**Clinical Guideline**
**John Hunter Hospital**

**Short Course Antibiotics for Intra-abdominal Sepsis - Adult**

<table>
<thead>
<tr>
<th>Sites where Clinical Guideline applies</th>
<th>JHH</th>
</tr>
</thead>
<tbody>
<tr>
<td>This Clinical Guideline applies to:</td>
<td></td>
</tr>
<tr>
<td>1. Adults</td>
<td>Yes</td>
</tr>
<tr>
<td>2. Children up to 16 years</td>
<td>No</td>
</tr>
<tr>
<td>3. Neonates – less than 29 days</td>
<td>No</td>
</tr>
</tbody>
</table>

**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

**Keywords**
Antibiotic, intra-abdominal, sepsis, stewardship, diverticulitis, appendicitis, cholangitis, cholecystitis, peritonitis, pancreatitis, liver abscess

**Document registration number**

**Replaces existing document?**
No

**Registration number and dates of superseded documents**

**Related Legislation, Australian Standard, NSW Ministry of Health Policy Directive or Guideline, National Safety and Quality Health Service Standard (NSQHSS) and/or other, HNE Health Document, Professional Guideline, Code of Practice or Ethics:**
- National Safety & Quality Health Standard 3.14
- Therapeutic Guidelines: Antibiotic, Therapeutic Guidelines®, Melbourne, Victoria 2014

**Position responsible for Clinical Guideline Governance and authorised by**
Director Infectious Diseases JHH

**Clinical Guideline contact officer**
Lisa Harris

**Contact details**
49213635

**Date authorised**
13 April 2017

**This document contains advice on therapeutics**
Yes
Approval gained from JHH Quality Use of Medicines Committee on 13 April 2017

**Issue date**
April 2017

**Review date**
April 2020

**TRIM number**
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.

RISK CATEGORY: Clinical Care & Patient Safety

SUMMARY
Successful treatment of intra-abdominal infections usually requires both effective source control and the use of antibiotics.

**Where source control is possible**, a fixed duration of 4 days of antibiotic treatment gives similar outcomes to that of traditionally longer courses ≥ 8–14 days and results in lower antibiotic exposure and decreased drug adverse events including diarrhoea and phlebitis.

Non-compliance with empirical antibiotic guidelines for intra-abdominal infections is associated with increased morbidity and mortality, particularly where risk factors for multidrug-resistant bacteria exist.

GLOSSARY

<table>
<thead>
<tr>
<th>Acronym or Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>HNELHD</td>
<td>Hunter New England Local Health District</td>
</tr>
<tr>
<td><em>E. coli</em></td>
<td><em>Escherichia coli</em></td>
</tr>
<tr>
<td>TDM</td>
<td>Therapeutic drug monitoring</td>
</tr>
</tbody>
</table>
GUIDELINE

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.

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 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 72\% 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

<table>
<thead>
<tr>
<th></th>
<th>1,651</th>
<th>100%</th>
</tr>
</thead>
<tbody>
<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>
</tr>
</tbody>
</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 Table 3) 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.

Intra-abdominal Sepsis - Adult

- most Enterobacteriaceae 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)

4 *E. coli, Klebsiella, Enterobacter* species and other species. For recent cumulative antibiograms, see Pathology North antibiograms.
### Table 2 Empirical treatment of intra-abdominal infections

*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 [7] 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—7 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>
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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</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute diverticulitis</td>
<td>For uncomplicated cases, antibiotics are not required²</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>
<td>amoxicillin/clavulanate orally 875+125 mg 12-hourly OR in penicillin allergic patient, trimethoprim/sulfamethoxazole orally 160+800 mg 12-hourly PLUS metronidazole orally 400 mg 12-hourly</td>
</tr>
<tr>
<td>Peritonitis due to perforated viscus (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 MRO⁹ 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 PLUS metronidazole orally 400 mg 12-hourly</td>
</tr>
</tbody>
</table>

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, Andresson 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.
Table 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\(^{11}\) (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](#) for further information (available on PPG) and Therapeutic Guidelines: Antibiotic, Edition 15, Appendix 2.

**IMPLEMENTATION PLAN**

- The guideline will be available on the Policy, Procedures and Guidelines
- Infectious Diseases and Gastroenterology/General Surgeons have been consulted in the development of this guideline and have agree to the treatment recommendations
- The guideline will be further disseminated to staff on ward J3S and to the surgeons by the Antimicrobial Stewardship Working Party and the clinical pharmacists
- Medical and Nursing staff will receive education from Pharmacy, Infectious Diseases & Clinical Microbiology
- JHH Antimicrobial Stewardship Working Party is responsible for updating this guideline

**MONITORING AND AUDITING PLAN**

- 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

\(^{11}\) 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)
CONSULTATION WITH KEY STAKEHOLDERS

- Surgical Departments – pending
- Pharmacy Department
- Infectious Diseases and Immunology
- JHH Quality Use of Medicines Committee and Antimicrobial Stewardship Working Party

FEEDBACK

Any feedback on this document should be sent to the Contact Officer listed on the front page.
**Clinical Audit Tool** – Only create a new and separate audit tool where necessary. Clinical Audits should be amalgamated and embedded within a Clinical Audit Program

*(National Standard 1: 1.7.2 The use of agreed clinical guidelines by the clinical workforce is monitored)*

<table>
<thead>
<tr>
<th>Criterion no.</th>
<th>Criterion</th>
<th>Exceptions</th>
<th>Definition of terms and/or general guidance</th>
<th>Data source</th>
<th>Frequency</th>
<th>Position Responsible</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Compliance with guideline recommendations</td>
<td>None.</td>
<td>All cases comply with guidelines</td>
<td>Patient health record.</td>
<td>12 monthly</td>
<td>QUM Pharmacist</td>
</tr>
</tbody>
</table>