Guidelines for the Selection of Anti-infective Agents for Complicated Intra-abdominal Infections

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EXECUTIVE SUMMARY

These guidelines, from the Infectious Diseases Society of America (IDSA), the Surgical Infection Society, the American Society for Microbiology, and the Society of Infectious Disease Pharmacists, contain evidence-based recommendations for selection of antimicrobial therapy for adult patients with complicated intra-abdominal infections. Complicated intra-abdominal infections extend beyond the hollow viscus of origin into the peritoneal space and are associated either with abscess formation or with peritonitis. These guidelines also address timing of initiation of antibiotic therapy, when and what to culture, modification of therapy based on culture results, and duration of therapy.

Infecting flora. The anticipated infecting flora in these infections and, therefore, the agent(s) selected are determined by whether the infection is community acquired or health care associated. Health care–associated intra-abdominal infections are most commonly acquired as complications of previous elective or emergent intra-abdominal operations and are caused by nosocomial isolates particular to the site of the operation and to the specific hospital and unit.

For community-acquired infections, the location of the gastrointestinal perforation (stomach, duodenum, jejunum, ileum, appendix, or colon) defines the infecting flora. Established infection beyond the proximal small bowel is caused by facultative and aerobic gram-negative organisms; infections beyond the proximal ileum also can be caused by a variety of anaerobic microorganisms.

Microbiologic evaluation. Given the activity of common regimens against the anaerobic organisms identified in community-acquired infections, microbiologic workup for specimens from such infections should be limited to identification and susceptibility testing of facultative and aerobic gram-negative bacilli. Susceptibility profiles for *Bacteroides fragilis* group isolates demonstrate substantial resistance to clindamycin, cefotetan, cefoxitin, and quinolones, and these agents should not be used alone empirically in contexts in which *B. fragilis* is likely to be encountered.

Recommended regimens. These infections may be managed with a variety of single- and multiple-agent regimens. The antimicrobials and combinations of antimicrobials listed in table 1 are considered appropriate for the treatment of community-acquired intra-abdominal infections. No regimen has been consistently demonstrated to be superior or inferior. Although many of the listed regimens have been studied in prospective clinical trials, many such studies have serious design flaws. Recommendations are, therefore, based in part on in vitro activities.

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Table 1. Recommended agents for treatment of community-acquired complicated intra-abdominal infections.

Type of therapy	Agent(s) recommended for mild-to-moderate infections	Agent(s) recommended for high-severity infections
Single agent		
β-lactam/β-lactamase inhibitor combinations	Ampicillin/sulbactam,[a] ticarcillin/clavulanic acid	Piperacillin/tazobactam
Carbapenems	Ertapenem	Imipenem/cilastatin, meropenem
Combination regimen		
Cephalosporin based	Cefazolin or cefuroxime plus metronidazole	Third/fourth-generation cephalosporin (cefotaxime, ceftriaxone, ceftizoxime, ceftazidime, cefepime) plus metronidazole
Fluoroquinolone based	Ciprofloxacin, levofloxacin, moxifloxacin or gatifloxacin, each in combination with metronidazole[b]	Ciprofloxacin in combination with metronidazole
Monobactam based		Aztreonam plus metronidazole

[a] Because increasing resistance of *Escherichia coli* to ampicillin and to ampicillin/sulbactam has been reported, local susceptibility profiles should be reviewed before use.

[b] Because increasing resistance of *Bacteroides fragilis* group isolates to available quinolones has been reported, these agents should be used in combination with metronidazole. A trial of moxifloxacin without metronidazole is ongoing.

Community-acquired infections. For patients with community-acquired infections of mild-to-moderate severity, agents that have a narrower spectrum of activity and that are not commonly used for nosocomial infections, such as ampicillin/sulbactam, cefazolin or cefuroxime plus metronidazole, ticarcillin/clavulanate, ertapenem, and quinolones plus metronidazole, are preferable to agents that have broader coverage against gram-negative organisms and/or greater risk of toxicity. Cost is an important factor in the selection of a specific regimen. Patients with more-severe infections, as defined by accepted physiologic scoring systems, or patients deemed to have immunosuppression resulting either from medical therapy or from acute or chronic disease, might benefit from regimens with a broader spectrum of activity against facultative and aerobic gram-negative organisms. Recommended regimens include meropenem, imipenem/cilastatin, third- or fourth-generation cephalosporins (cefotaxime, ceftriaxone, ceftizoxime, ceftazidime, and cefepime) plus metronidazole, ciprofloxacin plus metronidazole, and piperacillin/tazobactam.

