# Chapter 137: Intra-Abdominal Infections

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## KEY CONCEPTS

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1. Most intra-abdominal infections are caused by a defect in the gastrointestinal (GI) tract and are best treated by surgical drainage, resection, and/or repair.
2. Primary peritonitis is generally caused by a single organism (*Staphylococcus aureus* in patients undergoing chronic ambulatory peritoneal dialysis [CAPD] or *Escherichia coli* in patients with cirrhosis).
3. Secondary peritonitis is usually caused by a mixture of bacteria, including enteric gram-negative bacilli and anaerobes, which enhance the pathogenic potential of the bacteria.
4. For peritonitis, early and effective IV fluid resuscitation and electrolyte replacement therapy are essential. A common cause of early death is tissue hypoperfusion precipitated by inadequate intravascular volume.
5. Treatment is generally initiated on a "presumptive" or empirical basis and should be based on the likely pathogen(s), local resistance patterns, and severity of illness.
6. Antimicrobial regimens for secondary peritonitis, determined by the severity of illness and microbiology data, include: (a) third-generation cephalosporin (ceftriaxone) with metronidazole, (b) piperacillin/tazobactam, (c) a carbapenem (imipenem, meropenem, or ertapenem), or (d) a quinolone (levofloxacin or ciprofloxacin) plus metronidazole or moxifloxacin alone.
7. Treatment of patients with peritoneal dialysis-associated peritonitis should include an antistaphylococcal antimicrobial, such as a first-generation cephalosporin (cefazolin) or vancomycin, as well as an agent with significant gram-negative bacterial activity such as a third-generation cephalosporin or aminoglycoside; intraperitoneal administration is preferred.
8. The duration of antimicrobial treatment should be 4 days after achievement of source control for most secondary peritonitis infections.
9. Patients treated for intra-abdominal infections should be assessed for the occurrence of drug-related adverse effects, particularly hypersensitivity reactions (β-lactam antimicrobials), diarrhea (most agents), fungal infections (most agents), and nephrotoxicity (aminoglycosides).

## BEYOND THE BOOK

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Activity 1:

Answer the questions for the case below on the basis of the information contained within the chapter and develop a treatment plan following the

patient care process.

Case: A 59-year-old woman with history of cirrhosis secondary to alcohol abuse is admitted from an outside hospital for altered mental status and concern for hepatic encephalopathy. The patient lives at home, and the day before admission, the patient told her spouse that her stomach was hurting. The spouse expresses concern that the patient was not receiving lactulose for the past 1.5 weeks and missed her recent liver clinic appointment. The patient was initially admitted for less than 24 hours to an outside hospital and received unknown antibiotics before transfer to the current hospital. On exam, the patient is drowsy and not very responsive to questions. Patient appears jaundiced and is complaining of abdominal pain. No nausea, vomiting, or shortness of breath is observed.

Home medications:

Folic acid 1 mg orally every day

Lactulose 10 g orally twice a day

Magnesium oxide 400 mg orally twice a day

Pantoprazole 40 mg orally every day

Potassium chloride 20 mEq orally twice a day

Hydrochlorothiazide 25 mg orally every day

Spironolactone 25 mg orally every day

ALL: NKDA

Pertinent Labs:

Total bilirubin 11.5 mg/dL (197 µmol/L)

Direct bilirubin 3.9 mg/dL (67 µmol/L)

Alkaline phosphatase 68 U/L (1.13 µkat/L)

AST/ALT 65/27 U/L (1.08/0.45 µkat/L)

Albumin 2.3 g/dL (23 g/L)

Creatinine 0.7 mg/dL (62 µmol/L)

WBC 14.8 × $10^9$/L (14,800/µL)

Hemoglobin 8.9 g/dL (89 g/L; 5.52 mmol/L)

Platelets 92 × $10^9$/L (92,000/µL)

INR 3.2

No significant culture history

Vitals: Pulse 106 BPM, Respiratory rate 24 BPM, BP 145/65 mm Hg, $O_2$ Saturation 96% (0.96) on room air, Tmax 38°C

Diagnostic paracentesis on admission: Ascites fluid cell count/differential; Color: Yellow, cloudy; WBC: 8,080 cells/µL (8.08 × $10^9$/L); RBC: 5,280 cells/µL (5.28 × $10^9$/L); Neutrophil: 74% (0.74); Gram stain: negative

1. How do you classify this patient's infection?

A. Cholecystitis

B. Cholangitis

C. Spontaneous bacterial peritonitis

D. Secondary bacterial peritonitis

2. What laboratory data and patient symptoms support the diagnosis above?

3. What are the likely pathogens that could cause this syndrome?

4. What empiric therapy do you initiate?

A. Cefepime

B. Cefepime + metronidazole

C. Ceftriaxone

D. Ceftriaxone + metronidazole

E. Meropenem

Answers to Postclass Beyond the Book Activity 1 exercise:

1. C.

2. The patient has liver cirrhosis, which is a risk factor for spontaneous bacterial peritonitis (SBP). They present with fever, abdominal pain, and an ascitic fluid with >250/µL ($0.25 \times 10^9$/L) PMN, which is suggestive of SBP. Although the Gram stain of the ascitic fluid was negative, the Gram stain is often negative with low inoculum infections and/or in patients who have received antibiotic therapy.

3. SBP is typically monomicrobial. The most common pathogens are *Streptococcus* species and Enterobacterales such as *Escherichia coli* and *Klebsiella* spp. Notably, anaerobes are not a common cause of SBP.

4. C. Ceftriaxone is the correct response, given it provides adequate empiric activity for the pathogens listed in question 3. Furthermore, it does not provide unnecessary broad coverage for anaerobes (responses B, D, and E are incorrect) or *Pseudomonas* (responses A, B, and E are incorrect).

Activity 2: Watch the video entitled “Diverticulosis and Diverticulitis Assessment” by Picmonic (https://www.picmonic.com/pathways/nursing/courses/standard/medical-surgical-nursing-pathophysiology-296/inflammatory-intestinal-disorders-1421/diverticulosis-and-diverticulitis-assessment_1147). This 1.5-minute video provides a general overview of diverticulosis and diverticulitis. The video is useful to enhance student understanding regarding the COLLECT and ASSESS steps in the patient care process.

## INTRODUCTION

Intra-abdominal infections are those contained within the peritoneal cavity or retroperitoneal space. The peritoneal cavity extends from the undersurface of the diaphragm to the floor of the pelvis and contains the stomach, small bowel, large bowel, liver, gallbladder, and spleen. The duodenum, pancreas, kidneys, adrenal glands, great vessels (aorta and vena cava), and most mesenteric vascular structures reside in the retroperitoneum. Intra-abdominal infections may be generalized or localized, complicated or uncomplicated, and community- or healthcare-associated. Uncomplicated intra-abdominal infections are confined within visceral structures, such as the liver, gallbladder, spleen, pancreas, kidney, or female reproductive organs, and do not extend into the peritoneum, while complicated intra-abdominal infections involve anatomical disruption, extend beyond a single organ, and yield peritonitis and/or abscess.

Community-acquired intra-abdominal infections are usually caused by the patient's own microflora, are present within 48 hours of admission to the hospital, and occur in patients that do not have significant history of healthcare exposure (ie, presence of an invasive device; known methicillin-resistant *Staphylococcus aureus* [MRSA] infection or colonization; or healthcare facility residence, dialysis, or surgery in the prior 12 months). Healthcare-associated intra-abdominal infections can be classified as either community-onset or hospital-onset. Community-onset infection occurs in patients presenting from the community with the aforementioned healthcare exposure risk factors, while hospital-onset infection is defined by infection occurring after 48 hours of hospitalization.[1]

*Peritonitis* is defined as the acute inflammatory response of the peritoneal lining to microorganisms, chemicals, or foreign-body injury. This chapter deals only with peritonitis of infectious origin. An *abscess* is a purulent collection of fluid separated from surrounding tissue by a wall consisting of inflammatory cells and adjacent organs. It usually contains necrotic debris, bacteria, and inflammatory cells. These processes differ considerably in presentation and approach to treatment.

## EPIDEMIOLOGY

Peritonitis may be classified as primary, secondary, or tertiary. Primary peritonitis, also called *spontaneous bacterial peritonitis*, is an infection of the peritoneal cavity without an evident source in the abdomen. Bacteria may be transported from the bloodstream to the peritoneal cavity, where the inflammatory process begins. In secondary peritonitis, a focal disease process is evident within the abdomen. Secondary peritonitis may involve perforation of the gastrointestinal (GI) tract (possibly because of ulceration, ischemia, or obstruction), postoperative peritonitis, or posttraumatic peritonitis (blunt or penetrating trauma). Tertiary peritonitis occurs in critically ill patients, and it persists or recurs at least 48 hours after attempted management of primary or secondary peritonitis.[2,3]

1 Primary peritonitis occurs in both children and adults, although the incidence and mortality rates in both populations have been declining.[4] Primary peritonitis develops in up to 10% to 30% of patients with alcoholic cirrhosis.[4-7] Patients undergoing chronic ambulatory peritoneal dialysis (CAPD) average one episode of peritonitis every 20 to 33 months.[8,9] Secondary peritonitis may be caused by perforation of a peptic ulcer; traumatic perforation of the stomach, small or large bowel, uterus, or urinary bladder; appendicitis; pancreatitis; diverticulitis; bowel infarction; inflammatory bowel disease; cholecystitis; operative contamination of the peritoneum; or diseases of the female genital tract, such as septic abortion, postoperative uterine infection, endometritis, and salpingitis. Diverticulitis is the eighth most frequent diagnosis for outpatients in the United States and is responsible for over 216,000 hospital admissions in 2012.[10] Appendicitis is also a common cause of intra-abdominal infections. More than 300,000 appendectomies are performed in the United States for suspected appendicitis each year.[11] Most healthcare-associated intra-abdominal infections occur as complications following intra-abdominal surgeries.

