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# Intra-abdominal Infections Treatment Protocol

**Abbreviations**

IV: Intravenous
PO: Oral
GI: Gastrointestinal
g: Gram
mg: Milligram
kg: Kilogram
dL: Deciliter
h: Hours
q24hr: Every 24 hours
q12hr: Every 12 hours
q8hr: Every 8 hours
q6hr: Every 6 hours
SCr: Serum Creatinine
TMP-SMX: Trimethoprim-sulfamethoxazole
DS: Double strength
SS: Single strength
SIRS: Systemic inflammatory response syndrome
PCN: Penicillin
MDR-GNR: Multidrug-resistant Gram-negative rods
SBP: Spontaneous bacterial peritonitis
MRSA: Methicillin-resistant Staphylococcus *aureus*

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## Introduction

- Infections within the abdominal cavity typically arise because of inflammation or disruption of the gastrointestinal tract.
- Intra-abdominal infections are the second most common cause of infectious mortality in intensive care units.
- Antimicrobial therapy should be initiated once a patient receives a diagnosis of an intra-abdominal infection or once such an infection is considered likely.
- For patients without septic shock, antimicrobial therapy should be started in the emergency department.
- Satisfactory antimicrobial drug levels should be maintained during a source control intervention, which may necessitate additional administration of antimicrobials just before initiation of the procedure.

**Purpose:**

- In 2021 one of the most indication reported through Antimicrobial stewardship program was intra-abdominal infection at MOH hospitals
- **This treatment protocol** to support MOH hospitals in activating /launching / improving the antimicrobials stewardship program.

**Aim and scope:**

- The protocol aims to provide an evidence based, safe and cost-effective treatment guide for intrabdominal infections in the inpatient setting
- For hospital-acquired infections, the choice between the recommended agents should be based on local resistance data (i.e., the antibiogram)

**Targeted population**: Hospitalized immunocompetent patients who are diagnosed with Intra-abdominal infections.

**Targeted end users:** Physicians, pharmacists/clinical pharmacists, and nurses.

**Setup**: Inpatient setting.

**Methodology:**
These recommendations are based on the high quality of evidence along with expert opinions maintaining the best practices guidelines and taking into consideration the local resources, and cultural variation.

**Conflict of interest:** This protocol was developed based on valid scientific evidence, critical assessment of that evidence, and objective clinical judgment that relates the evidence to the needs of practitioners and patients.

**Funding:** No fund was provided

**Updating:** First version of this protocol created in 2022. The protocol will be updated every three years or if any changes or updates released by international/national guidelines, pharmacotherapy references or MOH formulary

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# INTRA-ABDOMINAL INFECTIONS IN ADULTS

## Introduction:

## Classification of Intra-abdominal infection in adults:

Two classifications are used to subdivide INTRA-ABDOMINAL INFECTIONS:

- Uncomplicated
- Complicated, considering infection extent; and community-acquired, healthcare-associated or hospital-acquired, regarding the place of acquisition.

According to the Infectious Diseases Society of America (IDSA), complicated **Intra-abdominal infections** is defined as an infection that extends beyond the wall of a hollow viscus of origin into the abdominal cavity while being associated with an abscess or peritonitis.

**Factors indicating healthcare-associated intra-abdominal infection:**

A patient is considered to have healthcare-associated intra-abdominal infection if any of the following factors is met:

1. Hospitalized for at least 48 hours during the previous 90 days
2. Residing in a skilled nursing or long-term care facility during the previous 30 days
3. Received IV infusion therapy, wound care, or renal replacement therapy within the previous 30 days
4. Received several days of broad-spectrum antimicrobial therapy within the previous 90 days
5. Have postoperative infection
6. Known to have been colonized or infected previously with a resistant pathogen

## SOURCE CONTROL:

Source control should be done within 24h of diagnosis. This may include draining of infected peritoneal fluid, resection of intra-abdominal abscess, cholecystectomy (only in case of severe cholecystitis), appendectomy (only in case of severe perforated appendicitis), repair of intestinal perforation, etc.

## EMPIRIC ANTIMICROBIAL THERAPY:

Empirical treatment is established by identifying whether the infection is healthcare- versus community-acquired, which organs are infected, and whether the infection is complicated or uncomplicated.

