Appendix 27 - INTRA-ABDOMINAL INFECTIONS (IAI)

[A] Selection of empiric antimicrobial therapy for adult patients with CA-IAI:

- The routine use of aminoglycoside-based regimens for the empiric treatment of patients with IAI is not recommended. These regimens may be useful for treatment of IAI in neonatal patients and in adults and children because of resistant gram-negative organisms, if other agents are not suitable.
- The use of selected oral agents with good bioavailability as a substitute for IV agents in the treatment of patients with IAI when the patient has return of adequate gastrointestinal function is recommended. Oral amoxicillin-clavulanic acid as an acceptable regimen to complete a short course of antimicrobial therapy for the treatment of IAI in adults and children older than one month with IAI.
- Oral moxifloxacin and Oral ciprofloxacin plus metronidazole are acceptable regimens in adults, not recommended for children unless other options are not suitable.
- Oral levofloxacin plus metronidazole, an oral first-, second-, or third-generation cephalosporin plus metronidazole, or oral trimethoprim-sulfamethoxazole plus metronidazole can be used as alternative regimens for the treatment of IAI in adults and children older than one month, if other oral agents are not suitable.
- **PE (Treatment Protocol Based on The Surgical Infection Society Revised Guidelines on the Management of Intra-Abdominal Infection 2017)**

[A-1] Lower-risk patients with CA-IAI:

- Treatment of Community Acquired-Intra-Abdominal Infections (CA-IAI) in lower-risk patients with narrower-spectrum antimicrobial agents having activity against the usual gram-negative Enterobacteriaceae, aerobic streptococci, and obligate anaerobic microorganisms associated with these infections. Not to use broader spectrum or additional agents specifically to provide antipseudomonal or anti-enterococcal coverage. Antifungal coverage is unnecessary for management of CA-IAI in lower-risk patients.

Table 1: Recommended Empiric Antimicrobial Regimens for Patients with Community Acquired Intra-Abdominal Infection

Lower-risk patients[a,b]	*Higher-risk patients*
Single agents	
Ertapenem	Piperacillin-tazobactam
Moxifloxacin[c]	Doripenem[f]
	Imipenem-cilastatin
	Meropenem[f]
Combination regimens	
Cefotaxime or ceftriaxone plus metronidazole[d]	Cefepime plus metronidazole[f,g]
Ciprofloxacin plus metronidazole[c,e]	Aztreonam plus metronidazole plus vancomycin[h]

C The Use of fluoroquinolones is suggested primarily for patients with significant reactions to b-lactam antibiotic agents.
d Cefuroxime plus metronidazole is also an option, is less well supported by contemporary data.
e If levofloxacin is the only fluoroquinolone available on a formulary, it may be substituted for ciprofloxacin. There is little evidence with regard to its efficacy, and it is not approved by the Food and Drug Administration for treatment of patients with complicated intra-abdominal infection.
f Use of an agent such as ampicillin or vancomycin effective against Enterococcus spp. can be considered in patients with severe sepsis-septic shock and other higher-risk patients who receive **DORIPENEM** or meropenem and should be added to a cephalosporin-based regimen.
g Ceftazidime plus metronidazole is also an option, is less well supported by contemporary data. h Aztreonam plus metronidazole plus vancomycin is an option for patients with significant reactions to b-lactam antibiotic agents, is less well supported by contemporary data.

ST: Cefotaxime or ceftriaxone plus metronidazole OR ertapenem monotherapy

- Cefotaxime or ceftriaxone plus metronidazole combinations or ertapenem monotherapy are the preferred antimicrobial agents for the management of CA-IAI in lower-risk adult patients.

ST: Moxifloxacin-Ciprofloxacin-Levofloxacin

- The use of a fluoroquinolone-based regimen for initial empiric antimicrobial therapy of CA-IAI in lower risk patients who have had major reactions to beta-lactam antibiotic agents.