## ETIOLOGY

Primary peritonitis in adults occurs most commonly in association with alcoholic cirrhosis, especially in its end stage, or with ascites caused by postnecrotic cirrhosis, chronic active hepatitis, acute viral hepatitis, congestive heart failure, malignancy, systemic lupus erythematosus, or nephritic syndrome. It may also result from the use of a peritoneal catheter for dialysis or CNS ventriculoperitoneal shunting for hydrocephalus. Rarely, primary peritonitis occurs without apparent underlying disease.

Potential causes of bacterial peritonitis include inflammatory processes of the GI tract or abdominal organs, bowel obstruction, vascular occlusions that may lead to gangrene of the intestines, and neoplasia that may cause intestinal perforation or obstruction (Table 137-1). Other possible causes include those resulting from traumatic injuries, postoperative infections, or solid organ transplant in the abdomen.

Diverticulitis arises from inflammation of diverticula, intestinal protrusions into the surrounding muscle layer, and can be considered as both uncomplicated and complicated intra-abdominal infections. Risk factors for diverticulitis include smoking, physical inactivity, obesity, diets low in fiber and high in processed carbohydrates and red meat, and use of nonsteroidal anti-inflammatory drugs (NSAIDs).[10]

TABLE 137-1

**Causes of Bacterial Peritonitis**

| |
|---|
| **Primary (spontaneous) bacterial peritonitis** |
| Cirrhosis with ascites |
| Nephrotic syndrome |
| Peritoneal dialysis (may be secondary to catheter site infection) |
| **Secondary bacterial peritonitis** |
| Miscellaneous causes |
| Diverticulitis |
| Appendicitis |
| Inflammatory bowel diseases |
| Salpingitis |
| Biliary tract infections |
| Necrotizing pancreatitis |
| Neoplasms |
| Intestinal obstruction |
| Perforation |
| Mechanical GI problems |
| Any cause of small bowel obstruction (adhesions, hernia) |
| Vascular causes |
| Mesenteric arterial or venous occlusion (atrial fibrillation) |
| Mesenteric ischemia without occlusion |
| Trauma |
| Blunt abdominal trauma with rupture of intestine |
| Penetrating abdominal trauma |
| Iatrogenic intestinal perforation (endoscopy) |
| Intraoperative events |
| Solid organ transplant in the abdomen |
| Peritoneal contamination during abdominal operation |
| Leakage from GI anastomosis |

GI, gastrointestinal.

Abscesses are the result of chronic inflammation and may occur without preceding generalized peritonitis. They may be located within one of the spaces of the peritoneal cavity or within one of the visceral organs and may range from a few milliliters to a liter or more in volume. These collections often have a fibrinous capsule and may take from a few weeks to years to form.

The causes of intra-abdominal abscess overlap those of peritonitis and, in fact, may occur sequentially or simultaneously. Appendicitis is the most frequent cause of abscesses. Other potential causes of intra-abdominal abscess include pancreatitis, diverticulitis, lesions of the biliary tract, genitourinary tract infections, perforation in the abdomen, trauma, and leaking intestinal anastomoses. In addition, pelvic inflammatory disease in women may lead to formation of a tubo-ovarian abscess. For some diseases, such as appendicitis and diverticulitis, abscesses occur more frequently than generalized peritonitis. Protein–calorie malnutrition, antecedent steroid therapy, and diabetes mellitus may also contribute to the formation of an intra-abdominal abscess.

## Microflora of the Gastrointestinal Tract and Female Genital Tract

A full appreciation of intra-abdominal infections requires an understanding of the normal microflora within the GI tract. There are striking differences

in bacterial species and concentrations of flora within the various segments of the GI tract (Table 137-2), and this bacterial environment usually determines the severity of infectious processes in the abdomen. Generally, the low gastric pH eradicates bacteria that enter the stomach. With achlorhydria, bacterial counts may rise to $10^5$ to $10^7$ organisms/mL ($10^8$ to $10^{10}$/L). The normally low bacterial count may also increase by 1,000- or 10,000-fold with gastric outlet obstruction, hemorrhage, gastric cancer, and in patients receiving histamine 2 (H2)-receptor antagonists, proton pump inhibitors, or antacids.[12,13] A two- to threefold increase in spontaneous bacterial peritonitis has been demonstrated with the use of proton pump inhibitors.[12]

TABLE 137-2

**Usual Microflora of the GI Tract**

| Site | Commonly Found Bacteria | Approximate Concentration (No. of Organisms/mL [$\times 10^3$/L]) | |
|---|---|---|---|
| | | Aerobes | Anaerobes |
| Stomach[a] | *Streptococcus, Lactobacillus* | 10-100 | Rare |
| Biliary tract | Normally sterile (*Escherichia coli, Klebsiella*, or enterococci in some patients) | 0 | 0 |
| Proximal small bowel | *Streptococcus* (including enterococci), *E. coli, Klebsiella, Lactobacillus*, diphtheroids | 100 | Few |
| Distal ileum | *E. coli, Klebsiella, Enterobacter*, enterococci, *Bacteroides fragilis, Clostridium*, peptostreptococci | $10^4$-$10^6$ | $10^5$-$10^7$ |
| Colon | *Bacteroides* spp., peptostreptococci, *Clostridium, E. coli, Klebsiella*, enterococci, *Enterobacter*, *Candida*, and many others | $10^5$-$10^8$ | $10^9$-$10^{11}$ |

GI, gastrointestinal.

[a]With achlorhydria, acid suppressive therapy, gastric cancer, or gastric outlet obstruction, bacterial counts may rise to $10^5$/mL ($10^8$/L).

The biliary tract (gallbladder and bile ducts) is sterile in most healthy individuals, but in people older than 70 years, those with acute cholecystitis, jaundice, or common bile duct stones, it is likely to be colonized by aerobic gram-negative bacilli (particularly *E. coli* and *Klebsiella* spp.) and enterococci.[14,15] Patients with biliary tract bacterial colonization are at greater risk of intra-abdominal infection.

In the distal ileum, bacterial counts of aerobes and anaerobes are quite high. In the colon, there may be 500 to 600 different types of bacteria in stool, with concentrations often reaching $10^{11}$ organisms/mL ($10^{14}$/L), and anaerobic bacteria outnumbering aerobic bacteria by more than 1,000 to 1.[16,17] Fortunately, most colonic bacteria are not pathogens because they cannot survive in environments outside the colon. Perforation of the colon results in the release of large numbers of anaerobic and aerobic bacteria into the peritoneum.

The colonic flora generally remains the same unless exposed to a broad spectrum of antimicrobials or a GI infectious process. In either case, the flora may change due to the antibiotic or infectious process and is often replaced by more pathogenic bacteria. Depending on the type of antibiotic and spectrum, the duration of use, route of administration, and distribution to the GI tract, antibiotics can cause shifts in the normal GI microflora leading to increased drug resistance.[18]

The lower female genital tract is generally colonized by a large number of aerobic and anaerobic bacteria. Anaerobes may number $10^9$ organisms/mL ($10^{12}$/L) and often include lactobacilli, eubacteria, clostridia, anaerobic streptococci, and, less frequently, *Bacteroides fragilis.* Aerobic bacteria most often are streptococci and *Staphylococcus epidermidis*, and these may number $10^8$ organisms/mL ($10^{11}$/L).

## PATHOPHYSIOLOGY

Intra-abdominal infection results from bacterial entry into the peritoneal or retroperitoneal spaces or from bacterial collections within intra-abdominal organs. In primary peritonitis, bacteria may enter the abdomen via the bloodstream or the lymphatic system by transmigration through the bowel wall, through an indwelling peritoneal dialysis catheter, or via the fallopian tubes in females. Hematogenous bacterial spread (through the bloodstream) occurs more frequently with tuberculosis peritonitis or peritonitis associated with cirrhotic ascites. When peritonitis results from peritoneal dialysis, skin surface flora is introduced via the peritoneal catheter. In secondary peritonitis, bacteria most often enter the peritoneum or retroperitoneum as a result of perforation of the GI or female genital tracts caused by diseases or traumatic injuries. In addition, peritonitis or abscesses may result from contamination of the peritoneum during a surgical procedure or from an anastomotic leak. In diverticulitis, it is postulated that stool particles accumulate within the diverticula to either erode into the abdominal cavity or form an abscess.[10]

The physiologic characteristics of the peritoneal cavity determine the nature of the response to infection or inflammation within it. The peritoneum is lined by a highly permeable serous membrane with a surface area approximately that of skin. The peritoneal cavity is lubricated with less than 100 mL of sterile, clear yellow fluid, normally with fewer than 250 WBC cells/μL ($0.25 \times 10^9$/L), a specific gravity below 1.016, and protein content below 3 g/dL (30 g/L).[4,19] These conditions change drastically with peritoneal infection or inflammation, as described below.

