Intra-abdominal Infections

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Learning Objectives
1. Classify patient intra-abdominal infections by etiology and severity.
2. Design an appropriate plan for supportive care of the hospitalized patient with intra-abdominal infection.
3. Develop an appropriate empiric antimicrobial regimen for the patient with intra-abdominal infection.
4. Analyze the impact of peritoneal pharmacokinetics and pharmacodynamics on antimicrobial selection and dosing.
5. Justify the use of empiric antifungal therapy in the patient with intra-abdominal infection.
6. Assess the need for directed therapy active against enterococci in the patient with intra-abdominal infection.
7. Evaluate microbiologic reports to guide changes in empiric antimicrobial therapy.
8. Evaluate the role of antimicrobial stewardship in an institutional approach to therapy in patients with intra-abdominal infection.

Introduction

Intra-abdominal infection represents a broad range of infections with three overlapping types predominating: individual organ infections, generalized peritonitis, and abscesses. Although these infections typically are treated in the inpatient setting, they have origins and diagnoses that include community-based care.

Pathophysiology

The pathophysiology of intra-abdominal infections is variable and depends on the specific infection type. Organ-specific infections (e.g., appendicitis, cholecystitis, cholangitis) are typically the result of primary or secondary bacterial infections caused by enteric organisms in the hepatobiliary tree or intestinal tract. These infections are often contained in the organ system; however, they can also progress to generalized infection of the peritoneal space or abscess formation. Certain patient characteristics (e.g., liver failure, peritoneal dialysis, surgical procedures, penetrating trauma) can lead to direct infection of the peritoneal cavity in the absence of individual organ infections.

Generalized peritonitis is commonly divided into primary, secondary, and tertiary types. Primary peritonitis results when organisms are either externally introduced into the peritoneum (e.g., peritoneal dialysis infections) or translocated into the peritoneal fluid (e.g., liver failure). In adult patients with liver failure and ascites, this syndrome is typically termed spontaneous bacterial peritonitis (SBP). Secondary peritonitis generally arises from perforation of the gastrointestinal (GI) tract and spillage of bacterial contents, or from extension of individual organ infections into the peritoneal

Baseline Review Resources

The goal of PSAP is to provide only the most recent (past 3–5 years) information or topics. Chapters do not provide an overall review. Suggested resources for background information on this topic include:

Tertiary peritonitis refers to severe recurrent or persistent peritonitis after previously adequate control of primary or secondary disease. An example of tertiary peritonitis is the postsurgical patient who has successful surgical removal and repair of a ruptured appendix and initially responds to therapy, but then progresses to a “new” peritonitis and multiple organ dysfunction. Classification of tertiary disease is less commonly delineated clinically; instead, most severe illness is classified under the general term complicated intra-abdominal infection. Abscesses can complicate individual infections and occur within or adjacent to GI organs or the peritoneum.

Microbiology
The microbiology of intra-abdominal infections also depends on the pathophysiology involved. For primary peritonitis in adult patients with ascites and secondary peritonitis, the organisms typically arise from the GI tract. The microbiology of the GI tract changes as it progresses from the stomach to the small and then large intestines, with gram-positive and gram-negative aerobes ceding to more obligate anaerobes. The microbiology of single-organ infections is dictated by their location in the digestive tract. In patients receiving peritoneal dialysis or with abdominal traumas, skin or exogenous flora can be introduced. Primary peritonitis of all types is typically mono-microbial, with a single organism entering the peritoneal cavity. Secondary peritonitis, by virtue of its contamination by intestinal flora, is typically a multi-organism infection with mixed aerobic and anaerobic flora. (Table 2-1).

Table 2-1. Common Pathogens Isolated from Complicated Intra-abdominal Infections in Adults

<table>
<thead>
<tr>
<th>Organism</th>
<th>Percentage of Patients*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram-negative aerobes</td>
<td></td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>60</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>12</td>
</tr>
<tr>
<td><em>Citrobacter spp.</em></td>
<td>6</td>
</tr>
<tr>
<td><em>Enterobacter spp.</em></td>
<td>5</td>
</tr>
<tr>
<td><em>Klebsiella spp.</em></td>
<td>15</td>
</tr>
<tr>
<td><em>Proteus spp.</em></td>
<td>6</td>
</tr>
<tr>
<td>Gram-positive aerobes</td>
<td></td>
</tr>
<tr>
<td><em>Streptococcus spp.</em></td>
<td>41</td>
</tr>
<tr>
<td><em>Enterococcus faecium</em></td>
<td>3</td>
</tr>
<tr>
<td><em>Enterococcus faecalis</em></td>
<td>7</td>
</tr>
<tr>
<td>Other enterococci</td>
<td>11</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>5</td>
</tr>
<tr>
<td>Anaerobes</td>
<td></td>
</tr>
<tr>
<td><em>Bacteroides fragilis</em></td>
<td>23</td>
</tr>
<tr>
<td>Other <em>Bacteroides spp.</em></td>
<td>26</td>
</tr>
<tr>
<td><em>Fusobacterium spp.</em></td>
<td>3</td>
</tr>
<tr>
<td><em>Peptostreptococcus spp.</em></td>
<td>8</td>
</tr>
<tr>
<td><em>Clostridium spp.</em></td>
<td>8</td>
</tr>
</tbody>
</table>

*Some patients had more than one isolate.