Health care–associated infections. Postoperative (nosocomial) infections are caused by more-resistant flora, which may include *Pseudomonas aeruginosa, Enterobacter* species, *Proteus* species, methicillin-resistant *Staphylococcus aureus,* enterococci, and *Candida* species. For these infections, complex multidrug regimens are recommended, because adequate empirical therapy appears to be important in reducing mortality. Local nosocomial resistance patterns should dictate empirical treatment, and treatment should be altered on the basis of the results of a thorough microbiologic workup of infected fluid. These infections remain an important area for clinical research.

Multiple implementation strategies should be used to maximize adherence to these recommendations. These include obtaining feedback from microbiologists, nurses, pharmacists, and physicians before local publication of selected regimens; use of lectures and publications; small-group interactive sessions; and computer-assisted care. Compliance may be monitored through pharmacy-based drug utilization reviews and through review of microbiology records.

INTRODUCTION

Complicated intra-abdominal infections are problems in clinical practice and consume substantial hospital resources. These resources include emergency department services, imaging services, operating room time, laboratory services, antibiotic therapy, and in-hospital care of variable intensity. Outcomes are heavily influenced by the rapidity of diagnosis and appropriate intervention and by the timeliness and efficacy of anti-infective therapy.

A wide range of individual antimicrobial agents and combinations of agents is available for use in complicated intra-abdominal infections. There are convincing data that absent or inadequate empirical and definitive antibiotic therapy results in both increased failure rates and increased mortality [1–5]. Conversely, unnecessary or needlessly broad therapy is associated with its own problems. Cost remains an important issue in antimicrobial agent selection. Various patient- and agent-specific toxicities may occur, including superinfection and organ toxicity. Acquisition of intrinsically drug-resistant organisms and selective pressure for resistance within the unit, hospital, or community is of increasing concern [6, 7].

Development of these guidelines. These evidence-based guidelines were developed by an expert panel using the IDSA Guidelines Development process and have been endorsed by the IDSA, the Surgical Infection Society, the American Society for Microbiology, and the Society of Infectious Disease Phar-

macists [8]. In addition, these guidelines conform with prevention strategies recommended in the Centers for Disease Control and Prevention's Campaign to Prevent Antimicrobial Resistance in Healthcare Settings (available at http://www.cdc.gov/drugresistance/healthcare/default.htm). The expert panel developed a clinical framework for managing intra-abdominal infections and reviewed studies on the site of origin of the intra-abdominal infections, their microbiology, the laboratory approach to infections, and the selection and duration of antibiotic therapy. The Therapeutic Agents Committee of the Surgical Infection Society recently completed an extensive review of published articles on the use of antimicrobials [9] that was used to develop the Surgical Infection Society Guidelines on Antimicrobial Therapy for Intra-abdominal Infections [10]. That work served as the initial review of clinical trials of antibiotic agents for the present guideline.

Purpose of these guidelines. These guidelines are intended to define the types of infections that require antimicrobial therapy; categorize these infections and the microorganisms likely to be involved in each type of infection; and describe appropriate specimen processing, the use of specific antimicrobial agents or combination regimens appropriate for treatment, and the timing and duration of such therapy. The impact of therapy on the occurrence of antibiotic resistance is considered.

Scope of these guidelines. Complicated intra-abdominal infections are defined as infections that extend beyond the hollow viscus of origin into the peritoneal space and that are associated either with abscess formation or peritonitis. These infections require either operative or percutaneous intervention to resolve. The current guidelines will not address intraparenchymal abscesses of the liver or spleen, infections arising in the genitourinary system, or infections of the retroperitoneum, with the exception of pancreatic infections. These guidelines are not intended to address infections occurring in children <18 years of age or primary peritonitis.