After bacteria are introduced into the peritoneal cavity, there is an immediate response to contain the invasion. Humoral and cellular defenses respond first, then the omentum adheres to the affected area. A limited bacterial inoculum is handled rapidly by defense mechanisms, including complement activation and a leukocyte response. Under certain conditions, bacteria are not contained and disseminate throughout the peritoneal cavity, resulting in peritonitis. This is more likely to occur in the presence of a foreign body, hematoma, dead tissue, a large bacterial inoculum, continuing bacterial contamination, and contamination involving a mixture of synergistic organisms.

When bacteria become dispersed throughout the peritoneum, the inflammatory process involves most of the peritoneal lining. There is an outpouring into the peritoneum of fluid containing leukocytes, fibrin, and other proteins that form exudates on the inflamed peritoneal surfaces and begin to form adhesions between peritoneal structures. This process, combined with a paralysis of the intestines (ileus), may result in confinement of the contamination to one or more locations within the peritoneum. Fluid also begins to collect in the bowel lumen and wall, and distension may result.

The fluid and protein shift into the abdomen (called *third-spacing*) may be so dramatic that circulating blood volume is decreased, which may cause a decrease in cardiac output leading to hypovolemic shock. Accompanying fever, vomiting, or diarrhea may worsen the fluid imbalance. A reflex sympathetic response, manifested by perspiration, tachycardia, and vasoconstriction, may be evident. With an inflamed peritoneum, bacteria and endotoxins are absorbed easily into the bloodstream (translocation), and this may result in septic shock.[4,5,19] Other foreign substances present in the peritoneal cavity potentiate peritonitis. These adjuvants, notably feces, dead tissues, barium, mucus, bile, and blood, have detrimental effects on host defense mechanisms, particularly on bacterial phagocytosis.

Many of the manifestations of intra-abdominal infections, particularly peritonitis, result from cytokine activity. Inflammatory cytokines, such as tumor necrosis factor-α (TNF-α), interleukin (IL) 1, IL-6, IL-8, and interferon-γ (INF-γ), are produced by macrophages and neutrophils in response to bacteria and bacterial products or in response to tissue injury resulting from the surgical incision.[4,19] These cytokines produce wide-ranging effects on the vascular endothelium of organs, particularly the liver, lungs, kidneys, and heart. With uncontrolled activation of these mediators, sepsis may result (see Chapter 142, “Sepsis and Septic Shock”).[20-22]

Peritonitis may result in death because of the effects on major organ systems. Fluid shifts, cytokines, and microorganism toxins may result in hypovolemia, hypoperfusion, and shock. Hypoalbuminemia may result from protein loss into the peritoneum, exacerbating intravascular volume loss. Pulmonary function may be compromised by the inflamed peritoneum, producing splinting (muscle rigidity caused by pain) that inhibits adequate diaphragmatic movement leading to atelectasis and pneumonia. Increased lung vascular permeability and resulting shunting of blood may induce onset of acute respiratory distress syndrome and associated hypoxemia and hypercarbia. With fluid loss and hypotension, renal and hepatic perfusion may be compromised, and acute renal and hepatic failures are potential threats.

If peritoneal contamination is localized but bacterial elimination is incomplete, an abscess results. This collection of necrotic tissue, bacteria, and WBCs may be at single or multiple sites and may be within one of the spaces of the peritoneal cavity or in one of the visceral organs. The location of the

abscess is often related to the site of primary disease. For example, abscesses resulting from appendicitis tend to appear in the right lower quadrant or the pelvis; those resulting from diverticulitis tend to appear in the left lower quadrant or pelvis.

An abscess begins by the combined action of inflammatory cells (such as neutrophils), bacteria, fibrin, and other inflammatory mediators. Bacteria may release heparinases that cause local thrombosis and tissue necrosis or fibrinolysins, collagenases, or other enzymes that allow extension of the process into surrounding tissues. Neutrophils gathered in the abscess cavity die in 3 to 5 days, releasing lysosomal enzymes that liquefy the core of the abscess. A mature abscess may have a fibrinous capsule that isolates bacteria and the liquid core from antimicrobials and immunologic defenses.

Within the abscess, the oxygen tension is low, and anaerobic bacteria thrive; thus, the size of the abscess may increase because it is hypertonic, resulting in an additional influx of fluid. Hypertonicity promotes the formation of L-form bacteria, which are resistant to antimicrobial agents that disrupt cell walls. Abscess formation may continue and mature for long periods of time and may not be readily evident to either patient or physician. In some instances, the abscess may resolve spontaneously, and, infrequently, it may erode into adjacent organs or rupture and cause diffuse peritonitis. If the abscess erodes through the skin, it may result in an enterocutaneous fistula, connecting the peritoneum to skin, or in a draining sinus tract.

The overall outcome of an intra-abdominal infection depends on key factors: patient-specific risk factors, inoculum size, virulence of the contaminating organisms, the presence of adjuvants within the peritoneal cavity that facilitate infection, the adequacy of host defenses, source control, and the adequacy of initial treatment.[23-25]

## Microbiology of Intra-Abdominal Infection

2 The prevalence of pathogens has not appreciably changed in community-onset intra-abdominal infection, although susceptibility to antibiotics has decreased over time. Primary bacterial peritonitis is often caused by a single organism. In children, the pathogen is usually group A *Streptococcus*, *E. coli*, *Streptococcus pneumoniae*, or *Bacteroides* species.[26-29] When peritonitis occurs in association with cirrhotic ascites, *E. coli* is isolated most frequently. Other potential pathogens are: *Haemophilus influenzae*, *Klebsiella* spp., *Pseudomonas* spp., anaerobes, and *S. pneumoniae*.[30] Occasionally, primary peritonitis may be caused by *Mycobacterium tuberculosis.* Peritonitis in patients undergoing peritoneal dialysis is caused most often by common skin organisms, such as coagulase-negative staphylococci, *S. aureus*, streptococci, and enterococci. Gram-negative bacteria associated with peritoneal dialysis infections include *E. coli*, *Klebsiella* spp., and *Pseudomonas* spp.[9] The mortality rate from primary peritonitis caused by gram-negative bacteria is much greater than that from gram-positive bacteria.[4,5]

3 Because of the diverse bacteria present in the GI tract, secondary intra-abdominal infections are often polymicrobial.[16] The mean number of different bacterial species isolated from infected intra-abdominal sites ranged from 2.9 to 3.7, including an average of 1.3 to 1.6 aerobes and 1.7 to 2.1 anaerobes.[30,31] With proper anaerobic specimen collection, anaerobic organisms are isolated in most patients. In one report of patients with gangrenous and perforated appendicitis, an average of 10.2 different organisms was isolated from each patient, including 2.7 aerobes and 7.5 anaerobes.[32] Purely aerobic or anaerobic infections are uncommon, as are infections caused by fungi. Table 137-3 gives the frequencies with which specific bacteria were isolated from patients with peritonitis and other intra-abdominal infections.[33,34] Nosocomial infections tend to have a more diverse array of pathogens, are more likely to involve *Pseudomonas* spp., and have a higher likelihood of multidrug-resistance compared with isolates from community-acquired infections.[35]

TABLE 137-3

**Pathogens Isolated from Patients with Intra-Abdominal Infection**

| | Secondary Peritonitis[33,35] (%) | Community-Acquired Infection[35] (%) | Nosocomial Infection[35] (%) |
|---|---|---|---|
| **Gram-Negative Bacteria** | | | |
| *Escherichia coli* | 32-61 | 29 | 22.5 |
| *Enterobacter* | 8-26 | 5.2 | 8.0 |
| *Klebsiella* | 6-26 | 2.8 | 4.5 |
| *Proteus* | 4-23 | 1.7 | 2.4 |
| *Pseudomonas* | 5-13 | 5 | 13 |
| **Gram-Positive Bacteria** | | | |
| *Enterococcus* | 18-24 | 10.6 | 18 |
| *Streptococcus* | 6-55 | 13.7 | 10 |
| *Staphylococcus* | 6-16 | 3.1 | 4.8 |
| **Anaerobic Bacteria** | | | |
| *Bacteroides* | 25-80 | 13.7 | 10.3 |
| *Clostridium* | 5-18 | 3.5 | 3.4 |
| **Fungi** | 2-5 | 3 | 4 |

Visceral organ abscesses differ in character from the typical intra-abdominal abscess. Hepatic abscesses may be polymicrobial (involving *E. coli*, *Klebsiella* spp., and anaerobes) or occasionally may be caused by amoeba.[17] Pancreatic abscesses are often polymicrobial, involving enteric bacteria that ascend through the biliary system. Splenic abscesses usually result from hematogenous dissemination of bacteria, such as *E. coli, S. aureus*, *Proteus mirabilis*, *Enterococcus* spp., and *Klebsiella pneumoniae*, as well as anaerobes.[17] Pelvic inflammatory disease is associated initially with *Neisseria gonorrhoeae* or *Chlamydia trachomatis.* However, tubo-ovarian abscesses are usually polymicrobial, having a mix of gram-positive and gram-negative aerobes and anaerobes.