Diagnosis of intra-abdominal infection is based on signs and symptoms and advanced imaging studies of the internal organs and peritoneal wall. Surgical exploration, typical for many organ infections and secondary or tertiary peritonitis, allows visualization of infected tissues and direct culture results. In addition, drainage and examination of peritoneal fluid or fluid from abscesses can help determine infection.

Severity of Illness
Classification of severity of illness is an important decision point in selection of antimicrobial therapy. In general, more severely ill patients are treated with therapy that is more aggressive and that includes a broader spectrum of activity. The exact definitions of mild, moderate, or severe illness are not completely
agreed on clinically. Recent guidelines from the Infectious Diseases Society of America suggest that a *complicated* intra-abdominal infection is an intra-abdominal infection coupled with any one of the following indicators of severe illness: Acute Physiology and Chronic Health Evaluation II (APACHE II) scores greater than 15, advanced age, comorbidity and degree of organ dysfunction, low albumin concentration, poor nutritional status, degree of peritoneal involvement, inability to control the infection source, or malignancy.

**TREATMENT**

The four main treatment goals of intra-abdominal infections are to (1) restore and maintain vital functions; (2) repair physical defects, if possible; (3) eradicate pathogens; and (4) reduce morbidity and mortality.

**Fluid Resuscitation**

Support of vital functions is the first step in the treatment of intra-abdominal infections, and fluid resuscitation and supportive care are imperative. Administration of crystalloids is generally recommended to restore intravascular volume and improve perfusion. In addition to vital signs, urine output should be monitored to ensure proper hydration. Fluid therapy in primary peritonitis should be carefully monitored because the typical patient often has fluid disturbances caused by underlying kidney or liver impairment as well as third spacing of fluids into multiple tissues. Patients who have sepsis may require aggressive fluid therapy with colloids or crystalloids and vasopressors for hemodynamic instability.

**Source Control**

Source control is important in intra-abdominal infections because defects in internal organs are often the portals for microbial entry into the peritoneal space. Infected and non-viable tissues, including organ tissues, often require surgical removal and repair to control the source of infection. In primary peritonitis, catheter care and foreign body removal is imperative for eradication of infection sources. There is no usual surgical requirement for patients with liver ascites and SBP. Abscesses are typically a later complication of infection, with the body responding by sequestering the infected tissues and resultant pathogens. Surgical drainage of large abscesses is preferred where possible.

**Empiric Antibiotic Therapy**

After stabilization of vital functions and attempts at source control, antimicrobial therapy is the mainstay of intra-abdominal infection management. Data are conflicting on the clinical impact of rapid initiation of appropriate antibiotic therapy in a variety of infections. Although it is intuitively important to begin therapy directed against the pathogens recovered in culture, some studies fail to show alterations in clinical course with early initiation of concordant antimicrobials. In patients with complicated secondary infections and sepsis, antimicrobial therapy is recommended within 1 hour of presentation. However, in less severely ill patients, initiation of antimicrobial therapy directed against common pathogens within 8 hours of presentation to clinical care has been recommended by experts without supporting clinical data.

**Primary Peritonitis**

Primary peritonitis is typified by the isolation of a single disease-causing pathogen. In patients receiving peritoneal dialysis, empiric antibiotic selections for primary peritonitis are directed against both gram-positive and gram-negative aerobic pathogens. Although staphylococci predominate, gram-negative pathogens are increasing; this is because of the routine colonization of dialysis catheters with common organisms on the skin, as well as enteric gram-negative organisms. In SBP with cirrhotic ascites, the primary pathogens are streptococci and enteric gram-negative bacilli. Because of the presence of fluid in the peritoneal space (dialysate or ascitic), fluid culture is a mainstay for diagnosis and antibiotic selection.

**Organ Infections**

Appendicitis can result in a variety of severities of illness, with perforation a possible cause of secondary peritonitis. Appendix removal remains the common treatment of disease, although conservative therapy with only antimicrobials has been favorable in limited studies. Preoperative coverage with cefoxitin or cefotetan is recommended, with a perforated or gangrenous appendix necessitating broader-spectrum coverage to include both enteric gram-negative organisms and anaerobes similar to secondary peritonitis.

Empiric therapy for simple biliary infections, (e.g., cholecystitis) should include targeted therapy against gram-negative aerobes such as *Escherichia coli* and *Klebsiella pneumoniae*, rather than anaerobic pathogens. Cefuroxime or ceftriaxone are recommended for these uncomplicated infections. Severe cholecystitis or any form of cholangitis would necessitate broad-spectrum coverage to include anaerobic pathogens similar to secondary peritonitis treatment.

Pancreatitis is not typically an infectious process, and it rarely requires antimicrobial therapy. Only infected necrotic pancreatitis requires treatment, with little role for antibiotic prophylaxis.

Abscesses are generally best treated with drainage, with antimicrobials serving a complimentary role in eradicating residual pathogens. When abscesses cannot be drained (e.g., because of location, numbers, or size), antimicrobials are directed against likely pathogens including gram-negative enteric pathogens and
anaerobes. The variable activity of antimicrobial classes within the acidic microenvironment of abscesses has been shown experimentally; however, few clinical data are available to suggest the superiority of one class over another if equal antibacterial spectra are achieved.