Target audience. The target audience for these guidelines is the physician and pharmacy practitioners who are responsible for antibiotic selection for antimicrobial therapy and the laboratory personnel who are responsible for the processing of specimens obtained at intervention for intra-abdominal infections.

Identification of relevant clinical trials. The bases for these guidelines are published articles on the use of antimicrobials to treat intra-abdominal infections published between 1990 and 2003. The 1990 cutoff was selected because relevant literature up to 1990 was the subject of a previous guideline [11]. The MEDLINE database was searched using multiple strategies, in which the names of specific antimicrobials or more general descriptors (such as "cephalosporins") were paired with words and phrases indicating an intra-abdominal infection (such as "peritonitis" and "appendicitis"). This search included studies that were in the MEDLINE database as of 1 February 2003. The Cochrane Database was also searched for other prospective trials, although none were identified.

Scientific review. Using this methodology, the published studies used to create recommendations were categorized according to study design and quality; then, the recommendations developed from these studies were graded according to the strength of evidence behind them. For particular recommendations and statements, the strength of the supporting evidence and quality of the data are rated by use of an IDSA–United States Public Health Service grading system (table 2) [8].

WHICH PATIENTS REQUIRE THERAPEUTIC ADMINISTRATION OF ANTIMICROBIALS?

Bowel injuries due to penetrating, blunt, or iatrogenic trauma that are repaired within 12 h and intraoperative contamination of the operative field by enteric contents under other circumstances should be treated with antibiotics for ⩽24 h (A-1). For acute perforations of the stomach, duodenum, and proximal jejunum in the absence of antacid therapy or malignancy, therapy is also considered to be prophylactic (B-2) [12, 13]. Similarly, acute appendicitis without evidence of gangrene, perforation, abscess, or peritonitis requires only prophylactic administration of inexpensive regimens active against facultative and obligate anaerobes (A-1).

Acute cholecystitis is often an inflammatory but noninfectious disease. If infection is suspected on the basis of clinical and radiographic findings, urgent intervention may be indicated, and antimicrobial therapy should provide coverage against Enterobacteriaceae (B-2) [14]. Activity against enterococci is not required, because their pathogenicity in biliary tract infections has not been demonstrated. Coverage against anaerobes is warranted in treatment of patients with previous bile duct–bowel anastomosis (C-3).

Infections occurring during the course of acute necrotizing pancreatitis are due to microbial flora similar to that found in infections resulting from colonic perforations [15]. Antibiotic choices appropriate for other types of intra-abdominal infection are considered appropriate for the empirical treatment of infected necrotizing pancreatitis. The administration of prophylactic antibiotics to patients with severe necrotizing pancreatitis before the diagnosis of infection is a common but unproved practice [16]. If a patient with diagnosed infection has previously been treated with an antibiotic, that patient should be treated as if he or she had a health care–associated infection (B-3).

TIMING OF EMPIRICAL ANTIBIOTIC TREATMENT

Established infection is defined primarily by the history of the illness and by the findings at the time of operative or percu-

Table 2. Infectious Diseases Society of America–United States Public Health Service grading system for rating recommendations in clinical guidelines.

Category, grade	Definition
Strength of recommendation	
A	Good evidence to support a recommendation for use
B	Moderate evidence to support a recommendation for use
C	Poor evidence to support a recommendation
D	Moderate evidence to support a recommendation against use
E	Good evidence to support a recommendation against use
Quality of evidence	
1	Evidence from ⩾1 properly randomized, controlled trial
2	Evidence from ⩾1 well-designed clinical trial, without randomization; from cohort or case-controlled analytic studies (preferably from >1 center); from multiple time-series; or from dramatic results from uncontrolled experiments
3	Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

taneous intervention. Evidence of established infection includes the presence of a systemic and local inflammatory response, the latter as indicated by the presence of a purulent exudate and inflamed tissue.

