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Guidelines for antimicrobial therapy of intra-abdominal infections in adults

Infectious Diseases Society of Taiwan; Taiwan Surgical Society of Gastroenterology; Medical Foundation in Memory of Dr. Deh-Lin Cheng; Foundation of Professor Wei-Chuan Hsieh for Infectious Diseases Research and Education; CY Lee's Research Foundation for Pediatric Infectious Diseases and Vaccines

Intra-abdominal infections are important in daily clinical practice. Outcomes are heavily influenced by timely, accurate diagnoses and appropriate surgical and radiological intervention and by the timeliness and efficacy of antimicrobial therapy. Selection of antimicrobial agents is not only a choice between old versus new or single-agent versus combination therapy, but depends on the clinical status of patients, spectrum of activity, timing and duration of therapy, dose and dosing frequency, drug interactions and tolerability, adequacy of drug levels and prior antibiotic treatment. In addition, antimicrobial agents should be used carefully to avoid or prevent antimicrobial resistance.

A series of symposia was held over the last two years in order to develop these guidelines. Participants included experts in the fields of infectious diseases, gastroenterology and general surgery.

A consensus conference for establishing guidelines for antimicrobial therapy for intra-abdominal infections in Taiwan was held on March 8, 2008 following a symposium on intra-abdominal infections held in conjunction with the Infections Diseases Society of Taiwan, Taiwan Surgical Society of Gastroenterology, the Medical Foundation in Memory of Dr. Deh-Lin Cheng, Foundation of Professor Wei-Chuan Hsieh for Infectious Diseases Research and Education, and CY Lee's Research Foundation for Pediatric Infectious Diseases and Vaccines.* Three principles are maintained in establishing these guidelines:

1. Guidelines are based on local epidemiology and susceptibility patterns of pathogens.
2. Antimicrobial agents recommended in the guidelines are agents already marketed in Taiwan.
3. Guidelines are based on academic principles rather than the regulations of the Bureau of National Health Insurance on antibiotic usage.

Special considerations are given to include primary hepatic abscess, mainly due to *Klebsiella pneumoniae*, and spontaneous bacterial peritonitis due to its high prevalence in Taiwan. Many recommendations are still based on expert opinion and unpublished data, due to a paucity of well-designed, randomized, controlled clinical trials in this region.

These guidelines are approved by the board of the Infectious Diseases Society of Taiwan, and a copy will be sent to physicians in all hospitals in Taiwan. These guidelines are published in the *Journal of Microbiology, Immunology and Infection*, and are also available at the Journal's website (www.jmii.org). The guidelines will be updated and revised as necessary, to serve as an easily accessible reference for all physicians in Taiwan.

Guidelines for antimicrobial therapy of intra-abdominal infections in adults

Diagnosis	Drugs of choice	Alternative[a]
1. Intra-abdominal infections		
Mild to moderate severity	Ampicillin-sulbactam	Third-generation cephalosporins[i] + metronidazole[g]
	Amoxicillin-clavulanate	Ertapenem
	Second-generation cephalosporins (cephamycins)[f]	Moxifloxacin
	Cefazolin or cefuroxime + metronidazole[g]	Tigecycline
High severity[b]	Piperacillin, piperacillin-tazobactam or ticarcillin-clavulanate	Ciprofloxacin or levofloxacin (750 mg) + metronidazole[g]
	Flomoxef	Aztreonam + metronidazole[g]
	Third- or fourth-generation cephalosporins[h] + metronidazole[g]	Imipenem or meropenem

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Note:
1. Addition of aminoglycosides[c] is optional.
2. The duration of treatment is variable and depends on the type of infection found, adequacy of control of focus, the status of host defenses, and the response to treatment. Patients who have localized peritonitis or an intra-abdominal abscess (if abscess is completely drained) and who are not immunocompromised can be treated for a relatively brief period (7 to 10 days), whereas patients with generalized peritonitis and who are more ill require a longer duration of treatment (10 to 14 days) to 2 to 4 weeks of intravenous therapy followed by prolonged oral antibiotic course (if needed) if drainage is incomplete. Antimicrobial therapy should continue until there are clear signs that the infection has resolved.
3. Continued evidence of infection, e.g., fever, elevated white blood cell count, gastrointestinal tract function, indicates persistent intra-abdominal infection or the occurrence of nosocomial infection at another site. This should prompt appropriate diagnostic investigations.