**Secondary Peritonitis**

In secondary peritonitis, the multiple mixed aerobic and anaerobic nature of the infection necessitates coverage with a broad-spectrum regimen that covers true anaerobes such as *Bacteroides fragilis*. The likely mix of aerobic pathogens dictates the choice of specific agents. Community-associated infections are less likely to be caused by resistant pathogens than hospital-acquired infections. Hospital-acquired infections require broader coverage and empiric coverage of hospital endemic pathogens such as *Pseudomonas aeruginosa* or methicillin-resistant *Staphylococcus aureus* (MRSA) (Table 2-2).

Single-agent therapy with β-lactam/β-lactamase inhibitor combinations or carbapenems is the mainstay of treatment for secondary peritonitis. Severe β-lactam allergy complicates first-line therapy because carbapenems (particularly imipenem and, to a lesser extent, meropenem) have cross-sensitivity rates similar to penicillins and cephalosporins. Moxifloxacin, the only widely available fluoroquinolone with reasonable anaerobic activity, was deemed non-inferior to other standard therapies in some studies. Many clinicians, however, remain wary of moxifloxacin’s anaerobic coverage and avoid its use as a single agent except for mild infection.

Combination therapy directed against gram-negative pathogens combined with metronidazole is another option. Two more traditional therapy options, the cephamycins (cefotetan and cefoxitin) and clindamycin, have become obsolete for empiric treatment of intra-abdominal infections because of rising anaerobic resistance. Ampicillin/sulbactam, another common community-acquired mixed aerobic/anaerobic antimicrobial, should be reserved for use when local susceptibilities are adequate against *E. coli*, because national resistance rates are high.

**Pediatric Infections**

Pediatric antimicrobial recommendations for intra-abdominal infection therapy follow many of the same guidelines as those for adults, with attention to unique safety issues. Antimicrobial spectrum should be determined by severity of illness, origin of infection, and site of infection. Because of their unique toxicity issues, fluoroquinolones (cartilage toxicity) and tigecycline (tooth discoloration) are not usually recommended for pediatric patients.

**Peritoneal Fluid Pharmacokinetics/Pharmacodynamics**

Pharmacokinetic and pharmacodynamic modeling of antibacterial concentrations in peritoneal fluid have been investigated to determine both activity at the site of action and to compare the pharmacodynamic profiles with those obtained in the plasma. For most agents,
including cephalosporins and carbapenems, the results suggest similar pharmacokinetic parameters for a variety of antimicrobials within the peritoneal fluid. Organ-specific concentrations of antimicrobials are less widely reported, though most GI organs are well penetrated by antimicrobials. Agents with high biliary secretion (e.g., ceftriaxone) can provide very high luminary concentrations. At this time, it does not appear that peritoneal concentrations are more predictive of clinical outcomes than plasma concentrations, although a lack of concentration differences precludes making a significant comparison.

**Specific Pathogens**

**Enterococci**

Enterococci are part of the normal GI flora, though treatment with drugs devoid of enterococcal activity (e.g., cephalosporins) is clinically effective. This proves that coverage of every pathogen isolated from peritoneal fluid in a mixed infection is not required for cure. It is important to distinguish abscess or body fluid cultures from blood cultures, because enterococci in the blood necessitate directed antimicrobial treatment appropriate for local susceptibilities. Clinicians should consider coverage of enterococci when it is predominant in a normally sterile tissue or fluid culture or when the patient’s initial or subsequent clinical picture is severe or worsening in the face of enterococcal isolation without current drug coverage.

**Candida spp.**

Antifungal therapy directed against Candida spp. is also not recommended as empiric therapy for patients without fungemia, even though these are common gut flora. When cultured from the intra-abdominal space or blood, specific Candida coverage is recommended. Echinocandins are typically employed until speciation of the organisms is confirmed. This will allow coverage of Candida glabrata and Candida krusei, pathogens less likely to be susceptible to fluconazole. When Candida albicans isolation is confirmed, fluconazole remains the mainstay of therapy.

**Methicillin-Resistant S. aureus**

Empiric coverage of MRSA should be considered in hospital-associated infections, particularly in patients at high risk of colonization (i.e., those with known previous colonization, previous antimicrobial exposure, or other associated risks). When risk factors for MRSA are not present, specific empiric therapy is not recommended. When MRSA is isolated from intra-abdominal culture or blood culture, specific MRSA therapy should be added to antibiotic regimens. Vancomycin is the typical first-line therapy, assuming local susceptibilities suggest low minimum inhibitory concentration (MIC) values (generally 1 mcg/mL or less).

**Monitoring**

**Definitive Antimicrobial Selection**

As with all infections, identification of pathogens from culture should guide alterations in antimicrobial therapy. Isolating a single pathogen from primary peritonitis cultures allows narrowing of coverage to a single antimicrobial after susceptibilities are reported. In secondary peritonitis, intra-abdominal culture results are more difficult to interpret. Mixed aerobic gram-negative enteric pathogens and anaerobic pathogens are expected in secondary peritonitis, and both groups need to be covered even if representative pathogens are not isolated. Anaerobes, for example, are notoriously difficult to culture, and their absence in clinical cultures cannot guarantee their lack of contribution to the disease. Anti-anaerobic therapy should be maintained during the treatment course in all secondary infections. Similarly, gram-negative enteric pathogens must continue to be covered even in the absence of documented cultures.

The presence of resistant pathogens (e.g., *Pseudomonas* spp., extended-spectrum β-lactamase producers) in intra-abdominal cultures would typically dictate the expansion of coverage to include these organisms. Isolation of enterococci, even as one of many pathogens isolated, is not immediately considered a requirement for adding directed antimicrobial coverage. True positive blood cultures with any pathogen necessitate antimicrobial treatment directed at the isolate.