## Bacterial Synergism

The size of the bacterial inoculum and the number and types of bacterial species present in intra-abdominal infections influence patient outcome. The combination of aerobic and anaerobic organisms appears to greatly increase the severity of infection. In animal studies, combinations of aerobic and anaerobic bacteria were much more lethal than infections caused by aerobes or anaerobes alone.

Facultative bacteria may provide an environment conducive to the growth of anaerobic bacteria.[16] Although many bacteria isolated in mixed infections are nonpathogenic by themselves, their presence may be essential for the pathogenicity of the bacterial mixture.[23] The role of facultative bacteria in mixed infections can include (a) promotion of an appropriate environment for anaerobic bacterial growth through oxygen consumption, (b)

production of nutrients necessary for anaerobes, and (c) production of extracellular enzymes that promote tissue invasion by anaerobes.

Rat models of intra-abdominal infection demonstrate that uncontrolled infection with an implanted mix of aerobes and anaerobes leads to a two-stage (biphasic) infectious process. There is an early peritonitis phase with a high mortality rate and isolation of *E. coli* from blood and a late abscess formation phase in all survivors with isolation of anaerobes such as *B. fragilis* and *Fusobacterium varium*. These experiments and others support the concept that aerobic enteric organisms and anaerobes are pathogens in intra-abdominal infections. Aerobic bacteria, particularly *E. coli*, appear responsible for the early mortality from peritonitis, whereas anaerobic bacteria are major pathogens in abscesses, with *B. fragilis* predominating.[36]

*Enterococcus* can be isolated from many intra-abdominal infections in humans, but its role as a pathogen is not clear. Enterococcal infection occurs more commonly in postoperative peritonitis, in the presence of specific risk factors indicating failure of the host's defenses (immunocompromised patients), or with the use of broad-spectrum antibiotics.[37,38]

## CLINICAL PRESENTATION

Intra-abdominal infections have a wide spectrum of clinical features often depending on the specific disease process, the location and magnitude of bacterial contamination, and concurrent host factors. Peritonitis is usually recognized easily, but intra-abdominal abscesses may often continue for considerable periods of time, either going unrecognized or being attributed to an unrelated disease process. Patients with primary and secondary peritonitis present quite differently (Table 137-4).[4,5,19,39-41]

TABLE 137-4

**Clinical Presentation of Peritonitis**

| Primary Peritonitis |
|---|
| **General** |
| The patient may not be in acute distress, particularly with peritoneal dialysis |
| **Signs and symptoms** |
| The patient may complain of loss of appetite, bloating, nausea, vomiting (sometimes with diarrhea), and abdominal tenderness |
| Temperature may be only mildly elevated or not elevated in patients undergoing peritoneal dialysis |
| Bowel sounds are hypoactive |
| The cirrhotic patient may have worsening encephalopathy |
| Cloudy dialysate fluid with peritoneal dialysis |
| **Laboratory tests** |
| The patient's WBC count may be only mildly elevated |
| Ascitic fluid usually contains greater than 250 leukocytes/$mm^3$ ($0.25 \times 10^9$/L), and bacteria may be evident on Gram stain of a centrifuged specimen |
| In 60%-80% of patients with cirrhotic ascites, the Gram stain is negative |
| **Other diagnostic tests** |
| Culture of peritoneal dialysate or ascitic fluid is typically positive, particularly if collected prior to initiation of antibiotics |
| In conjunction with clinical findings, procalcitonin may be helpful for limiting duration of antibiotic therapy in secondary and tertiary peritonitis |
| **Secondary Peritonitis** |
| **Signs and symptoms** |
| Generalized abdominal pain |
| Tachypnea |
| Tachycardia |
| Nausea and vomiting |
| Temperature is normal initially then increases to 37.8-38.9°C (100-102°F) within the first few hours and may continue to rise for the next several hours |
| Hypotension, hypoperfusion, and shock if volume is not restored |
| Decreased urine output due to vascular volume depletion |
| **Physical examination** |
| Voluntary abdominal guarding changing to involuntary guarding and a "board-like abdomen" |
| Abdominal tenderness and distension |
| Faint bowel sounds that cease over time |
| **Laboratory tests** |
| Leukocytosis (15,000-20,000 WBC/$mm^3$ [$15 \times 10^9$ to $20 \times 10^9$/L]), with neutrophils predominating and an elevated percentage of immature neutrophils (bands) |
| Elevated hematocrit and blood urea nitrogen because of dehydration |
| Patient progresses from early alkalosis because of hyperventilation and vomiting to metabolic acidosis |
| **Other diagnostic tests** |
| Abdominal radiographs may be useful because free air in the abdomen (indicating intestinal perforation) or distension of the small or large bowel is often evident |

WBC, white blood cell.

Primary peritonitis can develop over a period of days to weeks and is usually a more indolent process than secondary peritonitis. The first sign of peritonitis may be a cloudy dialysate in patients undergoing peritoneal dialysis or worsening encephalopathy in a cirrhotic patient.

The patient with generalized bacterial peritonitis presents most often in acute distress. The patient lies still, usually on his or her back, possibly with the hips slightly flexed. Any movement of the patient, including rocking the bed or breathing, worsens the generalized abdominal pain.

If peritonitis continues untreated, the patient may experience hypovolemic shock from third-space fluid loss into the peritoneum, bowel wall, and lumen. This may be accompanied by sepsis because the inflamed peritoneum absorbs bacteria and toxins into mesenteric blood vessels and lymph nodes, initiating production of inflammatory cytokines. Hypovolemic shock is the major factor contributing to mortality in the early stage of peritonitis.

Intra-abdominal abscesses may pose a difficult diagnostic challenge because the symptoms are neither specific nor dramatic. The patient may complain of abdominal pain or discomfort, but these symptoms are not reliable. Fever is usually present; often it is low grade, but it may be high, with a spiking pattern. The patient may have a paralytic ileus and abdominal distension. The abdominal examination is unreliable; tenderness and pain may be present, and a mass may be palpated.

Peritonitis may result from an abscess that ruptures, spreading bacteria and toxins throughout the peritoneum. In other patients, the entry of bacterial toxins into the systemic circulation from the abscess may lead to sepsis and progressive multisystem organ failure (eg, renal, hepatic, pulmonary, or cardiovascular).

Laboratory studies are not generally helpful in the diagnosis of intra-abdominal abscesses, although most patients will have leukocytosis. C-reactive protein has been suggested, but due to its lack of specificity, it is not very useful. Procalcitonin has been postulated to be of use, but its exact utility still must be determined. Some patients may have positive blood cultures, whereas others, particularly patients with diabetes, may have hyperglycemia. The finding of *Bacteroides* or enteric bacteria in the bloodstream is often indicative of an intra-abdominal infectious process.

Radiographic methods are used to make the diagnosis of an intra-abdominal abscess. Plain radiographs may show air–fluid levels or a shift of normal intra-abdominal contents by the abscess mass. GI contrast studies may also demonstrate this displacement of abdominal structures. Both of these modalities provide indirect evidence of abscess presence but are not generally helpful in precisely locating the abscess.

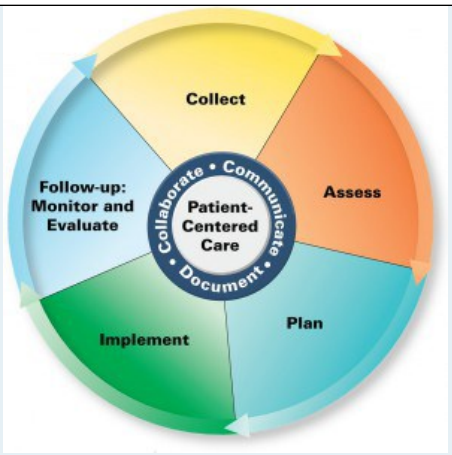
Ultrasound is the primary diagnostic method used when an intra-abdominal abscess is suspected. The procedure may be done at the bedside, which is particularly helpful when the patient is in the intensive care unit.

Computed tomography (CT) scanning is the preferred modality used to evaluate the abdomen for the presence of an abscess and is the imaging study of greatest value. If not contraindicated, an oral radiocontrast agent should be given to allow differentiation of the abscess from the bowel. IV radiocontrast material will be taken up preferentially in the wall of the abscess, creating a unique radiographic appearance, so-called rim enhancement. Magnetic resonance imaging offers no significant advantage when compared with CT scanning.

Intra-abdominal infection caused by disease processes at specific sites often produces characteristic manifestations that are helpful in diagnosis. For example, a patient with diverticulitis may exhibit stabbing left-lower-quadrant abdominal pain and constipation. Fever and leukocytosis are frequently present, and a tender mass is sometimes palpable. With appendicitis, the findings may be inconsistent, but many patients have a sudden onset of periumbilical or epigastric pain that is usually colicky and later shifts to the right lower quadrant. The location of pain may vary because the appendix can be in many locations (eg, retrocecal or pelvic) in the abdomen. A mass may be palpable on abdominal, pelvic, or rectal examination. The patient's temperature is generally mildly elevated early and then increases. If perforation and peritonitis occur, findings would include diffuse abdominal pain, rigidity, and sustained fever. More often, however, appendiceal perforation results in a local abscess.