ST: Ciprofloxacin plus metronidazole OR moxifloxacin monotherapy

- Cefotaxime or ceftriaxone plus metronidazole combinations or ertapenem monotherapy are the preferred antimicrobial agents for the management of CA-IAI in lower-risk patients. Ciprofloxacin plus metronidazole combination or moxifloxacin monotherapy should be used as alternatives for the management of CA-IAI in lower-risk patients who have serious b-lactam allergies.

ST: Levofloxacin plus metronidazole

- Ciprofloxacin plus metronidazole combination or moxifloxacin monotherapy are used for the management of CA-IAI in lower-risk patients who have serious b-lactam allergies as alternatives. Levofloxacin plus metronidazole should be used as an alternative only if no other fluoroquinolone is available. [ciprofloxacin and moxifloxacin are preferred]

ST: Cefuroxime plus metronidazole OR CEFOPERAZONE-sulbactam

- Cefotaxime or ceftriaxone plus metronidazole combinations or ertapenem monotherapy are the preferred antimicrobial agents for the management of CA-IAI in lower-risk patients. Cefuroxime plus metronidazole or CEFOPERAZONE-sulbactam, where available, are used as alternative empiric antimicrobial regimens for the management of CA-IAI in lower-risk patients.

PA: Patients with perforated appendicitis

- Treatment of patients with perforated appendicitis should be with the same agents or regimens recommended for other lower-risk patients with CA-IAI, unless they meet criteria identifying them as higher-risk patients or at risk for having resistant pathogens, and this should be confirmed by the prescriber.

[A-2] Higher risk patients with CA-IAI:

- Treatment of CA-IAI in higher-risk patients should be with broader-spectrum empiric antimicrobial agents to ensure coverage of less common gram-negative pathogens potentially involved in these infections.
- Piperacillin-tazobactam, imipenem CILASTATIN, meropenem, DORIPENEM, or cefepime plus metronidazole are recommended as the preferred antimicrobial agents for empiric treatment of CA-IAI in higher-risk patients

Table 2: Factors Potentially Identifying Patients with Intra-Abdominal Infection at Higher Risk

Phenotypic/physiologic risk factors
Advanced age (≥70 y)
Malignancy
Significant cardiovascular compromise
Significant liver disease or cirrhosis
Significant renal disease
Hypoalbuminemia
Extent of infection/adequacy of initial source control
Diffuse, generalized peritonitis
Elevated MPI score
Delayed initial source control
Inability to achieve adequate source control
Microbiologic characteristics
Suspected infection with resistant pathogens

MPI = Mannheim Peritonitis Index.

ST: Ceftazidime plus Metronidazole

- Piperacillin-tazobactam, imipenem CILASTATIN, meropenem, DORIPENEM, or cefepime plus metronidazole are the preferred antimicrobial agents for empiric treatment of CA-IAI in higher-risk patients. Ceftazidime plus metronidazole can be used as an alternative regimen for these patients.
- **The addition of an adjunctive** aminoglycoside or fluoroquinolone to a b-lactam agent for empiric management of CA-IAI in higher-risk patients is not recommended.

ST: An aztreonam based regimen

- An aztreonam based regimen is recommended for initial empiric therapy of CA-IAI in higher-risk patients who have had major reactions to beta-lactam antibiotic agents.

ST: Aztreonam plus metronidazole plus vancomycin

- Aztreonam plus metronidazole plus vancomycin as combination therapy is used as alternative for empiric treatment of CA-IAI in higher-risk patients who are with a severe reaction to beta-lactam agents.

CU: Ampicillin or Vancomycin

- The addition of ampicillin or vancomycin is recommended for empiric anti-enterococcal management or coverage of CA-IAI in higher risk patients, if the patient is not being treated with piperacillin-tazobactam or imipenem-CILASTATIN.

Empiric Antifungal Therapy

- Routine use of empiric antifungal therapy for management of CA-IAI in higher-risk patients is not recommend, empiric antifungal therapy should be considered for critically ill patients with CA-IAI because of upper gastrointestinal perforations.

PA-CU: Fluconazole

- Fluconazole should be added for pre-emptive management of IAI in non-critically ill adults and children who are at high risk for intra-abdominal candidiasis, and for pathogen-directed treatment of non-critically ill patients infected with susceptible strains of C. albicans, and this should be confirmed by the prescriber.