**Evaluation of Clinical Outcomes**

Clinical outcomes, in addition to microbiology results, should continue to dictate therapy changes. Further surgical intervention is often required, and inadequate source control must be considered and the need to change antimicrobial therapy evaluated. The general standard for monitoring efficacy is observing a clinical improvement in the initial signs and symptoms of infection. In patients with complicated intra-abdominal infections, improvement should generally be observed within 2–3 days. In patients with severe illness, response may be delayed.

**Therapy Duration**

Primary peritonitis is typically treated for 5 days in patients with cirrhosis and ascites and for a minimum of 14 days in patients receiving peritoneal dialysis (although longer durations are suggested for resistant pathogens). Most secondary intra-abdominal infections can be treated with 4–7 days of therapy. Individual patient response should dictate duration, with longer durations typically reserved for severely ill patients who have responded slowly to treatment or for cases in which source control has been difficult and prolonged. The presence of undrained abscesses may necessitate longer therapy (e.g., several weeks) that is often guided by imaging of the abscesses and tracking of their resolution.
**Oral Antimicrobials**

Oral antimicrobials can be considered for step-down therapy in secondary peritonitis or specific organ infections, providing that orally bioavailable agents with the appropriate microbiologic spectrum are available. Intravenous-to-oral conversion in the patient with an intra-abdominal infection requires some caution. The presence of gastrointestinal complications caused by infection (e.g., ileus, peritonitis, nausea, gut edema secondary to third spacing) may compromise absorption of oral agents, including those with otherwise excellent bioavailability. Together with an improving clinical picture, toleration of normal feeding should be used as a guide for consideration of a switch to oral antimicrobial therapy.

**Prophylaxis**

Spontaneous bacterial peritonitis in patients with cirrhosis and ascites is the only intra-abdominal infection in which primary prophylaxis is sometimes indicated. Supporting evidence is strongest for primary prophylaxis of patients with ascites and active acute upper GI bleeding. Seven-day courses of ceftriaxone or a fluoroquinolone are suggested during active bleeds. Data are less strong for primary prophylaxis in non-acutely bleeding patients; however, low ascitic protein concentrations and additional risk factors (e.g., high bilirubin or low sodium) influence the decision to begin therapy (Box 2-1). Underlying liver failure and bacterial translocation into ascitic fluid has led to the recommendation of indefinite antimicrobials for secondary prophylaxis (i.e., after an episode of SBP) in patients with cirrhosis.

The predominance of gram-negative enteric pathogens has led to the use of fluoroquinolones as the preferred prophylactic agent for these patients with ascites. Norfloxacin used in daily therapy has the most available clinical data. Although limited data suggest that weekly ciprofloxacin therapy is as effective, increased resistance with this regimen is a concern. In addition, selection of more gram-positive infections continues to be reported during prophylaxis.

**Role of the Pharmacist**

**Pharmacoeconomics**

Few data on pharmacoeconomics are available for the treatment of intra-abdominal infections. Limited data suggest that some treatment modalities are more cost-effective because of their greater likelihood of having activity against common pathogens. A prospective study of different dosing strategies of piperacillin-tazobactam (continuous vs. intermittent infusion) in complicated intra-abdominal infections failed to show a cost benefit, partly because of the relatively minor cost of antibacterial therapy compared with the high overall cost of hospitalization. Limited data suggest that treatment of complicated intra-abdominal infections with orally bioavailable agents allows cost reductions compared with all intravenous alternatives. Because many of these studies were small or not prospective, the pharmacoeconomic data are not sufficient for generalized treatment recommendations.

**Appropriate Antimicrobial Use**

The pharmacist plays a vital role in all areas of drug therapy for patients with intra-abdominal infection. In the initial and maintenance phases, selection and monitoring of fluid and vasopressor needs is an important pharmacist role. Another major role surrounds the appropriate selection, dosing, and monitoring of antimicrobial therapy. Knowledge of local antimicrobial resistance rates and pathogens common to the health system is imperative in making proper empiric therapy choices. Drug dosing can also be complicated by underlying organ dysfunctions inherent in this patient population, as well as the fluctuation of organ function with acute illness or sepsis. Monitoring of drug concentrations is important, when appropriate, and it should follow usual standards for acute or severe infections. Additional vigilance in making rational dosing decisions for antimicrobials that do not require therapeutic drug monitoring is another vital pharmacist role. This includes adjustments to maximize pharmacodynamic parameters when dealing with organ dysfunctions, as well as patient weight, fluid shifts, and variable infecting organisms.