## PATIENT CARE PROCESS

**Patient Care Process for Treatment of Intra-Abdominal Infections**




### Collect

- Patient characteristics (eg, age, sex, weight, body mass index)
- Patient history (past medical, family, social—dietary habits, tobacco use, alcohol use, substance abuse) and surgical operations (site, date, procedure)
- Medication history at hospital admission (prescription and non-non-prescription medications and supplements), drug allergies, and intolerances; previous antibiotic use, inpatient and outpatient, dose and duration
- Microbiologic results from blood, intra-abdominal fluids, and other sources, and obtain susceptibility results when they are available
- Laboratory results for infection, major organ function (particularly kidney and liver), and immune status

### Assess

- Hemodynamic status (eg, MAP, HR)
- Estimate creatinine clearance for drug dosing
- Review all culture results and consider anaerobic bacteria even though they may not be isolated in cultures

### Plan*

- Determine initial empiric treatment and monitoring plan
- Establish antimicrobial monitoring goals for microbiologic and clinical outcomes
- Consider other medications that may be needed during treatment or post-surgery (ie, fluids, analgesics, medications for nausea and vomiting, thrombosis prevention)
- Check for drug interactions and dose adjustments based on end-organ function

### Implement

- Initiate an empiric antimicrobial regimen, modify therapy once microbiologic data is available, and establish a tentative stop date
- De-escalate antimicrobial therapy as appropriate based on response and microbiologic data
- Discontinue adjunct medications when not needed or indicated
- Assess patient as needed for response to surgical control, medications, and other treatments

- Use measures to minimize adverse events to medications and assess for occurrence of adverse events
- Assess pain control and progress of gastrointestinal function
- Change to oral medications when appropriate after patient resumes oral feeding

**Follow-up: Monitor and Evaluate**

- Determine whether patient shows improvement with signs and symptoms of infection within 2 to 3 days after antimicrobials are initiated and surgical source control is completed
- The patient should be reassessed continually to determine the success or failure of therapies
- Monitor for emergence of resistant bacterial isolates in blood or other sources and change antimicrobials if needed
- Monitor for occurrence of secondary infections such as respiratory and urinary tract
- Upon hospital discharge, determine which medications the patient should be discharged with and provide counseling; discontinue unnecessary medications

**Collaborate with patient, caregiver(s), and other healthcare professionals.*

# TREATMENT

## Desired Outcome

The primary goals of treatment are correction of the intra-abdominal disease processes or injuries that have caused infection and the drainage of purulent collections (abscesses). A secondary objective is to achieve a resolution of infection without major organ system complications (pulmonary, hepatic, cardiovascular, or renal failure) or adverse drug effects. Ideally, the patient should be discharged from the hospital after treatment with full function for self-care and routine daily activities.

## General Approach to Treatment

The treatment of intra-abdominal infection most often requires hospitalization and the coordinated use of three major modalities: (a) prompt surgical control and drainage of the infected site, (b) hemodynamic resuscitation and support of vital organ functions, and (c) early administration of appropriate antimicrobial therapy to treat infection not eradicated by surgery.[16]

Antimicrobials are an important adjunct to drainage procedures in the treatment of secondary intra-abdominal infections; however, the use of antimicrobial agents without surgical source control is usually inadequate. For most cases of primary peritonitis, drainage procedures may not be required, and antimicrobial agents become the mainstay of therapy.

4 In the early phase of serious intra-abdominal infections, attention should be given to the maintenance of organ system functions. With generalized peritonitis, initial large volumes of IV fluids are required to restore vascular volume, to improve cardiovascular function, and to maintain adequate tissue perfusion and oxygenation. Adequate urine output should be maintained to ensure adequate resuscitation and proper renal function. Respiratory function can be assisted by a variety of methods, including oxygen therapy, pulmonary physiotherapy, and ventilatory support in severely ill patients. Often the critically ill patient with intra-abdominal infection will require intensive care management, particularly if there is cardiovascular or respiratory instability. In addition, isolation procedures may be required if the infectious process poses a threat to other hospitalized patients.

An important component of therapy is nutrition. Intra-abdominal infections often involve the GI tract or disrupt its function (ie, paralytic ileus). The return of GI motility may take days, weeks, and, occasionally, months. In the interim, enteral or parenteral nutrition, as indicated, facilitates improved immune function and wound healing to ensure recovery. Additional information pertaining to enteral and parenteral nutrition can be found elsewhere in this book (Chapters 165 and 166).

## Nonpharmacologic Treatment

### Drainage Procedures

Primary peritonitis is treated with antimicrobials and rarely requires drainage. Secondary peritonitis requires surgical correction of the underlying pathology. The drainage of the purulent material is the critical component of management of an intra-abdominal abscess. Without adequate drainage of the abscess, antimicrobial therapy and fluid resuscitation can be expected to fail.

Secondary peritonitis is treated surgically; this is often called *source control*, which refers to all the physical measures undertaken to eradicate the focus of infection.[5,16] At the time of laparotomy (surgical opening and exploration of the abdomen), attempts are made to correct the cause of the peritonitis. This may include patching a perforated ulcer with omentum, removal of a segment of perforated colon, or excision of a portion of gangrenous small intestine. In addition, the surgeon may elect to leave the abdomen open after the laparotomy, plan a re-laparotomy at a later time regardless of the patient's condition, or perform re-laparotomy if the patient develops reinfection.[5,16] The goal of all these procedures is to repair or remove the inflamed or gangrenous tissue and to prevent further bacterial contamination. The presence of active inflammation increases the difficulty of the surgical procedure, which results in a higher morbidity and mortality rate than if the same procedures were performed in an elective setting without inflammation. Electing to leave the abdomen open after surgery is usually to prevent abdominal compartment syndrome; however, this is unnecessary when fluid collections can be removed with percutaneous catheter drainage.[42]

The presence of active inflammation may make it technically impossible to perform the definitive surgical procedure. In this situation, attempts are made to provide drainage of the infected or gangrenous structures. If an intra-abdominal abscess, separate from any intra-abdominal organ, is discovered during an exploratory laparotomy, it may be debrided, excised, or drained. If the intra-abdominal abscess involves an abdominal structure, then a resection of part or of the entire organ may be required. An example of this situation is an abscess associated with diverticular disease of the colon. Management may include drainage of the abscess and resection of the involved part of the colon. All foreign material, necrotic tissue, feces, blood, or purulent material should be removed from the operative field, and the peritoneum should be copiously irrigated with 0.9% sodium chloride to decrease the concentrations of bacteria or other noxious substances.

After an abscess is located, it must be drained. This may be performed surgically or with percutaneous, image-guided techniques.[5,16,43] Typically, image-guided techniques use ultrasonography or CT scanning. The management of an intra-abdominal abscess with percutaneous catheter drainage may be sufficient to resolve the infection. Some patients may require a subsequent procedure to treat the underlying GI conditions; however, a significant advantage is obtained by first draining the abscess percutaneously. This allows the surgical procedure to be performed on a patient who is no longer suffering from the systemic manifestations of uncontrolled infection. Drainage techniques may be performed using endoscopy or laparoscopy. These minimal-access techniques may offer advantages when compared with traditional surgery but will probably be used less often than radiologically assisted percutaneous drainage techniques.

The most valuable microbiologic information may be obtained at the time of percutaneous or operative abscess drainage. If purulent material or presumably infected fluid is found, it is best to aspirate 2 to 3 mL into a syringe, remove any air, and tightly cap the syringe. The specimen should be promptly delivered to the microbiology laboratory, where a Gram stain should be performed immediately, and cultures prepared for identification of aerobic and anaerobic bacteria. If no fluid is available for collection, culture swab devices may be applied to the infected area; however, anaerobic organisms often are not isolated from swabs.

### Fluid Therapy

4 Patients should be evaluated for signs of hypovolemia, hypoperfusion, and shock. Initial effective fluid repletion and management are required for successful management of intra-abdominal infections. Fluid therapy is instituted for the purposes of achieving or maintaining intravascular volume to ensure adequate cardiac output, tissue perfusion, and correction of acidosis. Loss of fluid through vomiting, diarrhea, or nasogastric suction contributes to fluid depletion. A more thorough discussion of sepsis and septic shock, including fluid resuscitation, is presented elsewhere in this book (Chapters e42 and 142).

In patients with peritonitis, hypovolemia is often accompanied by metabolic acidosis. Although serum lactate is not a direct measure of tissue perfusion, it may serve as a surrogate marker representing tissue hypoxia and is therefore recommended by the Surviving Sepsis Campaign 2021

update to guide fluid administration. In those patients with sepsis hypoperfusion or septic shock, IV fluids should consist of a 30 mL/kg bolus of crystalloids with additional fluids targeting predefined therapeutic goals.[44-46] Initial fluid resuscitation should be completed within 3 hours of hypoperfusion recognition. Thereafter, fluids may be required at a rate of 1 L/hr or higher. Once targeted therapeutic goals are reached, judicious use of fluids should be used, as a sustained positive fluid balance after initial resuscitation may be harmful.[16,47] Maintenance fluids should be instituted with 0.9% sodium chloride, 5% dextrose, and 0.45% sodium chloride, or a balanced crystalloid solution.[48] The administration rate should be based on estimated daily fluid loss through urine and nasogastric suction, including 0.5 to 1 L for insensible fluid loss. Potassium can be included in maintenance fluids if the patient is experiencing vomiting, diarrhea, or has nasogastric suction.