Once the diagnosis of intra-abdominal infection is suspected, it is appropriate to begin antimicrobial therapy before an exact diagnosis is established and before results of appropriate cultures are available. The goals of antibiotic therapy for intra-abdominal infection are to eliminate infecting microorganisms, to decrease the likelihood of recurrence, and to shorten the time to resolution of signs and symptoms of infection. Infecting microorganisms heavily contaminate surgical wounds, and it is important that effective antimicrobial therapy be begun before any intervention, so that subsequent surgical-site infection can be prevented.

Antibiotics should be administered after fluid resuscitation has been initiated, so that adequate visceral perfusion can be restored and better drug distribution is possible. Particularly in the case of aminoglycosides, nephrotoxicity is exacerbated by impaired renal perfusion [17].

SELECTION OF EMPIRICAL ANTIBIOTIC REGIMENS

Infections derived from the stomach, duodenum, biliary system, and proximal small bowel can be caused by gram-positive and gram-negative aerobic and facultative organisms. Infections derived from distal small-bowel perforations can be caused by gram-negative facultative and aerobic organisms with variable density. Perforations of this type often evolve into localized abscesses, with peritonitis developing only after rupture of the abscess. Anaerobes, such as *B. fragilis,* are commonly present. Colon-derived intra-abdominal infections can be caused by facultative and obligate anaerobic organisms. Streptococci and enterococci are also commonly present. By far the most common gram-negative facultative organism is *Escherichia coli.*

Antibiotics used for empirical treatment of community-acquired intra-abdominal infections should, therefore, be active against enteric gram-negative aerobic and facultative bacilli and β-lactam–susceptible gram-positive cocci (A-1). Coverage against obligate anaerobic bacilli should be provided for distal small-bowel and colon-derived infections and for more-proximal gastrointestinal perforations when obstruction is present (A-1).

Table 3 details agents and regimens that may be used to treat intra-abdominal infections and that have been adequately studied in clinical trials [45]. We note that studies in which sample sizes are too small to define equivalence or detect differences between various regimens provide little useful data. Studies that are not subject to peer review are, similarly, of little use.

The expanded gram-negative bacterial spectrum of some agents shown to be effective in clinical trials is not advantageous for patients with community-acquired infections, and unnecessary use of such agents may contribute to the emergence of antimicrobial resistance. In particular, agents that are used to treat nosocomial infections in the intensive care unit should not be routinely used to treat community-acquired infections (B-2) [7, 46].

For patients with mild-to-moderate community-acquired infections, agents that have a narrower spectrum of activity, such as ampicillin/sulbactam, cefazolin or cefuroxime/metronidazole, ticarcillin/clavulanate, and ertapenem are preferable to more costly agents that have broader coverage against gram-negative organisms and/or greater risk of toxicity (A-1). Generic agents have cost advantages.

Aminoglycosides have relatively narrow therapeutic ranges and are associated with ototoxicity and nephrotoxicity. Because of the availability of less toxic agents demonstrated to be of

Table 3. Agents and regimens that may be used for treatment of intra-abdominal infections and have been subjected to randomized, prospective clinical trials.

Type of therapy, agent(s)	Reference(s)
Single agent	
β-lactam/β-lactamase inhibitor combinations	
Ampicillin/sulbactam	[18]
Piperacillin/tazobactam	[19–22]
Ticarcillin/clavulanic acid	[23, 24]
Carbapenems	
Ertapenem	[25]
Imipenem/cilistatin	[21, 23, 26–35]
Meropenem	[30, 36–40]
Cephalosporins	
Cefotetan	[41]
Cefoxitin	[32]
Combination regimen	
Aminoglycoside-based regimens	
Gentamicin, tobramycin, netilmicin, or amikacin plus an antianaerobe (clindamycin or metronidazole)	[24, 35, 38, 42]
Cephalosporin-based regimens	
Cefuroxime plus metronidazole	[20, 43]
Ceftriaxone, cefotaxime, or cefepime, each in combination with metronidazole	[29, 40, 42, 44]
Quinolone-based regimens: ciprofloxacin plus metronidazole	[19, 26]