**Antimicrobial Stewardship**

Broad oversight of antimicrobial stewardship within the health system is another role of the pharmacist in managing intra-abdominal infections. Protocols for individual drug use and criteria for restrictions or

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**Box 2-1. Antimicrobial Prophylaxis in Spontaneous Bacterial Peritonitis without Active Bleeding**

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary prophylaxis</strong></td>
<td>Norfloxacin</td>
</tr>
<tr>
<td>Ascitic fluid protein concentration &lt; 1.5 g/dL</td>
<td>400 mg PO daily</td>
</tr>
<tr>
<td><strong>Plus</strong> one of the following</td>
<td></td>
</tr>
<tr>
<td>Serum creatinine ≥ 1.2 mg/dL</td>
<td>Ciprofloxacin</td>
</tr>
<tr>
<td>BUN ≥ 25 mg/dL</td>
<td>500 mg PO daily</td>
</tr>
<tr>
<td>Serum sodium ≤ 130 mEq/L</td>
<td>750 mg PO weekly</td>
</tr>
<tr>
<td>Child-Pugh ≥ 9 with</td>
<td>Trimeprprim/sulfamethoxazole</td>
</tr>
<tr>
<td>bilirubin ≥ 3 mg/dL</td>
<td>160 mg/800 mg PO five times/week</td>
</tr>
</tbody>
</table>

**Secondary prophylaxis**

Previous peritonitis

BUN = blood urea nitrogen; PO = by mouth.
oversight of certain antimicrobials or antimicrobial classes can improve patient outcomes while ensuring appropriate use and limiting emergence of resistance. Formulary management and prospective audits of patient therapy are other ways the pharmacist can improve outcomes from antimicrobial therapy in intra-abdominal infections.

**Conclusion**

Intra-abdominal infections encompass a broad range of infections that share many similarities. Knowledge of the differences in the pathogen types seen in these infections and of the proper selection and monitoring of drug therapy is imperative. Pharmacists are vital team members in the treatment of patients with intra-abdominal infections.

**Annotated Bibliography**


   This 2010 guideline is an update of the 2003 version and is endorsed by the American Society for Microbiology, the American Society of Health-System Pharmacists, the Pediatric Infectious Diseases Society, and the Society of Infectious Diseases Pharmacists. As such, this is the primary guideline used for complicated intra-abdominal infections in the United States. This update provides substantially more evidence and background information than the 2003 report. Owing to its recent publication, it includes recommendations with all the currently relevant antimicrobials. Primary changes in this edition include the recommendation of moxifloxacin as a single agent for mild-moderate infections, a stronger emphasis on initiation of antifungal therapy with intra-abdominal cultures, and a discussion of 20% prevalence of multidrug resistance and the resulting changes in empiric therapy. Although the focus of the review is on generalized intra-abdominal infections, it also includes recommendations for biliary infections such as cholecystitis and cholangitis. Comments on primary peritonitis in patients with liver or kidney failure are included. As with any expert guideline, several recommendations are based primarily on expert opinion. This article is required reading for any hospital or critical care pharmacist.


   Pancreatitis is often included in intra-abdominal infections but typically is not an infectious process. These guidelines reaffirm the limited instances in which antimicrobial therapy is warranted in pancreatitis. Specifically, antimicrobials are not recommended for routine pancreatitis or for prophylaxis of necrotic pancreatitis. Antimicrobials are reserved for the specific diagnosis of infected necrotic pancreatitis. This diagnosis is often made intra-operatively, and surgical debridement is a mainstay of therapy. Antimicrobial selection should be guided by culture and susceptibilities. These guidelines are important in the creation of protocols surrounding pancreatitis and are helpful in providing evidence to assist in curtailing inappropriate antimicrobial use.


   This article updates the 2005 publication on the diagnosis and treatment of primary peritonitis in patients receiving peritoneal dialysis; written by the International Society for Peritoneal Dialysis, these recommendations are widely considered the gold standard for treatment of this infection. Of importance, this guideline synthesizes the recommended dosing of antimicrobials that are instilled directly into the peritoneal cavity with the dialysate. This route of administration is recommended for both its local and systemic activity.


   Because they are able to pool results from clinical studies, meta-analyses are the strongest form of available evidence. The Cochrane Library is widely regarded as the most authoritative source of meta-analyses. This analysis included 17 trials and almost 1900 patients. The authors’ conclusions were that antibiotic prophylaxis in patients with cirrhosis and upper GI bleeds (usually esophageal varices) is beneficial in preventing infection and mortality versus placebo. No conclusions could be drawn about the most effective antimicrobial regimen. This analysis is important in highlighting the current understanding of prophylaxis and in understanding where evidence in the literature is lacking.


   This meta-analysis presents the strongest and best delineated evidence of its kind. The methodology is impeccable and extremely transparent, as is that in all the Cochrane Reviews. Unlike the very positive results for prophylaxis in patients with cirrhosis and upper GI bleeding, only mild advantages were observed in patients with ascites alone. Clinically, based on other guidelines, prophylaxis is sometimes recommended in nonbleeding patients with low ascitic protein.
concentrations and other risk factors. The Cochrane Review is an important pooled finding because it highlights the poor quality of evidence in many of the studies. The gray areas in the efficacy of prophylaxis are combined with the concern for development of antimicrobial resistance with prolonged prophylaxis.


Large in vitro susceptibility reports are important evidence in guiding the empiric selection of antimicrobials, particularly when individual health systems lack sufficient data to provide local resistance rates. Anaerobes are notoriously difficult to culture and are not easy to test for susceptibility in clinical laboratories. The authors compare the susceptibilities for the important Bacteroides spp. and other anaerobes from intra-abdominal infections in the early 2000s in the United States. Overall susceptibility rates of B. fragilis, considered the prototypical true anaerobe, were 88% for moxifloxacin, 85.5% for levofloxacin, 90% for clindamycin, 98% for ampicillin/sulbactam, 99% for cefoxitin, and 100% for metronidazole. Susceptibilities for other Bacteroides spp. are variable, with lower rates for the fluoroquinolones. The susceptibility rates for moxifloxacin against some anaerobes are much lower than for other antibiotic classes (e.g., carbapenems, β-lactam/β-lactamase inhibitors). This concern and other resistance rates have led to the recommendation of moxifloxacin for only mild-moderate infections.