## Pharmacologic Treatment

### Antimicrobial Therapy

The goals of antimicrobial therapy are: (a) to eliminate the intra-abdominal infection and prevent the establishment of metastatic foci of infection or bacteremia, (b) to reduce suppurative complications (eg, abscess formation) after bacterial contamination, and (c) to prevent local spread of existing infection. After suppuration has occurred, a cure by antibiotic therapy alone is very difficult to achieve; antimicrobials may serve to improve the results obtained with surgery.

5 An empirical antimicrobial regimen should be started as soon as the presence of intra-abdominal infection is suspected. The Surviving Sepsis Campaign Guidelines recommend that antimicrobial therapy is administered immediately and within 1 hour of the recognition of sepsis or septic shock.[46] Therapy must be initiated based on the likely pathogens, potential resistance, and severity of patient illness. Resistance is common among gram-negative pathogens to fluoroquinolones and ampicillin/sulbactam; this emphasizes the importance of using local susceptibility data to guide empiric therapy and tailoring the antibiotic regimen based on susceptibility results.[49] Predominant pathogens, as discussed in the preceding section, vary depending on the site of intra-abdominal infection and the underlying disease process. Table 137-5 lists the likely pathogens against which antimicrobial agents should be directed.

TABLE 137-5

**Likely Intra-Abdominal Pathogens**

| Type of Infection | Aerobes | Anaerobes |
|---|---|---|
| **Primary (Spontaneous) Bacterial Peritonitis** | | |
| Children | Group A *Streptococcus*, *E. coli*, pneumococci | — |
| Cirrhosis | *E. coli*, *Klebsiella*, pneumococci (many others) | — |
| Peritoneal dialysis | *Staphylococcus*, *Streptococcus*, *E. coli*, *Klebsiella*, *Pseudomonas* | — |
| **Secondary Bacterial Peritonitis** | | |
| Gastroduodenal | *Streptococcus*, *E. coli* | — |
| Biliary tract | *E. coli*, *Klebsiella*, enterococci | *Clostridium* or *Bacteroides* (infrequent) |
| Small or large bowel | *E. coli*, *Klebsiella*, *Proteus* | *B. fragilis* and other *Bacteroides*, *Clostridium* |
| Appendicitis | *E. coli*, *Pseudomonas* | *Bacteroides* |
| Abscesses | *E. coli*, *Klebsiella*, *Streptococcus*, enterococci | *B. fragilis* and other *Bacteroides*, *Clostridium*, anaerobic cocci |
| Liver | *E. coli*, *Klebsiella*, *Streptococcus*, enterococci, *Staphylococcus*, amoeba | *Bacteroides* (infrequent) |
| Spleen | *Staphylococcus*, *Streptococcus*, *E. coli*, *Salmonella* | — |

### Antimicrobial Experience

Many studies have been conducted evaluating or comparing the effectiveness of antimicrobials for the treatment of intra-abdominal infections. Substantial differences in patient outcomes between specific agents have not generally been demonstrated.[50]

Important findings from over 20 years of clinical trials regarding selection of antimicrobials for intra-abdominal infections are the following:

1. Antimicrobial regimens used for secondary infections should cover a broad spectrum of aerobic and anaerobic bacteria from the GI tract. The local epidemiology of resistant pathogens, patient-specific risk factors for resistant pathogens, and patient severity of illness should guide empiric treatment.

2. Resistance is prevalent among *B. fragilis* to clindamycin and Enterobacterales to ampicillin/sulbactam and quinolones, and therefore these agents should not be routinely used empirically for complicated intra-abdominal infections.[51,52]

3. If the causative pathogens are susceptible and the patient has clinically responded, antimicrobial treatment can be completed orally with amoxicillin/clavulanate, metronidazole with either ciprofloxacin or levofloxacin, or moxifloxacin.[53]

4. Four days of antimicrobial treatment after adequate source control is sufficient for most intra-abdominal infections.[16,54,55]

Intra-abdominal infections present in many different ways and with a wide spectrum of severity. The regimen employed and duration of treatment depends on the specific clinical circumstances (ie, the nature of the underlying disease process, severity of illness, and risk of resistant pathogens).

**Recommendations**

6 For most intra-abdominal infections, the antimicrobial regimen should be effective against both aerobic and anaerobic bacteria.[55,56] When initial antimicrobial therapy is inactive, morbidity and mortality rates are higher than when initially active therapy is used.[55] Generally, agents with activity against enteric gram-negative bacilli, such as *E. coli* and *Klebsiella* spp., and anaerobes, including *B. fragilis,* should be administered. If most of the organisms can be eliminated through drainage or antimicrobials, the synergistic effect may be removed, and the patient's defenses may be able to resolve the remaining infection.

Table 137-6 lists the agents recommended by the Infectious Diseases Society of America (IDSA) and the Surgical Infection Society (SIS) for the treatment of community-acquired complicated intra-abdominal infections.[16,55] These recommendations were formulated using an evidence-based approach. Table 137-7 lists additional evidence-based recommendations for the treatment of complicated intra-abdominal infections. Choosing empiric antibiotic therapy based on these recommendations within the IDSA/SIS guidelines has been associated with a decreased time to active therapy for patients with community-onset complicated intra-abdominal infection.[57] Although most community-acquired infections are of mild-to-moderate severity, healthcare-associated infections tend to be more severe, more difficult to treat, and more common due to resistant pathogens. Table 137-8 presents guidelines for treatment and alternative regimens for specific situations. These are general guidelines; such a table cannot incorporate many factors, including local resistance patterns to commonly used agents such as quinolones.

TABLE 137-6

**Recommended Agents for the Treatment of Community-Acquired Complicated Intra-Abdominal Infections in Adults**

| Agents Recommended for Mild-to-Moderate Infections | Agents Recommended for High Severity Infections |
|---|---|
| **Single Agent** | |
| Cefoxitin[a] | Piperacillin/tazobactam |
| Moxifloxacin[b] | Imipenem/cilastatin,[c] meropenem,[c] meropenem/vaborbactam,[d] imipenem/relebactam[d] |
| Ertapenem[c] | |
| Eravacycline[d] | |
| **Combination Regimens** | |
| Cefazolin,[a] cefuroxime,[a] ceftriaxone, or cefotaxime each in combination with metronidazole | Cefepime, ceftazidime, cefiderocol,[d] ceftazidime/avibactam,[d] or ceftolozane/tazobactam[d] each in combination with metronidazole |
| Ciprofloxacin[b] or levofloxacin[b] each in combination with metronidazole | Ciprofloxacin[b] or levofloxacin[b] each in combination with metronidazole |

[a]Empiric first- and second-generation cephalosporin use should be avoided unless local antibiograms show >80% to 90% susceptibility of *E. coli* to these agents.

[b]Use of quinolones may be associated with treatment failure due to increasing resistance of enteric pathogens including *E. coli*. Empiric quinolone use should be avoided unless local antibiograms show >80% to 90% susceptibility of *E. coli* to quinolones.

[c]Carbapenems should be reserved for settings where there is a high risk of resistance to other agents (ie, extended-spectrum β-lactamase [ESBL]-producing pathogens).

[d]These broad-spectrum agents should be reserved for patients infected with Enterobacterales that are resistant to all other β-lactams. Ceftazidime/avibactam, meropenem/vaborbactam, and imipenem/relebactam are preferred for KPC-producing pathogens. Ceftolozane/tazobactam may have activity against multidrug-resistant *Pseudomonas*; however, susceptibility must be confirmed.

*Data from References 16,55,58, and 59.*

TABLE 137-7

**Evidence-Based Recommendations for Treatment of Complicated Intra-Abdominal Infections**

| | Grade of Recommendation[a] |
|---|---|
| **Elements of Appropriate Intervention** | |
| An appropriate source control procedure to drain infected foci, control ongoing peritoneal contamination by diversion or resection, and restore anatomic and physiological function to the extent feasible is recommended for nearly all patients with intra-abdominal infections | B-2 |