- ***HEALTHCARE-ASSOCIATED INTRA-ABDOMINAL INFECTIONS*** *(table 1)*

| Regimen | Empiric antibiotic regimens for health care-associated intra-abdominal infections adults |
|---|---|
| **Single agent regimen** | Imipenem-cilastatin 500 mg IV q6h |
| | Meropenem 1 g IV q8h |
| | Piperacillin-tazobactam 4.5 g IV q6h |
| **Combination therapy** | **ONE of the following:** |
| | Cefepime 2 g IV q8h **Or** |
| | Ceftazidime 2 g IV q8h |
| | **PLUS:** |
| | Metronidazole 500 mg IV or PO q8h |
| | **PLUS ONE of the following (in some cases*)**: |
| | Ampicillin 2 g IV q4h **Or** |
| | Vancomycin 15 to 20 mg/kg IV q8h to q12h |

* Add ampicillin or vancomycin to a cephalosporin-based regimen to provide enterococcal coverage, particularly in those with postoperative infection, prior use of antibiotics that select for *Enterococcus*, immunocompromising condition, valvular heart disease, or prosthetic intravascular materials.

- ***- COMMUNITY-ACQUIRED INFECTION*** *(table 2)*

| Regimen | Community-Acquired infection in Adults | |
|---|---|---|
| | **Mild to moderate infection*** | **Severe infection or high risk[1]** |
| **Single agent** | Ertapenem 1 g IV q24h | Imipenem-cilastatin 500 mg IV q6h |
| | Piperacillin-tazobactam 3.375 g IV q6h | Meropenem 1 g IV q8h |
| | Moxifloxacin 400 mg IV q24h | Piperacillin/tazobactam 4.5 g IV q6h |
| **Combination therapy** | **One of the following** | |
| | Cefazolin 1 to 2 g IV q8h | Cefepime 2 g IV q8h |
| | Cefuroxime 1.5 g IV q8h | |
| | Cefotaxime 2 g IV q8h | Ceftazidime 2 g IV q8h |
| | Ceftriaxone 2 g IV q24h | |
| | **High-risk allergy/contraindications to beta-lactams:** Ciprofloxacin 400 mg IV q12h or 500 mg PO q12h | The combination of vancomycin, aztreonam, and metronidazole is an alternative for those who cannot use beta-lactams or carbapenems (e.g., because of severe allergic reactions, such as anaphylaxis, angioedema, or urticaria). |
| | Levofloxacin 750 mg IV or PO q24h | |
| | Plus metronidazole[2] **500 mg IV or PO q8h | Plus metronidazole[2] 500 mg IV or PO q8h |

**Includes perforated appendicitis, abscessed appendix, and other infections of mild to moderate severity.*
*** For most uncomplicated biliary infections of mild to moderate severity, the addition of metronidazole is **not** necessary.*
[1]*Includes severe physiologic disturbance, septic shock, older, or immunocompromised patients.*
[2]*Because of increasing resistance of Escherichia coli to fluoroquinolones, local population susceptibility profiles and isolate susceptibility should be reviewed.*

**NOTES:**

- Microbiological cultures should be collected before the initiation of antimicrobial therapy.
- Always prefer using beta-lactam-based regimen over fluoroquinolones and aztreonam regimens unless the patient has documented severe beta-lactam allergy (such as anaphylaxis, angioedema, or urticaria). This is due to risk of emergence of bacterial resistance to fluoroquinolones.
- Coverage for methicillin-resistant *Staphylococcus aureus* (MRSA):

- For patients colonized with MRSA (as known by nasal swab PCR), prior treatment failure, or advanced age (≥ 65 years).
- Use vancomycin (15 to 20 mg/kg IV every 8 to 12 hours) or teicoplanin (loading dose of 6 mg/kg every 12h for 3 doses, then maintenance dose of 6 mg/kg q24h). Alternatives: linezolid (600 mg IV or PO q12h) or daptomycin (6 to 8 mg/kg IV q24h).

- Tigecycline is not recommended for empiric therapy unless other agents are not suitable.
- Antifungal coverage: Only if fungal infection is confirmed in cultures.
- Empiric coverage should be considered in patients with recurrent gastrointestinal perforations (i.e., tertiary peritonitis).
- Anaerobic coverage (i.e., metronidazole) is not necessary for patients with community-acquired cholecystitis/cholangitis of mild-moderate severity, unless a biliary-enteric anastomosis or emphysematous cholecystitis is present.
- Definitive antimicrobial therapy should be guided by microbiological culture and susceptibility results as soon as they become available.
- Treatment based on blood cultures should be considered if the organism grew in ≥ 2 blood cultures.
- Switching to oral antibiotics is acceptable after initial recovery from infection if patient can tolerate oral diet.