Although not limited to patients with intra-abdominal infection, this study of candidemia (n=230) has important consequences for the treatment of Candida infections of all types. The study included patients at four diverse medical centers from 2002–2005, a period likely to mimic current species and susceptibilities of Candida. Species was not a predictor of response, although most cultures were C. albicans (54%) or C. glabrata (17%). A delay in fluconazole from the time cultures were drawn until therapy initiation increased mortality from 15% (no delay) to 24% (1-day delay), 36% (2-day delay), and 41% (3-day or longer delay). This underscores the need to begin antifungal therapy promptly when the suggestion of infection is high. The answer to this clinical question is often difficult and may require better yeast identification techniques.


For many clinicians, the most appropriate situations in which to use tigecycline remain unsettled. Its inclusion in the new Infectious Diseases Society of America guidelines for mild/moderate intra-abdominal infection was questioned by some, although clinical data are supportive. The authors of this study reviewed both clinical and pharmacokinetic/dynamic parameters that were associated with successful patient outcomes. Lower patient body weight, absence of Pseudomonas spp., lower APACHE II scores, non-Hispanic race, appendicitis or cholecystitis, and an area-under-the-curve to minimum inhibitory concentration (AUC/MIC) ratio greater than 3.1 were indicative of better outcomes. The most compelling findings from this study are the pharmacodynamic parameters associated with clinical success. Knowing these targets can allow more rational dosing, particularly for the increasing number of obese patients who may require altered dosing schemes.


This trial, the first major clinical trial leading to the approval of moxifloxacin for intra-abdominal infection, revealed non-inferiority for moxifloxacin versus the wider-spectrum piperacillin/tazobactam-containing regimen. This was an important article because some clinicians considered the in vitro activity against anaerobes borderline. Other trials followed this one, which all suggested moxifloxacin non-inferiority with a potential role for this agent in mild-moderate intra-abdominal infections.


This article is one of several by these authors evaluating peritoneal fluid concentrations of antimicrobials. Traditional pharmacodynamics correlates plasma concentrations with bacteriologic and clinical outcomes. The relative importance of concentrations at target sites is less well understood. Meropenem concentrations in peritoneal fluid were similar to those in the plasma. Simulations using these peritoneal concentrations were performed to predict dosing likely to provide adequate time above the MIC profiles. This article, and others like it, may gain in importance as the clinical significance of peritoneal fluid concentrations versus plasma concentrations becomes better elucidated.

The authors investigated the incidence of vancomycin-resistant enterococcus (VRE) and its relationship to previous single-center hospital antibiotic use. The study used a time-series analysis to model the effects of hospital-wide defined daily dosages of antibiotics and any subsequent changes in VRE incidence. The authors found that glycopeptide use resulted in the greatest VRE incidence, followed by fluoroquinolone use and third- and fourth-generation cephalosporins. Combinations of β-lactams and β-lactamase inhibitors were inversely related to VRE incidence. This study adds to earlier studies that have suggested variable response to differential use of antibiotic classes. The model created, though far from perfect, explains most enterococcal resistance by hospital-wide antimicrobial use. These data also follow previous reports implicating broad-spectrum agents with little to no enterococcal coverage (cephalosporins and fluoroquinolones) and glycopeptides in VRE development. These data may enhance general antimicrobial stewardship and direct restrictions in outbreak settings.
Questions 21–23 pertain to the following case.
R.D. is a 48-year-old man brought to the emergency department today by his wife for nausea and abdominal pain and tenderness; he was admitted to the surgical intensive care unit (ICU) after removal of a ruptured appendix. R.D. has mild hypertension and no known drug allergies. He lives at home with his wife, where he works as a computer programmer. In surgery, abdominal cultures were obtained, and an infected appendix with diffuse peritonitis was noted. R.D., who received a cefoxitin dose preoperatively, has just arrived on the unit. His temperature is 100.8°F (38.2°C), with a blood pressure of 122/86 mm Hg and a respiratory rate (RR) of 22 breaths/minute. His laboratory results are aspartate aminotransferase (AST) 20 IU/L, alanine aminotransferase (ALT) 34 IU/L, serum creatinine 0.9 mg/dL, and serum albumin 3.8 g/dL.

21. Given his signs and symptoms, which one of the following is the best classification of R.D.'s infection?
   A. Community-acquired mild to moderate infection.
   B. Community-acquired severe infection.
   C. Hospital-associated infection.
   D. Community-acquired abscess.

22. Which one of the following is the best empiric therapy for R.D.?
   A. Ampicillin/sulbactam 3 g intravenously every 6 hours.
   B. Ampicillin 2 g intravenously every 6 hours and cefoxitin 2 g intravenously every 8 hours.
   C. Ertapenem 1 g intravenously every 24 hours.
   D. Meropenem 1 g intravenously every 8 hours.

23. Four days after surgery and the initiation of appropriate empiric antibacterial therapy, R.D. is clinically improving. He will be moved to a step-down unit. Before his transfer, his intra-operative microbiology results return. His cultures are positive for a variety of susceptible bacteria and Candida albicans. Which one of the following is best for R.D.?
   A. Change antibacterial therapy to oral agents.
   B. Discontinue antibacterial therapy.
   C. Add fluconazole 400 mg orally every 24 hours.
   D. Add caspofungin 70 mg intravenously once, followed by 50 mg intravenously every 12 hours.