NOTE. Trials were included if the sample size was sufficient to identify equivalence between different regimens. Note that, even though the results of clinical trials have supported the efficacy of certain regimens (aminoglycoside- or clindamycin-containing regimens, cefotetan, and cefoxitin), these agents are not recommended for current use in community-acquired intra-abdominal infections because of concerns about toxicity (aminoglycosides) or resistance in *Bacteroides fragilis*.

equal efficacy, aminoglycosides are not recommended for routine use in community-acquired intra-abdominal infections (A-1). These agents should be reserved for patients with allergies to β-lactam agents and even then are second choices to quinolone-based regimens. Aminoglycosides may be first-choice agents for empirical treatment of health care–associated intra-abdominal infections, depending on local susceptibility patterns of nosocomial isolates. Individualized administration of aminoglycosides is the preferred dosing regimen for patients receiving these agents for intra-abdominal infections (A-1). Cefoxitin and cefotetan cannot be recommended for use, because *B. fragilis* group microorganisms have increasingly been found to be resistant to these agents. That outcomes are worse for patients infected with *B. fragilis* who are treated with agents to which the organisms are resistant has been demonstrated repeatedly [47–49].

Cost considerations may play an important role in the selection of initial empirical antimicrobial therapy. Precise calculation of the expenses associated with the use of different regimens is difficult, and these costs are specific to the particular institution. Costs may differ markedly between regimens, depending on the frequency of administration and the need to monitor serum drug concentrations.

Completion of the antimicrobial course with oral forms of a quinolone plus metronidazole (A-1) or with oral amoxicillin/clavulanic acid (B-3) is acceptable for patients who are able to tolerate an oral diet [19, 26].

IDENTIFICATION OF HIGH-RISK PATIENTS

Several attempts have been made to identify clinical features in patients with peritonitis that increase the risk of adverse outcomes. These analyses have identified factors that are prognostic of death, rather than of the risk of recurrent infection, including higher APACHE II scores, poor nutritional status, significant cardiovascular disease, and inability to obtain adequate control of the source of infection [50–54]. Similarly, patients with immunosuppression resulting from medical therapy for transplantation, cancer, or inflammatory disease should receive broader-spectrum therapy. Patients with other acute and chronic diseases may also have immunosuppression, although this is difficult to define. For such patients, use of antimicrobial regimens with expanded spectra may be warranted, including meropenem, imipenem/cilastatin, piperacillin/tazobactam, ciprofloxacin plus metronidazole, or a third- or fourth-generation cephalosporin plus metronidazole (C-3).

Prolonged preoperative length of stay and prolonged (>2 days) preoperative antimicrobial therapy are significant predictors of antimicrobial failure leading to recurrent infection and suggest that organisms resistant to the empirical antimicrobial regimen may be responsible for infection [26, 27]. Such patients should be treated for nosocomial infection, as detailed in Health Care–Associated Intra-abdominal Infections (C-3).

DURATION OF THERAPY

Antimicrobial therapy for established infections should be continued until resolution of clinical signs of infection occurs, including normalization of temperature and WBC count and return of gastrointestinal function. The risk of subsequent treatment failure appears to be quite low for patients who have no clinical evidence of infection at the time of cessation of antimicrobial therapy [55].

For patients who have persistent or recurrent clinical evidence of intra-abdominal infection after 5–7 days of therapy, appropriate diagnostic investigation should be undertaken. This should include CT or ultrasonographic imaging, and antimicrobial therapy effective against the organisms initially identified should be continued (C-3). For patients with persistent

or recurrent intra-abdominal infections, additional intervention likely will be required to achieve source control. If a patient has persistent clinical symptoms and signs, but no evidence of a new or persistent infection is uncovered after a careful investigation, termination of antimicrobial therapy is warranted.

LABORATORY CONSIDERATIONS

In community-acquired infections, the encountered flora is routinely susceptible to recommended regimens. There is a strong case to be made against culturing samples from patients with perforated or gangrenous appendicitis. Several retrospective studies have examined the impact of performance of such cultures on outcome and have failed to identify any beneficial effect [56–58].