ST-CU: Voriconazole

- Voriconazole is recommended to be added for empiric or pathogen-directed management of IAI in non-critically ill adults and children older than one month who are suspected or proven to be infected with strains of Candida that are not susceptible to fluconazole.

ST-CU: Anidulafungin, CASPOFUNGIN, or Micafungin

- An echinocandin (anidulafungin, CASPOFUNGIN, or micafungin) should be added for empiric or pathogen directed management of IAI in severely ill adults and children older than one month who are suspected or proven to be infected with Candida spp.

ST: Ertapenem- DORIPENEM-Imipenem/CILASTATIN or Meropenem

- The use of ertapenem for empiric antimicrobial therapy of CA-IAI in lower-risk patients or a broad-spectrum carbapenem (DORIPENEM, imipenem-CILASTATIN, or meropenem) for CA-IAI in higher-risk patients, is recommended for patients at a high prevalence of ESBL-producing Enterobacteriaceae in the community.

[B] Selection of empiric antimicrobial therapy for adult patients with Hospital Acquired- Abdominal Infection (HA-IAI)

- All patients with HA-IAI be assessed with respect to their separate risks of infection from Enterococcus spp., MRSA, resistant gram-negative bacilli, and Candida spp.
- The broader-spectrum agents or regimens described for use in higher-risk patients with CA-IAI should be used for the initial empiric antimicrobial therapy of patients with HA-IAI.
- Other empiric agents should be added to the regimen according to the assessment of the patient's risk for an infection from Enterococcus spp., MRSA, resistant gram-negative bacilli, and Candida spp.

Table 3: Criteria for Healthcare- or Hospital Acquired Intra-Abdominal Infection

Infection developing greater than 48 h after initial source control.
Hospitalized for greater than 48 h during current admission or within the previous 90 d.
Residence in a skilled nursing or other long-term care facility within the previous 30 d.
Home infusion therapy, home wound care, or dialysis within the preceding 30 d.
Use of broad-spectrum antimicrobial therapy for 5 d or more during the preceding 90 d.

Table 4: Summary of Empiric Antimicrobial Therapy for Patients with Healthcare- or Hospital-Acquired Intra-Abdominal Infection

General approach	
Piperacillin-tazobactam, doripenem, imipenem-cilastatin, meropenem, or cefepime plus metronidazole, with ceftazidime plus metronidazole and aztreonam plus metronidazole plus vancomycin as potential alternatives	
Supplemental agents	
Potential pathogen	Recommendations
Enterococcus faecalis	Addition of ampicillin or vancomycin if not using piperacillin-tazobactam or imipenem-cilastatin
Enterococcus faecium	Vancomycin or teicoplanin
Vancomycin-resistant *Enterococcus* spp.	Daptomycin or linezolid
MRSA	Vancomycin, teicoplanin, daptomycin, or linezolid
ESBL-producing or AmpC-β-lactamase-producing Enterobacteriaceae	Use of a broad-spectrum carbapenem
KPC-producing Enterobacteriaceae	Combination therapy with a broad-spectrum carbapenem plus an aminoglycoside, polymyxin, or tigecycline; or ceftazidime-avibactam
MDR strains of *Pseudomonas aeruginosa*	Combination therapy with an aminoglycoside plus colistin, or ceftolozane-tazobactam or ceftazidime-avibactam
MDR strains of *Acinetobacter baumannii*	Combination therapy with a broad-spectrum carbapenem plus an aminoglycoside, polymyxin, or tigecycline
Candida albicans	An echinocandin (anidulafungin, caspofungin, micafungin) for critically ill patients, fluconazole for less critically ill patients
Non-*C. albicans* spp.	An echinocandin

MRSA =methicillin-resistant Staphylococcus aureus; ESBL= extended-spectrum beta-lactamase; KPC=Klebsiella pneumoniae **CARBAPENEMASE**.