Questions 24–26 pertain to the following case.
D.J. is a 37-year-old woman (weight 165 kg) who has severe intra-abdominal infection arising after gastric bypass surgery. Her initial surgery was complicated by perforation of the large bowel. She has type 2 diabetes mellitus, hypertension, and sleep apnea. She has no known drug allergies. On discovery of her postsurgical infection 2 days ago, D.J. was initiated on meropenem 2 g intravenously every 8 hours. She was returned to surgery to repair her bowel, where intra-abdominal cultures were obtained. Two days after her latest surgery, the cultures have returned with Pseudomonas aeruginosa, Bacteroides fragilis, and Enterococcus faecalis. Susceptibilities are pending.

24. Which one of the following is best for D.J.?
   A. Discontinue meropenem and begin piperacillin/tazobactam 4.5 g intravenously every 6 hours.
   B. Discontinue meropenem and begin imipenem/cilastatin 1 g intravenously every 6 hours.
   C. Continue meropenem and add vancomycin 2 g intravenously every 12 hours.
   D. Continue meropenem and add ampicillin 2 g intravenously every 6 hours.

25. Therapy is initiated, and 48 hours later, D.J. remains acutely ill, with continued fevers and declining vital signs. Blood cultures are obtained that have a preliminary result of yeast. Which one of the following would be best to add to D.J.’s therapy?
   A. Amphotericin B 0.7 mg/kg intravenously every 24 hours.
   B. Caspofungin 70 mg intravenously once, followed by 50 mg intravenously daily.
   C. Fluconazole 200 mg orally once daily.
   D. Liposomal amphotericin B 5 mg/kg intravenously daily.

26. Within 72 hours of initiation of antifungal therapy, D.J. is clinically stable and is transferred from the ICU. Follow-up blood cultures remain negative. She has now received 7 days of antibacterial therapy and 3 days of antifungal therapy. Which one of the following would be best for D.J.?
   A. Antibacterial therapy discontinued and antifungal therapy for 11 additional days.
   B. Antibacterial therapy for 6 more days and antifungal therapy for 4 more days.
   C. Antibacterial therapy for 2 more days and antifungal therapy for 2 more days.
D. Antibacterial therapy for 5 more days and antifungal therapy for 11 more days.

27. You are the antibiotic stewardship pharmacist in charge of determining appropriate use of broad-spectrum antimicrobials for a small community hospital. The susceptibility rates to cefoxitin, ertapenem, ticarcillin/clavulanic acid, and moxifloxacin are listed below.

<table>
<thead>
<tr>
<th></th>
<th>Cefoxitin</th>
<th>Ertapenem</th>
<th>Ticarcillin/ Clavulanic Acid</th>
<th>Moxifloxacin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudomonas spp.</td>
<td>N/A</td>
<td>97</td>
<td>88</td>
<td>N/A</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>86</td>
<td>100</td>
<td>92</td>
<td>88</td>
</tr>
<tr>
<td>Enterococcus</td>
<td>N/A</td>
<td>10</td>
<td>25</td>
<td>80</td>
</tr>
<tr>
<td>Bacteroides fragilis</td>
<td>89</td>
<td>99</td>
<td>96</td>
<td>84</td>
</tr>
</tbody>
</table>

N/A = not applicable.

Based on these susceptibilities, which one of the following would be most effective for empiric therapy against pathogens commonly identified in mild community-acquired intra-abdominal infections?

A. Cefoxitin.
B. Ertapenem.
C. Ticarcillin/clavulanate.
D. Moxifloxacin.

28. Your small community hospital has been struggling with VRE infections in the ICU. In the interest of antibiotic stewardship, the hospital staff is developing an antibiotic pathway for hospital-associated intra-abdominal infections. Which one of the following antibiotic regimens would best limit further enrichment of enterococcal antimicrobial resistance?

A. Piperacillin/tazobactam.
B. Ertapenem.
C. Ceftazidime and metronidazole.
D. Ciprofloxacin and metronidazole.

Questions 29 and 30 pertain to the following case.

L.Z. is a 63-year-old man with a history of alcohol abuse. He has ascites, and he is admitted to the hospital with a suggestion of spontaneous bacterial peritonitis (SBP). He does not have any active bleeding. Analysis of his ascitic fluid reveals protein 1.2 g/dL, a high white blood cell count and several bacteria.

29. Which one of the following would be best for L.Z.?

A. Ceftriaxone 1 g intravenously daily.
B. Piperacillin/tazobactam 4.5 g intravenously every 6 hours.
C. Ampicillin/sulbactam 3 g intravenously every 6 hours.
D. Ciprofloxacin 400 mg intravenously every 8 hours and metronidazole 500 mg intravenously every 8 hours.

30. L.Z. is successfully treated for his peritonitis in the hospital. Which one of the following would best prevent further SBP infections in L.Z.?

A. Ciprofloxacin once weekly.
B. Ceftriaxone once weekly.
C. Norfloxacin daily.
D. Trimethoprim/sulfamethoxazole daily.

Questions 31–33 pertain to the following case.

