Complete Summary

GUIDELINE TITLE

Guidelines for the selection of anti-infective agents for complicated intra-abdominal infections.

BIBLIOGRAPHIC SOURCE(S)

Solomkin JS, Mazuski JE, Baron EJ, Sawyer RG, Nathens AB, DiPiro JT, Buchman T, Dellinger EP, Jernigan J, Gorbach S, Chow AW, Bartlett J. Guidelines for the selection of anti-infective agents for complicated intra-abdominal infections. Clin Infect Dis 2003 Oct 15;37(8):997-1005. [71 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse (NGC): This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- July 08, 2008, Fluoroquinolones (ciprofloxacin, norfloxacin, ofloxacin, levofloxacin, moxifloxacin, gemifloxacin): A BOXED WARNING and Medication Guide are to be added to the prescribing information to strengthen existing warnings about the increased risk of developing tendinitis and tendon rupture in patients taking fluoroquinolones for systemic use.
- September 11, 2007, Rocephin (ceftriaxone sodium): Roche informed healthcare professionals about revisions made to the prescribing information for Rocephin to clarify the potential risk associated with concomitant use of Rocephin with calcium or calcium-containing solutions or products.

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SCOPE

DISEASE/CONDITION(S)

Complicated intra-abdominal infections including:

- Community-acquired infections where the gastrointestinal perforation may be located in the stomach, duodenum, jejunum, ileum, appendix, or colon
- Health care-associated infections most commonly acquired as complications of previous elective or emergent intra-abdominal operations

Note: These guidelines do not address primary peritonitis, intraparenchymal abscesses of the liver or spleen, infections arising in the genitourinary system, or infections of the retroperitoneum, with the exception of pancreatic infections.

GUIDELINE CATEGORY

Evaluation
Treatment

CLINICAL SPECIALTY

Colon and Rectal Surgery
Infectious Diseases
Internal Medicine
Pharmacology
Surgery

INTENDED USERS

Clinical Laboratory Personnel
Pharmacists
Physicians

GUIDELINE OBJECTIVE(S)

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.

TARGET POPULATION

Adult patients with complicated intra-abdominal infections that extend beyond the hollow viscus of origin into the peritoneal space and are associated either with abscess formation or with peritonitis

Note: These guidelines are not intended to address infections occurring in children <18 years of age.

INTERVENTIONS AND PRACTICES CONSIDERED

Evaluation

1. Identification of high-risk patients
2. Blood cultures
3. Gram stain
4. Computed tomography (CT) or ultrasonographic imaging

Treatment

1. Single agents:
    - Beta-lactam/Beta-lactamase inhibitor combinations
        - Ampicillin/sulbactam
        - Ticarcillin/clavulanic acid
        - Piperacillin/tazobactam
    - Carbapenems
        - Ertapenem
        - Imipenem/cilastatin
        - Meropenem
    - Cephalosporins
        - Cefotetan
        - Cefoxitin
2. Combination regimens
    - Aminoglycoside-based regimens
        - Gentamicin, tobramycin, netilmicin, or amikacin plus an antianaerobe (clindamycin or metronidazole)
    - Cephalosporin-based regimens
        - Cefazolin or cefuroxime plus metronidazole
        - Third/fourth-generation cephalosporin (cefotaxime, ceftriaxone, ceftizoxime, ceftazidime, cefepime) plus metronidazole
    - Fluoroquinolone-based regimens
        - Ciprofloxacin, levofloxacin, moxifloxacin or gatifloxacin, each in combination with metronidazole
        - Ciprofloxacin in combination with metronidazole
    - Monobactam-based regimens
        - Aztreonam plus metronidazole

MAJOR OUTCOMES CONSIDERED

- Outcomes associated with complicated intra-abdominal infections (e.g., patient mortality, failure rates, healthcare costs)
- Efficacy of anti-infective therapy, measured by clinical signs, temperature, white blood cell count, and gastrointestinal function

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

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. 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.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Quality of Evidence

1. Evidence from $\geq$1 properly randomized, controlled trial
2. Evidence from $\geq$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

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

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 published studies used to create recommendations were categorized according to study design and quality.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The evidence-based guidelines were developed by an expert panel using the Infectious Disease Society of America (IDSA) Guidelines Development process.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

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

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Definitions for the quality of the evidence (1-3) and strength of recommendation (A-E) are given at the end of the "Major Recommendations" field.