General approach

Piperacillin-tazobactam, DORIPENEM, imipenem-CILASTATIN, meropenem, or cefepime plus metronidazole, with ceftazidime plus metronidazole and aztreonam plus metronidazole plus vancomycin all as potential alternatives.

CU: Ampicillin OR Vancomycin:

- The Addition of ampicillin or vancomycin should be considered to the treatment regimen of HA-IAI, if not using piperacillin/tazobactam or imipenem-CILASTATIN as an empiric treating agent, because Enterococcus faecalis is potential pathogen.

CU-ST: Linezolid or Daptomycin

- Vancomycin or teicoplanin are the recommended agents for empiric antimicrobial therapy of HA-IAI in patients considered at risk for an infection from Enterococcus spp. Alternatively linezolid or daptomycin should be used for management of HA-IAI if patients known to be colonized with VRE or considered at high risk for infection from this organism.

CU-ST: Linezolid or Daptomycin

- Vancomycin or teicoplanin are the preferred agents, where available, for empiric antimicrobial therapy of HA-IAI in patients known to be colonized with MRSA or considered at high risk for infection from this organism, if being not available linezolid or daptomycin can be used as alternatives.

Antibacterial therapy for resistant gram-negative organisms

- Patients with HA-IAI who have received substantial previous broad-spectrum antimicrobial therapy, have had prolonged hospitalizations, have undergone multiple invasive interventions, or are known to have been colonized or infected with a resistant gram-negative organism is being considered at risk for infection from a **resistant gram-negative pathogen.**
- The use of local epidemiologic data and antibiograms for selecting empiric antimicrobial therapy of HA-IAI in patients considered at risk for infection with resistant gram-negative pathogens is highly recommended.

ST: Imipenem/CILASTATIN, Meropenem, DORIPENEM, CEFTOLOZANE -Tazobactam or Ceftazidime-Avibactam

- A broad-spectrum carbapenem: Imipenem/CILASTATIN, Meropenem, DORIPENEM, with CEFTOLOZANE - tazobactam or ceftazidime-avibactam are used as potential alternatives, for empiric antimicrobial therapy of HA-IAI in patients considered at risk for infection with ESBL producing Enterobacteriaceae. [CEFTOLOZANE - Tazobactam or Ceftazidime-Avibactam, clinical experience with these agents is still limited]

ST: Imipenem CILASTATIN, Meropenem, DORIPENEM, Ceftazidime-Avibactam

- A broad-spectrum carbapenem: Imipenem/CILASTATIN, Meropenem, DORIPENEM, and ceftazidime-avibactam are recommended as a potential alterative, for empiric antimicrobial therapy of HA-IAI in patients considered at risk for infection with Amp C–b-lactamase-producing Enterobacteriaceae. [but clinical experience using Ceftazidime-Avibactam to treat Amp C–b-lactamase producing gram-negative pathogens is quite limited]

ST: Combinations of a carbapenem with an aminoglycoside, Colistin, and/or tigecycline, or Ceftazidime avibactam.

- Combinations of a broad-spectrum carbapenem with an aminoglycoside, a polymyxin, and/or tigecycline, or ceftazidime avibactam should be considered, for empiric antimicrobial therapy of HA-IAI in patients considered at risk for infection with carbapenem-resistant Enterobacteriaceae, KPC-producing Enterobacteriaceae.

ST: CEFTOLOZANE-Tazobactam, ceftazidime-avibactam, an Aminoglycoside, and/or Colistin

- Combinations of a b-lactam, including CEFTOLOZANE-tazobactam, ceftazidime-avibactam, an aminoglycoside, and/or Colistin, should be considered for empiric antimicrobial therapy of HA-IAI in patients considered at risk for infection from MDR, XDR, or PDR strains of P. aeruginosa.

ST: A broad-spectrum Carbapenem plus Aminoglycoside, Colistin, and/or Tigecycline

- Combinations of a broad-spectrum carbapenem plus aminoglycoside, a polymyxin, and/or tigecycline should be considered for empiric antimicrobial therapy of HA-IAI in patients considered at risk for infection from MDR, XDR, or PDR strains of Acinetobacter spp.

