^9</td>
<td>amoxicillin/clavulanate 1.2 g IV 8-hourly</td>
<td>cefazolin 2 g IV 8-hourly PLUS metronidazole 500 mg IV 12-hourly</td>
<td>gentamicin IV PLUS clindamycin 600 mg IV 8-hourly</td>
<td>5–7 days total</td>
</tr>
<tr>
<td><strong>Peritonitis due to perforated viscus</strong> (includes complicated diverticulitis, appendicitis or cholecystitis) NB. Patients with MRSA, VRE or multi-resistant Gram negative colonisation may require additional therapy.</td>
<td>1. amoxicillin/clavulanate 1.2 g IV 8-hourly PLUS gentamicin OR, if high risk of MRO^10 or &gt; 3 days IV therapy needed, 2. piperacillin/tazobactam 4.5 g IV 8-hourly</td>
<td>ceftriaxone 1 g IV daily PLUS metronidazole 500 mg IV 12-hourly</td>
<td>gentamicin IV PLUS clindamycin 600 mg IV 8-hourly</td>
<td>If adequate source control achieved: 4 days after source control If inadequate source control (e.g. inadequate drainage): 7–10 days in total; switch to oral after clinical criteria satisfied. Treatment choice guided by positive culture results if available. The duration may need to be further prolonged if there are deep undrained collections—seek ID advice.</td>
<td>amoxicillin/clavulanate 875+125 mg 12-hourly OR in penicillin allergic patient, trimethoprim/sulfamethoxazole 160+800 mg 12-hourly</td>
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^9 Acute uncomplicated diverticulitis (AUD) is defined as diverticulitis without abscesses, perforation, colonic obstruction or fistula found by CT scanning of abdomen and pelvis. The decision to perform CT scan imaging is based on symptoms, suspicion of complications or in patients with new onset diverticulitis. Multiple RCTs have shown that antibiotic therapy provides no benefit in AUD with reported complication rates of approximately 2%. Isacson D, Thorisson A, Andreasson K et al. Outpatient non-antibiotic management of acute uncomplicated diverticulitis: a prospective study. International journal of colorectal disease. 2015 Sep;30(9):1229-34.

^10 Piperacillin/tazobactam is preferred for patients requiring repeat surgery for source control, inpatients with peritonitis who have resided more than 7 days in hospital or where patient clinical microbiology cultures indicate the need for an expanded spectrum. If Candida species, vancomycin-resistant enterococcus or other multi-resistant organism isolated, contact Infectious Diseases or Clinical Microbiology for further advice.
Appendix 2: Gentamicin dosing—not to be used beyond 48 hours without Infectious Diseases approval

| Severe sepsis | 7 mg/kg up to 640 mg  
|               | Base subsequent dosing on renal function as below |
| Ongoing therapy | GFR > 60 mL/min 4–5 mg/kg IV, 24 hourly for 2 further doses  
|                  | GFR 40–60 mL/min 4–5 mg/kg, 1 further dose at 36 hours  
|                  | GFR < 40mL/min give 4 mg/kg dose only |

Obese patients: use ideal body weight for aminoglycoside dose calculation\(^\text{11}\) (also see Table 2.32, Therapeutic Guidelines: Antibiotic, Edition 15.  
Empiric therapy: Use for a maximum of 48 hours as pending outcome of investigation.  
NO therapeutic monitoring (levels) required for short course treatment.  
Refer to [HDIS & HNELHD QUM Committee Fact Sheet: Aminoglycosides](https://www.hdh.org.au) for further information (available on PPG) and Therapeutic Guidelines: Antibiotic, Edition 15, Appendix 2.

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\(^\text{11}\) Ideal weight for men = 50 kg + 0.9 kg per cm over 152 cm (2.3 kg per inch over 5 feet). Ideal weight for women = 45.5 kg + 0.9 kg per cm over 152 cm (2.3 kg per inch over 5 feet)