2. Acute cholecystitis/cholangitis		
<24 h	Surgical intervention and no antimicrobial therapy	-
Mild[d]	Ampicillin-sulbactam Amoxicillin-clavulanate Second-generation cephalosporins (cephamycins)[f] Cefazolin or cefuroxime + metronidzole[g]	Moxifloxacin
Moderate to severe[e]	Piperacillin, piperacillin-tazobactam or ticarcillin-clavulanate Third- or fourth-generation cephalosporins[h] + metronidazole[g]	Aztreonam + metronidazole[g] Imipenem or meropenem

Note:
1. Addition of aminoglycosides[c] is optional.
2. When biliary obstruction is present, even an antimicrobial drug with excellent biliary excretion may not enter the biliary tract.

3. Hepatic abscess		
Primary (mainly *Klebsiella pneumoniae*)	Cefazolin or second-generation cephalosporins[i] ± aminoglycosides[c] Third-generation cephalosporins[i]	-
Biliary	As moderate to severe acute cholecystitis/cholangitis	-
Amebic	Metronidazole ± iodoquinol	-

Note: Percutaneous or surgical abscess drainage as early as possible is mandatory.

4. Spontaneous bacterial peritonitis		
	Cefazolin or second-generation cephalosporins[i]	Third-generation cephalosporins[i] Ampicillin-sulbactam Amoxicillin-clavulanate Piperacillin-tazobactam

[a]Alternative therapy includes the following considerations: allergy, pharmacology/pharmacokinetics, compliance, costs, and local resistance profiles.
[b]Advanced age; poor nutrition; low serum albumin; pre-existing disorders, such as significant cardiovascular disease; higher Acute Physiology And Chronic Health Evaluation II scores (≥15); inadequate source control during the initial operative procedure; resistant nosocomial microorganisms; immunosuppression resulting from medical therapy for transplantation, cancer, or inflammatory disease; or other acute/chronic diseases of difficult-to-define immunosuppression.
[c]Gentamicin, netilmicin, amikacin or isepamicin.
[d]In a healthy patient with no organ dysfunction and only mild inflammatory changes in the gallbladder, making cholecystectomy a safe and low-risk operative procedure.
[e]Moderate, any one of the following conditions: 1) elevated white blood cell count (>18,000/mm^3); 2) palpable tender mass in right upper quadrant; 3) duration of complaints >72 h; and 4) marked local inflammation (biliary peritonitis, pericholecystic abscess, hepatic abscess, gangrenous cholecystitis, emphysematous cholecystitis). Severe dysfunction in any of the following organ/systems: 1) cardiovascular dysfunction (hypotension requiring dopamine 5 μg/kg/min, or any dose of dobutamine); 2) neurological dysfunction (decreased level of consciousness); 3) respiratory dysfunction (partial pressure of oxygen/fraction of inspired oxygen ratio <300); 4) renal dysfunction (oliguria, creatinine >2.0 mg/dL); and 5) hepatic dysfunction (prothrombin time/international normalized ratio >1.5); hematological dysfunction (platelet count <100,000/mm^3).

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[f]Cefoxitin, cefotetan or cefmetazole.
[g]Other anti-anaerobic agents include clindamycin or chloramphenicol.
[h]Cefepime or cefpirome.
[i]Cefuroxime, cefoxitin, cefotetan and cefmetazole.
[j]Cefotaxime, ceftriaxone, ceftizoxime or ceftazidime.

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