Antifungal therapy:

PA: Fluconazole

- It is recommended fluconazole can be used for empiric antifungal therapy in less severely ill patients with HA-IAI considered at *risk for infections from Candida spp., and this should be confirmed by the prescriber.*

ST: Anidulafungin, CASPOFUNGIN, or Micafungin

- Recommended an echinocandin (anidulafungin, CASPOFUNGIN, or micafungin) should be used for empiric antifungal therapy of HA-IAI in severely ill patients considered at risk for infection from Candida spp.

ST: Anidulafungin, CASPOFUNGIN, Micafungin or Voriconazole

- It is recommended an echinocandin (anidulafungin, CASPOFUNGIN, or micafungin) or voriconazole should be used for empiric antifungal therapy of patients with HA-IAI considered at risk for infection because of a fluconazole-resistant non-C. albicans strain.

Duration of antimicrobial therapy:

- It is recommended that antimicrobial therapy be limited to 24 hours in patients:
  - With traumatic bowel perforations operated on within 12 hours, patients with gastroduodenal perforations operated on within 24 hours, patients with acute or gangrenous appendicitis in the absence of perforation, patients with acute or gangrenous cholecystitis in the absence of perforation, or patients with ischemic, non-perforated bowel.
  - It is recommended no more than four full days (96 h) of antimicrobial therapy for patients with IAI who had an adequate source control procedure.
  - It is recommended that no more than 5–7 days of antimicrobial therapy be provided to patients with established IAI in whom a definitive source control procedure is not performed.

Oral antimicrobial agents

- The use of selected oral agents with good bioavailability as a substitute for IV agents in the treatment of patients with IAI when the patient has return of adequate gastrointestinal function is recommended. Oral amoxicillin-clavulanic acid as an acceptable regimen to complete a short course of antimicrobial therapy for the treatment of IAI in adults and children older than one month with IAI.
- Moxifloxacin, ciprofloxacin or levofloxacin plus metronidazole, co-trimoxazole plus-metronidazole.
- Oral first-, second-, and third-generation cephalosporins, including cephalexin, cefadroxil, cefradine, cefuroxime, cefaclor, CEFPROZIL, cefdinir, and cefpodoxime, in combination with metronidazole, are potential options, as they have reasonable activity against non–ESBL-producing strains of E. coli

[C] Treatment of paediatric IAI

[C-1] Paediatric patients older than one month

Table 5: Recommended Empiric Antimicrobial Regimens for Pediatric Patients Older than One Month with Community-Acquired Intra-Abdominal Infection *
[More than 45 weeks' post-conceptual age]

Lower-risk patients	*Higher-risk patients*
Preferred regimens	
Cefotaxime or ceftriaxone plus metronidazole	Piperacillin-tazobactam
Ertapenem	Imipenem-cilastatin Meropenem
Alternative regimens	
Cefuroxime plus metronidazole	Ceftazidime or cefepime plus metronidazole[a] Aztreonam plus metronidazole plus vancomycin
Optional regimens	
Ciprofloxacin or levofloxacin plus metronidazole	

a-Use of an agent effective against Enterococcus spp. is suggested in patients with severe sepsis/septic shock who receive a cephalosporin-based regimen.

Table 6: Summary of Empiric Antimicrobial Therapy for Pediatric Patients Less than One Month Old with Intra-Abdominal Infection* **[Less than 45 weeks' post-conceptual age]**

General recommendation

Ampicillin, gentamicin, plus metronidazole
Ampicillin, cefotaxime, plus metronidazole
Meropenem

Additional agents

Potential pathogen	*Suggestion*
Enterococcus spp.	Use of ampicillin if *E. faecalis* is suspected, or use of vancomycin instead of ampicillin if a penicillin-resistant *Enterococcus* spp. is suspected
MRSA	Use of vancomycin if MRSA suspected
Candida spp.	Use of amphotericin B or fluconazole

ST: Ertapenem or a combination of cefotaxime or ceftriaxone plus metronidazole

- It is recommended ertapenem or a combination of cefotaxime or ceftriaxone plus metronidazole should be considered for empiric antimicrobial therapy of CA-IAI in lower-risk paediatric patients older than one month (45 weeks post-conceptional age)

ST: Cefuroxime and Metronidazole

- Ertapenem or a combination of cefotaxime or ceftriaxone plus metronidazole are considered preferred agents for empiric antimicrobial therapy of CA-IAI in lower-risk paediatric patients older than one month (45 weeks post-conceptional age). It is suggested cefuroxime plus metronidazole as an alternative regimen for empiric treatment of these paediatric patients.