There are, however, several concerns that prevent easy extrapolation of this observation to other types of intra-abdominal infection [55, 59]. The listed studies have been confined to pediatric populations with perforated, not abscessed, appendicitis. Treatment failure in this situation leading to recurrent infection is extremely uncommon. This is due in part to excision of the inflamed viscus; there remains no abscess rim or other infected tissue.

For other intra-abdominal infections, particularly those involving the colon, failure rates are substantially higher if empirical therapy is not active against any identified isolate [1, 2, 5]. Altering the regimen to cover identified isolates improves outcome (C-3) [4].

There are marked differences in susceptibility patterns within and between different communities. These epidemiologic data are of considerable value in defining the most suitable antimicrobial therapy for intra-abdominal infections. Certain communities have an inexplicably high incidence of *P. aeruginosa* in community-acquired appendicitis [2]. Therefore, local hospital antimicrobial susceptibility patterns should be heeded in selecting initial empirical therapy.

Identification and susceptibility testing of anaerobes (a tedious and expensive undertaking) appear to be unnecessary if broadly active anaerobic agents are used to treat infections in which anaerobes are frequently encountered (those with distal intestinal, appendiceal, and colonic sources) and if adequate drainage or debridement is achieved. Resistance repeatedly has been identified and found to be increasing for clindamycin, cefoxitin, cefotetan, piperacillin, and the quinolones [60–63].

Published multicenter surveys of anaerobic susceptibility that used the methods currently recommended by the NCCLS may be used as guides for therapy directed at the *B. fragilis* group [63, 64]. This statement is not intended to discourage hospitals from monitoring local resistance trends. If this is undertaken, the results should be published annually and compared with those for previous years [65]. Susceptibility testing of individual anaerobic isolates should be considered when there is persistent isolation of the organism, when bacteremia is present, and when prolonged therapy is needed.

HEALTH CARE–ASSOCIATED INTRA-ABDOMINAL INFECTIONS

In infections occurring after elective or emergent operations, a more resistant flora is routinely encountered [66]. Furthermore, there is evidence that not providing empirical therapy active against the subsequently identified pathogens is associated with significant increases in mortality and treatment failure (C-3) [66]. The organisms seen are similar to those seen in other nosocomial infections, and anaerobes are not frequently encountered. Antibiotic therapy for such infections should be guided by knowledge of the nosocomial flora seen at the particular hospital and its antimicrobial susceptibilities. This may require the use of multidrug regimens (e.g., an aminoglycoside or quinolone or a carbapenem and vancomycin).

WHAT MATERIAL SHOULD BE SENT FOR CULTURE?

Blood cultures do not provide additional clinically relevant information for patients with community-acquired intra-abdominal infections and are, therefore, not recommended for such patients (A-1). Specimens collected from the intra-abdominal focus of infection should be representative of the material associated with the clinical infection, and there is no benefit to obtaining multiple specimens. Both aerobic and anaerobic cultures can be performed using a single specimen, provided it is of sufficient volume (at least 0.5 cc of fluid or tissue) and is transported to the laboratory in an anaerobic transport system, rather than on a swab. Swabs do not provide appropriate specimens for anaerobic cultures.

WHEN SHOULD GRAM STAINING BE PERFORMED?

For community-acquired infections, there is no value in making a Gram stain of the infected material (B-2). For health care–associated infections, Gram staining may be valuable in defining the need for specific therapy for methicillin-resistant gram-positive organisms [66]. Local susceptibility patterns for *S. aureus* and for enterococci might warrant addition of vancomycin to the regimen until results of cultures and susceptibility testing are available. For enterococci, local susceptibilities should be monitored for ampicillin and vancomycin resistance.

INDICATIONS FOR ANTIFUNGAL THERAPY

Candida albicans or other fungi are isolated from ~20% of patients with acute perforations of the gastrointestinal tract [67]. Even when fungi are recovered, antifungal agents are unnecessary, unless the patient has recently received immunosuppressive therapy for neoplasm, transplantation, or inflammatory disease or has postoperative or recurrent intra-abdominal infection (B-2) [68, 69].