| | |
|---|---|
| **Community-Acquired Infections of Mild-to-Moderate Severity in Adults** | |
| Antibiotics used for empiric treatment of community-acquired intra-abdominal infections should be active against enteric gram-negative aerobic and facultative bacilli and enteric gram-positive streptococci | A-1 |
| For patients with mild-to-moderate, community-acquired infections, regimens with substantial anti-pseudomonal activity are not required (Table 137-6) | A-1 |
| Empiric coverage of *Enterococcus* is not necessary in patients with mild-to-moderate community-acquired intra-abdominal infection | A-1 |
| The use of agents listed as appropriate for high-severity, community-acquired infection and healthcare-associated infection is not recommended for patients with mild-to-moderate, community-acquired infection, because such regimens may carry a greater risk of toxicity and facilitate acquisition of more resistant organisms | B-2 |
| **High-Severity, Community-Acquired Infections in Adults**[b] | |
| The empiric use of antimicrobial regimens with broad-spectrum activity against gram-negative organisms including *Pseudomonas* spp., such as meropenem, imipenem/cilastatin, piperacillin–tazobactam, ciprofloxacin or levofloxacin in combination with metronidazole, or ceftazidime or cefepime in combination with metronidazole, is recommended for patients with high-severity, community-acquired intra-abdominal infection (Table 137-6) | A-1 |
| Aztreonam plus metronidazole is an alternative, but addition of an agent effective against gram-positive cocci is recommended | B-3 |
| **Healthcare-Associated Infections in Adults**[c] | |
| Empiric antibiotic therapy for healthcare-associated intra-abdominal infections should be driven by local microbiologic results | A-2 |
| To achieve empiric coverage of likely pathogens, multidrug regimens that include agents with expanded spectra of activity against gram-negative aerobic and facultative bacilli may be needed. These agents include meropenem, imipenem/cilastatin, piperacillin/tazobactam, or metronidazole combined with either cefepime or ceftazidime. For multidrug-resistant aerobic gram-negative pathogens, aminoglycosides, colistin, polymyxin B, meropenem/vaborbactam, imipenem/relebactam, eravacycline, cefiderocol, ceftazidime/avibactam, or ceftolozane/tazobactam may be required | B-3 |
| **Antimicrobial Agents Not Recommended** | |
| Ampicillin/sulbactam is not recommended for use because of high rates of resistance to this agent among community-acquired *E. coli* | B-2 |
| Quinolone-resistant *E. coli* have become common in some communities, and quinolones should not be used unless hospital surveys indicate 90% susceptibility of *E. coli* to quinolones | A-2 |
| Clindamycin is not recommended for use because of increasing prevalence of resistance to these agents among *Bacteroides fragilis* | B-2 |
| Because of the availability of less toxic agents demonstrated to be at least equally effective, aminoglycosides are not recommended for routine use in adults with community-acquired intra-abdominal infections | B-2 |
| **Oral Completion Therapy** | |

| | |
|---|---|
| For adults recovering from an intra-abdominal infection, completion of the antimicrobial course with oral forms of moxifloxacin, ciprofloxacin plus metronidazole, levofloxacin plus metronidazole, an oral cephalosporin with metronidazole, or amoxicillin/clavulanic acid is acceptable in patients able to tolerate an oral diet and in patients in whom susceptibility studies do not demonstrate resistance | B-2 |
| **Duration of Therapy** | |
| Antimicrobial therapy of established infection should be limited to 4 days, unless it is difficult to achieve adequate source control. Longer durations of therapy have not been associated with improved outcome | A-1 |
| For acute stomach and proximal jejunum perforations, in the absence of acid-reducing therapy or malignancy and when source control is achieved within 24 hours, prophylactic anti-infective therapy directed at aerobic gram-positive cocci for 24 hours is adequate | B-2 |
| Bowel injuries attributable to penetrating, blunt, or iatrogenic trauma that are repaired within 12 hours and any other intraoperative contamination of the operative field by enteric contents should be treated with antibiotics for ≤24 hours | A-1 |
| Acute appendicitis without evidence of perforation, abscess, or local peritonitis requires only prophylactic administration of narrow spectrum regimens active against aerobic and facultative and obligate anaerobes; treatment should be discontinued within 24 hours | A-1 |
| The administration of prophylactic antibiotics to patients with severe necrotizing pancreatitis prior to the diagnosis of infection is not recommended | A-1 |
| **Anaerobic Coverage** | |
| Coverage for obligate anaerobic bacilli should be provided for distal small bowel, appendiceal, and colon-derived infection and for more proximal GI perforations in the presence of obstruction or paralytic ileus | A-1 |
| **Antifungal Therapy** | |
| Antifungal therapy for patients with high-severity community-acquired or healthcare-associated infection is recommended if *Candida* is grown from intra-abdominal cultures | B-2 |
| **Anti-MRSA Therapy** | |
| Empiric antimicrobial coverage directed against MRSA should be provided to patients with healthcare-associated intra-abdominal infection who are known to be colonized with the organism or who are at risk of having an infection due to this organism because of prior treatment failure and significant antibiotic exposure | B-2 |
| Vancomycin is recommended for treatment of suspected or proven intra-abdominal infection due to MRSA | A-3 |
| **Antienterococcal Therapy** | |
| Antimicrobial therapy for enterococci should be given when enterococci are recovered from patients with high-severity community-acquired or healthcare-associated infection | B-III |
| Empiric antienterococcal therapy is recommended for patients with high-severity community-acquired infections and healthcare-associated intra-abdominal infections, particularly those with postoperative infection, those who have previously received cephalosporins or other antimicrobial agents selected for *Enterococcus* species, immunocompromised patients, and those with valvular heart disease or prosthetic intravascular materials | B-II |

| | |
|---|---|
| Initial empiric antienterococcal therapy should be directed against *Enterococcus faecalis*. Antibiotics that can potentially be used against this organism, on the basis of susceptibility testing of the individual isolate, include ampicillin, ampicillin/sulbactam, piperacillin/tazobactam, imipenem/cilastatin, and vancomycin | B-III |
| Empiric therapy directed against vancomycin-resistant *Enterococcus faecium* is not recommended unless the patient is at very high risk for an infection due to this organism, such as a liver transplant recipient with an intra-abdominal infection originating in the hepatobiliary tree or a patient known to be colonized with vancomycin-resistant *E. faecium* | B-III |

[a]Strength of recommendations: A, B, C = good, moderate, and poor evidence to support recommendation, respectively. 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, 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 communities.

[b]Criteria for high-severity community-acquired infection: sepsis or septic shock, APACHE II score ≥15, delay in initial intervention >24 hours, advanced age, comorbidity and degree of organ dysfunction, low albumin level, poor nutritional status, degree of peritoneal involvement or diffuse peritonitis, inability to achieve adequate debridement or control of drainage, and presence of malignancy.

[c]Criteria for classification of intra-abdominal infections as healthcare-associated infection vary. However, patients who develop an infection after surgery, reside in a long-term care facility, who were recently hospitalized, or who have other significant healthcare exposure can be considered to have a healthcare-associated intra-abdominal infection.

MRSA, methicillin-resistant *Staphylococcus aureus*.

*Data from References 16,55, and 58.*

TABLE 137-8

**Guidelines for Empiric Antimicrobial Agents for Intra-Abdominal Infections**

| | Primary Agents | Alternatives |
|---|---|---|
| **Primary (Spontaneous) Bacterial Peritonitis** | | |
| Cirrhosis | Ceftriaxone, cefotaxime | 1. Piperacillin/tazobactam, carbapenems<br>2. Aztreonam combined with an agent active against *Streptococcus* spp. (eg, vancomycin) or quinolones with significant *Streptococcus* spp. activity (levofloxacin, moxifloxacin) |
| Peritoneal dialysis | Initial empiric regimens should be active against both gram-positive (including *S. aureus*) and gram-negative pathogens: gram-positive agent (first-generation cephalosporin or vancomycin) plus a gram-negative agent (third-generation cephalosporin or aminoglycoside) | 1. Cefepime or carbapenems may be used alone<br>2. Aztreonam or an aminoglycoside may be used in place of ceftazidime or cefepime as long as combined with a gram-positive agent<br>3. Quinolones may be used in place of gram-negative agents if local susceptibilities allow |
| | 1. *Staphylococcus* spp.: oxacillin/nafcillin or first-generation cephalosporin | 1. Vancomycin should be used for methicillin-resistant *Staphylococcus* spp.<br>2. May consider addition of rifampin for 5-7 days |

| | | |
|---|---|---|
| | | with vancomycin |
| | 2. *Streptococcus* or *Enterococcus*: ampicillin | 1. Daptomycin or linezolid should ideally be used to treat vancomycin-resistant *Enterococcus* spp. not susceptible to ampicillin |
| | 3. Aerobic gram-negative bacilli: ceftazidime or cefepime | 1. The regimen should be based on in vitro sensitivity tests |
| | 4. *Pseudomonas aeruginosa*: two agents with differing mechanisms of action, such as an intraperitoneal ceftazidime or cefepime each combined with either tobramycin or oral ciprofloxacin | |
| **Secondary Bacterial Peritonitis** | | |
| Perforated peptic ulcer | First-generation cephalosporins | 1. Ceftriaxone, cefotaxime, or antianaerobic cephalosporins[a] |
| Other | Third- or fourth-generation cephalosporin with metronidazole, piperacillin–tazobactam or carbapenem | 1. Ciprofloxacin[b] or levofloxacin[b] each with metronidazole or moxifloxacin[b] alone<br>2. Aztreonam with vancomycin and metronidazole<br>3. Antianaerobic cephalosporins[a] |
| **Abscess** | | |
| General | Third- or fourth-generation cephalosporin with metronidazole or piperacillin/tazobactam | 1. Imipenem/cilastatin, meropenem, or ertapenem<br>2. Ciprofloxacin[b] or levofloxacin[b] each with metronidazole or moxifloxacin alone |
| Liver | As above | Use metronidazole if amoebic liver abscess is suspected |
| Spleen | Ceftriaxone or cefotaxime | Moxifloxacin[b] or levofloxacin[b] |
| **Other Intra-Abdominal Infections** | | |
| Appendicitis | Same management as for community-acquired complicated intra-abdominal infections as listed in Table 137-6[44] | |
| Community-acquired acute cholecystitis | Ceftriaxone or cefotaxime | Severe infection, piperacillin/tazobactam, antipseudomonal carbapenem, aztreonam with metronidazole |
| Cholangitis | Ceftriaxone or cefotaxime each with or without metronidazole | Vancomycin with aztreonam with or without metronidazole |
| Acute | Antianaerobic cephalosporins[a] or metronidazole with either ceftriaxone or | 1. Piperacillin/tazobactam or a carbapenem |

| | | |
|---|---|---|
| contamination from abdominal trauma | cefotaxime | 2. Ciprofloxacin[b] or levofloxacin[b] each with metronidazole or moxifloxacin alone |
| Diverticulitis | Cefazolin, cefuroxime, or ceftriaxone with metronidazole or ampicillin/sulbactam | Ciprofloxacin[b] or levofloxacin[b] each with metronidazole or moxifloxacin alone |

[a]Cefoxitin or ceftizoxime; these agents should be avoided empirically unless local antibiograms show >80% to 90% susceptibility of *E. coli* to these agents.