ST: Ciprofloxacin or levofloxacin plus metronidazole

- Ciprofloxacin or levofloxacin plus metronidazole as acceptable regimens for empiric treatment of selected paediatric patients with IAI if other agents cannot be used, particularly for those paediatric patients with life-threatening b-lactam reactions.

ST: Piperacillin-Tazobactam, Imipenem CILASTATIN, or Meropenem

- Piperacillin-tazobactam, imipenem CILASTATIN, or meropenem are the recommended agents for empiric antimicrobial therapy of CA-IAI in higher-risk paediatric older than one month (45 weeks post-conceptional age). It is also recommended to use these agents for empiric therapy of HA-IAI in paediatric patients.

ST: Ceftazidime or Cefepime plus Metronidazole

- Piperacillin-tazobactam, imipenem CILASTATIN, or meropenem are the recommended agents for empiric antimicrobial therapy of CA-IAI in higher-risk paediatric and HA-IAI in paediatric patients older than one month. Ceftazidime or Cefepime plus Metronidazole should be used as alternative regimens for empiric treatment of Higher risk CA-IAI or HA-IAI in these paediatric patients.

ST: Aztreonam plus metronidazole plus vancomycin

- Aztreonam plus metronidazole plus vancomycin combination therapy is as an acceptable regimen for empiric treatment of selected paediatric patients if other agents cannot be used, particularly for paediatric patients with life-threatening beta lactam reactions.

CU: Addition of Ampicillin or Vancomycin

- The addition of ampicillin or vancomycin to therapy, as empiric anti-enterococcal therapy of CA-IAI in higher-risk patients and those with HA-IAI if the patient is not being treated with piperacillin-tazobactam or imipenem-CILASTATIN.

Duration of Therapy

No more than five full days (120 h) of antimicrobial therapy of IAI in paediatric patients older than one month (45 weeks post-conceptional age) who have had adequate source control. It is not recommended to use of IV antibiotic agents beyond seven days for children with perforated appendicitis who have a post-operative abscess.

[C-2] Paediatric patients less than one month

PA: Ampicillin, Gentamicin, and Metronidazole or Clindamycin OR Ampicillin, Cefotaxime, and Metronidazole or Clindamycin OR Meropenem.

- It is suggested to use ampicillin, gentamicin, and metronidazole or clindamycin, OR ampicillin, cefotaxime, and metronidazole or clindamycin, OR Meropenem in paediatric patients less than one month of age (45 weeks post-conceptional age) with IAI, and this should be confirmed by prescriber.

AGE: Clindamycin

- Clindamycin is the recommended an anti-anaerobic agent in combination regimens for the empiric treatment of IAI in children under one month of age.

CU: Fluconazole or Amphotericin B

- In paediatric patients less than one month of age (45 weeks post-conceptional age) with IAI, Fluconazole or amphotericin B can be added if there is a suspected infection with Candida spp.

Duration of Therapy

A 7–10 days course of antimicrobial therapy for paediatric patients less than one month of age (45 weeks post-conceptional age), particularly for those with NEC. [Necrotizing enterocolitis]

PA: Consider limiting antimicrobial to 5–7 days in patients with established IAI in whom a definitive source control procedure is not performed, treatment can be extended for up to 10 days in certain cases, suggest a 7–10 days course of antimicrobial therapy for pediatric patients less than one month of age (45 weeks post-conceptional age), particularly for those with [necrotizing enterocolitis] NEC. and this should be confirmed by the prescriber