Anti-infective therapy for *Candida* should be withheld until the infecting species is identified (C-3). If *C. albicans* is found, fluconazole is an appropriate choice (B-2). For fluconazole-resistant *Candida* species, therapy with amphotericin B, caspofungin, or voriconazole is appropriate (B-3). The latter 2 agents cause substantially less toxicity than does amphotericin B and are specifically indicated for patients with renal dysfunction (A-1).

INDICATIONS FOR ANTIENTEROCOCCAL THERAPY

Numerous prospective, blinded, and randomized trials have compared regimens active against strains of *Enterococcus* routinely isolated from patients with community-acquired infections. In at least 6 of these studies, the comparator regimen did not have similar coverage [2, 18–20, 70, 71]. Nonetheless, none of these trials demonstrated an advantage to treating enterococcal infections. Routine coverage against *Enterococcus* is, therefore, not necessary for patients with community-acquired intra-abdominal infections (A-1). Antimicrobial therapy for enterococci should be given when enterococci are recovered from patients with health care–associated infections (B-3). The selection of appropriate antimicrobials should be guided by susceptibility testing.

PERFORMANCE MEASUREMENTS

The primary performance measurement for this guideline is a drug utilization review for patients with community-acquired and those with health care–associated intra-abdominal infection. Such reviews should correlate the empirical therapy provided with local susceptibility patterns.

AREAS FOR FUTURE RESEARCH

There are several aspects of treatment of intra-abdominal infection that require further study. The issue of appropriate specimen processing, including the role of antimicrobial susceptibility testing on a routine basis, requires close study. This may best be done by prospective observational studies. This type of study would also generate epidemiological data on community resistance patterns and community-specific microbiologic findings (e.g., an unanticipated incidence of multidrug-resistant organisms).

Definition of the appropriate duration of antimicrobial therapy is perhaps the most pressing need. The impact of prolonged therapy, driven by the availability of potent oral regimens, may have a significant effect on the incidence of resistant organisms in the community or in intermediate or chronic care facilities to which such patients are transferred from other institutions.

With regard to higher-risk patients, particularly those with health care–associated infections, poor clinical outcomes are still common. Given the infrequency of such patients, prospective comparative, randomized trials are unlikely to be performed, and other methodologies, including prospective observational studies, may be useful. The pattern of infecting organisms needs to be confirmed, and the impact of empirical therapy should be examined. In addition, duration of therapy for postoperative infections is an important variable that needs study.

DISCLOSURE OF FINANCIAL INTERESTS OR RELATIONSHIPS

Joseph S. Solomkin has received honoraria and travel expenses for consulting services from Merck, Ortho-McNeill, Pfizer, Bayer, and AstraZeneca. **John E. Mazuski** has received honoraria and travel expenses as a speaker for Wyeth Pharmaceuticals and as a consultant for Merck. He has been an investigator in research sponsored by Wyeth Pharmaceuticals, Bayer, Pfizer, and AstraZeneca Pharmaceuticals. **Ellen Jo Baron** has been a consultant with travel and honoraria provided by Ortho-McNeil, Bayer, Merck, and AstraZeneca Pharmaceuticals. Former research projects have been funded by Merck, Pfizer, and Bristol-Myers Squibb. She owns >$10,000 worth of stock in Merck. **Robert G. Sawyer** has received honoraria and travel expenses as a consultant for Pfizer and Merck. **Avery B. Nathens** has received honoraria and travel expenses for consulting services from Merck, Pfizer, and Wyeth. **Joseph T. DiPiro** has received honoraria and travel expenses for consulting services for Merck. **Timothy Buchman** has served as a local site investigator in clinical trials sponsored by Bayer and AstraZeneca. **E. Patchen Dellinger** has received honoraria and travel expenses for consulting services from Merck, Ortho-McNeill, Pfizer, Bayer, Wyeth, and AstraZeneca. **Sherwood Gorbach** has received honoraria and travel expenses for consulting services from Bayer. **Anthony W. Chow** has received honoraria and travel expenses for consulting services from Ortho-McNeill, Pfizer, Bayer, and AstraZeneca Pharmaceuticals.

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