**DURATION OF THERAPY:**

- GI perforations or severe biliary infections (cholecystitis or cholangitis) operated within 12-24h do not need more than 24h of therapy post-surgery.
- In case of adequate source control (e.g., adequate drainage of infected peritoneal fluid in case of peritonitis): 4 days.
- In case of adequate source control with initial bacteremia: 7 days.
- In case of inadequate source control: 5-7 days.
- In case of failed therapy (i.e., no clinical improvement after 4-7 days of therapy): repeat diagnostic investigation and consider non-infectious conditions.

## Spontaneous Bacterial Peritonitis

- **1st line:**

Ceftriaxone 2 g IV q24h

- **Alternative in patients with high-risk allergy/contraindication to beta-lactams *receiving* fluoroquinolone prophylaxis:**

Aztreonam* 2 g IV q8h + vancomycin*

- **Alternative in patients with high-risk allergy/contraindication to beta-lactams *NOT receiving* fluoroquinolone prophylaxis:**

Ciprofloxacin* 400 mg IV q8h

**Prophylaxis in Patients with Cirrhosis and GI Bleeds:**

- **1st line:**

Ceftriaxone 1 g IV q24h

- **Alternative in patients with high-risk allergy/contraindication to beta-lactams *receiving* fluoroquinolone prophylaxis:**

Aztreonam* 1 g IV q8h + vancomycin*

- **Alternative in patients with high-risk allergy/contraindication to beta-lactams *NOT receiving* fluoroquinolone prophylaxis:**

Ciprofloxacin* 400 mg IV q12h

* For patients with severe allergy to penicillins and cephalosporins, such as anaphylaxis, angioedema, or urticaria.

## Pancreatitis

- **Acute Pancreatitis without Necrosis or Abscess:** Antibiotics not recommended
- **Acute Necrotizing Pancreatitis with Sterile Necrosis:** Prophylaxis for sterile necrosis is not indicated.
- **Acute Necrotizing Pancreatitis in patients with hemodynamic instability, Persistent/worsening SIRS criteria after 7-10 days off antibiotic therapy, and Acute Necrotizing Pancreatitis with Proven Infection**: Start antibiotic therapy as outlined above (table 1 & 2).

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## Stepdown oral therapy

| If the patient is improving and tolerating oral diet. It should be guided by culture and susceptibility results (if available) |
|---|
| - Appendicitis<br>- Cholangitis and Cholecystitis<br>- Acute Uncomplicated Diverticulitis<br>- Secondary Peritonitis (infection associated with perforation or spillage of GI pathogens into the peritoneal cavity)<br>- Tertiary Peritonitis (Persistent infection associated with recurring GI perforation and/or anastomotic leakage after initial treatment for secondary peritonitis):<br>Amoxicillin-clavulanic acid* 875 mg PO q12h<br>**OR**<br>Moxifloxacin 400 mg PO q24h<br>**OR**<br>Metronidazole 500mg PO q8h + Cefuroxime* 500 mg PO q12h or cephalexin 500 mg PO q6h or cefixime 400 mg PO q24h or 200 mg PO q12h or cefpodoxime 200 mg PO q12h or cefadroxil 1 g q12h<br>**High-risk allergy/contraindications to beta-lactams OR MDR-GNR risk:**<br>Ciprofloxacin* 750 mg PO q12h + Metronidazole 500 mg PO q8h |
| - **Spontaneous Bacterial Peritonitis:**<br>Culture positive and clinically improving after 48-72h of IV therapy with oral antibiotic options feasible per culture and susceptibility results<br>Patients with culture-negative SBP who are hemodynamically stable and responding (exam, lab parameters, and repeat paracentesis if performed) after 48h of empiric therapy.<br>Oral step-down therapy options for patients with culture-negative SBP:<br>**1st line:**<br>Amoxicillin-clavulanate* 875 mg PO q12h<br>**Alternative in patients with low/medium-risk allergy to penicillins:**<br>Cefuroxime* 500 mg PO q12h<br>**High-risk allergy/contraindications4 to beta-lactams OR MDR-GNR risk**:<br>Ciprofloxacin* 750 mg PO q12h |
| -**Prophylaxis in Patients with Cirrhosis and GI Bleeds:**<br>Patients who are hemodynamically stable and whose bleeding is controlled (no further procedures or/and transfusions needed in past 24 hours) after 48 hours of prophylaxis Oral step-down therapy:<br>**1st line**:<br>Amoxicillin-clavulanate* 500 mg PO q12h<br>**Alternative in patients with low/medium-risk allergy to penicillins:**<br>Cefuroxime* 250 mg PO q12h<br>**Alternative in patients with high-risk allergy/contraindication to beta-lactams:**<br>Ciprofloxacin* 500 mg PO q24h |

*Adjust based on renal function

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