S.T. is a 76-year-old man (weight 64 kg) who resides in a nursing home. He is admitted to the hospital with an inability to keep food down and abdominal pains. S.T. has hypertension and dementia, and he reports anaphylaxis with previous ampicillin therapy. On admission, his vital signs include temperature 98.8°F (37.1°C), BP 100/65 mm Hg, heart rate 102 beats/minute, and RR 18 breaths/minute. His laboratory values are blood urea nitrogen (BUN) 26 mg/dL and serum creatinine 1.3 mg/dL. After returning from radiology, complicated intra-abdominal infection is high on the differential for this patient. Blood and urine cultures are pending.

31. Which one of the following is best as immediate therapy for S.T.?

A. Antibacterials.
B. Fluid resuscitation.
C. Vasopressors.
D. Antiemetics.

32. Which one of the following would be the best empiric antibacterial regimen to start in S.T.?

A. Imipenem 500 mg intravenously every 6 hours.
B. Ciprofloxacin 400 mg intravenously every 8 hours and metronidazole 500 mg intravenously every 8 hours.
C. Moxifloxacin 400 mg intravenously daily.
D. Cefepime 2 g intravenously every 8 hours and metronidazole 500 mg intravenously every 8 hours.

33. Shortly after therapy initiation, S.T. underwent surgery, where a section of infarcted small bowel and diffuse peritonitis were found. At 36 hours after surgery, he is in stable condition with moderate clinical improvement. Blood and urine cultures taken on admission have shown no growth to date; cultures obtained intraoperatively are positive for: Escherichia coli, E. faecalis, Bacteroides spp., and Prevotella spp. Susceptibilities are pending. Which one of the following would be best for S.T. at this time?
A. Add vancomycin 1 g intravenously every 12 hours.
B. Add ampicillin 2 g intravenously every 6 hours.
C. Change therapy to piperacillin/tazobactam 3.375 g intravenously every 6 hours.
D. Add gentamicin 55 mg/kg intravenously daily.

34. A 38-year-old woman on peritoneal dialysis presents to the renal clinic with malaise and feeling out of sorts for the past 2 days. She has end-stage kidney failure, uncontrolled hypertension, and multiple methicillin-resistant *Staphylococcus aureus* (MRSA) infections in the past 2 years. She has no known drug allergies. Blood and peritoneal fluid are sent for culture, with peritonitis suspected. Which one of the following would be the most appropriate empiric therapy for this patient?

A. Intraperitoneal vancomycin.
B. Intraperitoneal vancomycin and intraperitoneal ceftazidime.
C. Intravenous vancomycin and intravenous cefepime.
D. Intravenous vancomycin and intravenous metronidazole.

35. A 31-year-old woman with no significant medical history presents to the emergency department with upper quadrant abdominal pain. Physical examination is suggestive of cholecystitis. Ultrasonography confirms the diagnosis in the emergency department. The patient is in mild distress with no alteration in vital signs. Which one of the following is best for this patient?

A. Cefazolin 1 g intravenously every 8 hours.
B. Imipenem 1 g intravenously every 8 hours.
C. Gentamicin 5 mg/kg intravenously daily.
D. Vancomycin 1 g intravenously every 12 hours.

Questions 36–39 pertain to the following case.

E.Y. is a 48-year-old man who suffered a penetrating abdominal injury in a motor vehicle crash. Surgical repair of a small bowel perforation is undertaken, together with repair of several bone fractures. E.Y. receives 24 hours of prophylactic cefoxitin perioperatively. He has remained in the unit since his admission 10 days ago. After a period of stability, his clinical status has begun to deteriorate with new temperatures to 102°F (39°C) and hypotension unresponsive to fluids. Imaging reveals continued bowel leak and generalized peritonitis. Surgical repair is initiated.

36. Which one of the following is the best classification of E.Y.’s intraabdominal infection?

A. Moderate community-acquired secondary peritonitis.
B. Severe community-acquired primary peritonitis.
C. Hospital-acquired tertiary peritonitis.
D. Hospital-acquired primary peritonitis.

37. Which one of the following is best for empiric antimicrobial therapy in E.Y.?

A. Ceftazidime and metronidazole.
B. Piperacillin/tazobactam.
C. Meropenem and metronidazole.
D. Imipenem.

38. The culture results from E.Y.’s second surgery reveal *P. aeruginosa* and MRSA. Both organisms are susceptible to all the usual agents. Which one of the following is best for E.Y.?

A. Continue current therapy.
B. Change therapy to cefepime and vancomycin.
C. Add vancomycin.
D. Add an aminoglycoside and vancomycin.

39. During the next 5 days, E.Y.’s infection improves, together with his clinical stability. He has begun eating slowly and is undergoing preparation for transfer home for rehabilitation. After consulting with the infectious diseases team, the pharmacist determines that E.Y. will require 5 more days of therapy. No other cultures are confirmed. Which one of the following is best for E.Y.?

A. Home intravenous therapy because of a lack of oral options.
B. Change to oral therapy options with known susceptibility.
C. Intravenous therapy should be continued in the hospital.
D. Oral therapy for the agents received intravenously.

40. A 44-year-old woman presents with a mild community-acquired intra-abdominal infection that, on imaging, appears to be nonperforated appendicitis. No surgical procedures are under consideration. She has no significant medical history; however, she reports hives, but not anaphylaxis, with the administration of cefixime 3 years ago. She is admitted for antibiotic administration and observation. Which one of the following is the best empiric therapy for this patient?

A. Cefoxitin.
B. Moxifloxacin.
C. Aztreonam.
D. Cefazolin and metronidazole.