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 $\leq$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**).
- 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**).
- Coverage against anaerobes is warranted in treatment of patients with previous bile duct–bowel anastomosis (**C-3**).
- 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**).

Selection of Empirical Antibiotic Treatment

- Antibiotics used for empirical treatment of community-acquired intra-abdominal infections should, therefore, be active against enteric gram-negative aerobic and facultative bacilli and beta-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**).
- 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**).
- 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**).
- 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 equal efficacy, aminoglycosides are not recommended for routine use in community-acquired intra-abdominal infections (**A-1**).
- Individualized administration of aminoglycosides is the preferred dosing regimen for patients receiving these agents for intra-abdominal infections (**A-1**).
- 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.

Identification of High-risk Patients

- 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. Such patients should be treated for nosocomial infection, as detailed in Health Care–Associated Intra-abdominal Infections (**C-3**).

Duration of Therapy

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

Laboratory Considerations

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

Health Care-associated Intra-abdominal Infections

- In infections occurring after elective or emergent operations, a more resistant flora is routinely encountered. 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**).

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**).

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**).

Indications for Anti-fungal Therapy

- Even when fungi are recovered from patients, 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**).
- 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**).
- Caspofungin and voriconazole cause substantially less toxicity than does amphotericin B and are specifically indicated for patients with renal dysfunction (**A-1**).

Indications for Antienterococcal Therapy

- Routine coverage against *Enterococcus* is 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**).

Quality of Evidence

1. Evidence from $\geq$1 properly randomized, controlled trial
2. Evidence from $\geq$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

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

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Rapid diagnosis and appropriate intervention for complicated intra-abdominal infections
- Timely and effective anti-infective therapy

Subgroups Most Likely to Benefit

- 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.
- Caspofungin or voriconazole cause substantially less toxicity than does amphotericin B and are specifically indicated for patients with renal dysfunction

POTENTIAL HARMS

Aminoglycosides have relatively narrow therapeutic ranges and are associated with ototoxicity and nephrotoxicity.

CONTRAINDICATIONS

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Culturing samples is contraindicated in patients with perforated or gangrenous appendicitis.

QUALIFYING STATEMENTS

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Intra-abdominal infections may be managed with a variety of single- and multiple-agent regimens. 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.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

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.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Solomkin JS, Mazuski JE, Baron EJ, Sawyer RG, Nathens AB, DiPiro JT, Buchman T, Dellinger EP, Jernigan J, Gorbach S, Chow AW, Bartlett J. Guidelines for the selection of anti-infective agents for complicated intra-abdominal infections. Clin Infect Dis 2003 Oct 15;37(8):997-1005. [71 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2003 Oct 15

GUIDELINE DEVELOPER(S)

Infectious Diseases Society of America - Medical Specialty Society

SOURCE(S) OF FUNDING

Infectious Diseases Society of America (IDSA)

GUIDELINE COMMITTEE

Not stated

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

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.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the Infectious Disease Society of America (IDSA) Web site.

Print copies: Available from Infectious Diseases Society of America, 1300 Wilson Boulevard, Suite 300, Arlington, VA 22209.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Kish MA. Guide to development of practice guidelines. Clin Infect Dis 2001 Mar 15;32(6):851-4.

Electronic copies: Available from the Clinical Infectious Diseases Journal Web site.

Print copies: Available from Infectious Diseases Society of America, 1300 Wilson Boulevard, Suite 300, Arlington, VA 22209.

PATIENT RESOURCES

None available

NGC STATUS

This NGS summary was completed by ECRI on May 6, 2004. This summary was updated by ECRI on February 21, 2006 following the U.S. Food and Drug Administration (FDA) advisory on Tequin (gatifloxacin). This summary was updated by ECRI Institute on October 3, 2007 following the U.S. Food and Drug Administration (FDA) advisory on Rocephin (ceftriaxone sodium). This summary was updated by ECRI Institute on July 28, 2008 following the U.S. Food and Drug Administration advisory on fluoroquinolone antimicrobial drugs.

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