[b]Use of quinolones may be associated with treatment failure due to increasing resistance of enteric pathogens including *E. coli*. Empiric quinolone use should be avoided unless local antibiograms show >80% to 90% susceptibility of *E. coli* to quinolones.

*Data from References 55 and 60.*

Most patients with severe intra-abdominal infection, sepsis, or healthcare-associated infection should be placed on piperacillin/tazobactam, cefepime with metronidazole, or a carbapenem with *Pseudomonas* activity such as imipenem, or meropenem. In patients with IgE-mediated allergic reactions to β-lactams (hives/urticaria, bronchospasm, angioedema, or anaphylaxis), a combination therapy with aztreonam, vancomycin, and metronidazole may be used. The benefits of systemic preemptive antifungal therapy (with fluconazole or an echinocandin) as a means to prevent invasive candidiasis in patients with intra-abdominal infection have not been established.[61] However, patients with intra-abdominal infections are often at high risk for systemic candidiasis, given multiple risk factors may be present such as recent abdominal surgery, the presence of a central line, parenteral nutrition, and broad-spectrum antibiotic use.[16,55,62] When invasive candidiasis is suspected, generally an echinocandin should be used empirically because these patients are often severely ill and may be at risk for infection with a fluconazole-resistant *Candida* species.[62] As noted in Table 137-7, *Candida* should be treated if isolated from cultures in patients with high-severity, community-acquired or healthcare-associated infection.[16,62] If the *Candida* spp. is fluconazole susceptible and the patient is clinically improving, it is reasonable to de-escalate from an echinocandin to fluconazole.

Aminoglycoside-based treatment regimens are not routinely recommended due to their narrow therapeutic index (nephrotoxicity, ototoxicity) relative to the recommended agents such as β-lactams.[63,64] Aminoglycosides are reserved primarily for infections due to presumed or proven multidrug-resistant pathogen(s).[50,55]

If an aminoglycoside is required, the initial dosage should be determined based on the patient's weight and renal function. Traditionally, gentamicin and tobramycin were administered multiple times daily with specific peak (6-10 mcg/mL [mg/L; 13-21 µmol/L]) and trough (less than 1-2 mcg/mL [mg/L; less than 2-4 µmol/L]) serum concentration targets. Because aminoglycosides have concentration-dependent killing and have a relatively long postantibiotic effect for aerobic gram-negative bacilli, extended-interval dosing of aminoglycosides is possible. For most patients and indications, extended-interval aminoglycoside dosing (ie, 5-7 mg/kg once daily for tobramycin or gentamicin, 15-20 mg/kg once daily for amikacin) has replaced traditional dosing, given equivalent efficacy and decreased nephrotoxicity.[65-67]

Antimicrobial resistance continues to increase worldwide.[68-70] Enterobacterales producing extended-spectrum β-lactamases (ESBL) have been increasingly isolated from intra-abdominal cultures.[49,51] For patients with ESBL-producing pathogens, carbapenems are typically the drugs of choice. With the increased use of carbapenems, pathogens have continued to evolve with the development of β-lactamases that hydrolyze carbapenems (eg, *Klebsiella pneumoniae* carbapenemase [KPC]), multidrug-resistant *Pseudomonas* spp., and carbapenem-resistant *Acinetobacter* spp. Especially in patients with healthcare-associated intra-abdominal infections, these multidrug-resistant pathogens have forced clinicians to use more toxic and potentially less effective agents such as the polymyxins, tigecycline, and aminoglycosides. For example, the product labeling for tigecycline carries a Black Box Warning, as it has been associated with an increased risk of mortality relative to comparator agents, which is based on pooled data collected from randomized controlled trials including patients with intra-abdominal infections, skin and skin structure infections, and ventilator-associated pneumonia.[71-73] Accordingly, the 2017 SIS guidelines recommend against the use of tigecycline except potentially as part of a combination regimen for multidrug-resistant pathogens.[16] Three potential therapeutic options for multidrug-resistant pathogens, ceftolozane/tazobactam, ceftazidime/avibactam, and eravacycline have been FDA-approved for the treatment of complicated intra-abdominal infections in combination with

metronidazole.[66,67,74] Ceftolozane/tazobactam may be active against multidrug-resistant pathogens, particularly *Pseudomonas* spp., while ceftazidime/avibactam is active against KPC-producing Enterobacterales.

These agents may be more effective than colistin-based regimens for infections due to KPC-producing Enterobacterales.[59,75-77] However, it is not uncommon for organisms that are resistant to all other β-lactams to also be resistant to these three new agents, and so susceptibility must be confirmed. Despite this, these agents are highly valuable in terms of their activity against multidrug-resistant pathogens, and as such, their use should be reserved for patients with a suspected or confirmed infection due to a pathogen resistant to all other β-lactams. The limited safe-and-effective therapeutic options for resistant organisms highlight the need, from an individual patient and public health standpoint, for pharmacists and other clinicians to ensure that antimicrobials are selected appropriately, at the optimal dose, and for the correct duration.

With intra-abdominal contamination from the upper GI tract (perforation of a peptic ulcer or biliary tract disease), anaerobes such as *B. fragilis* are uncommon pathogens, and therefore other empiric agents such as ampicillin, penicillin, or first-generation cephalosporins are reasonable. Anaerobic coverage is also not necessary for primary peritonitis associated with cirrhosis, and cefotaxime or ceftriaxone remain the treatments of choice.[78]

Empiric coverage of *Enterococcus* in mild-to-moderate, community-acquired intra-abdominal infections is not recommended.[55] The failure of host defenses may be a critical factor in the pathogenicity of enterococci. In patients with high-severity, community-acquired intra-abdominal infections or patients with healthcare-associated infection, coverage of *Enterococcus faecalis* should be included in the initial regimen.[16,55] Ampicillin remains the drug of choice for this indication because it is active against the vast majority of *E. faecalis.* Notably, piperacillin/tazobactam and imipenem/cilastatin both have activity against ampicillin-susceptible *E. faecalis,* and therefore these may be elegant choices for empiric therapy of high-severity community-acquired or healthcare-associated intra-abdominal infections. Vancomycin may also be active against enterococci; however, rates of vancomycin-resistant enterococci are increasing, especially in select patient populations (eg, liver transplantation, immunocompromised patients).[79] Agents, including linezolid or daptomycin, are commonly used for vancomycin-resistant *Enterococcus* infections. Table 137-7 lists additional evidence-based recommendations for *Enterococcus* spp. coverage.

7 Intraperitoneal administration of antibiotics is preferred over IV therapy in the treatment of peritonitis that occurs in patients undergoing CAPD.[60,80] The International Society of Peritoneal Dialysis guidelines for the diagnosis and pharmacotherapy of peritoneal dialysis-associated infections provide antimicrobial dosing recommendations based on the modality of dialysis (continuous or intermittent).[60]

Given the peritoneal catheter exit site and tunnel is frequently the source of peritoneal dialysis-related peritonitis, prophylaxis with topic antibiotic cream or ointment to the catheter exit site reduces infections caused by *S. aureus* and gram-negative bacilli, including *Pseudomonas* spp.[81] When infection occurs, antimicrobial agents effective against both gram-positive skin flora (including *S. aureus*) and gram-negative organisms should be used for initial intraperitoneal empiric therapy. The most important factors to take into consideration for initial antimicrobial selection are the dialysis center's and the patient's history of infecting organisms and their sensitivities. For empiric intraperitoneal therapy, cefazolin or vancomycin in cases of high prevalence of MRSA or β-lactam allergy may be used for gram-positive coverage. Glycopeptide-containing regimens (vancomycin) were more likely to achieve complete cure compared to first-generation cephalosporins.[80,82] When vancomycin is used, it is preferred that it be given intraperitoneally via intermittent dosing (15-30 mg/kg every 5-7 days) and serum concentrations should be maintained above 15 mcg/mL (mg/L; 10.4 μmol/L).[83] When administered via intermittent dosing, generally the antibiotic should dwell for at least 6 hours. One of these gram-positive agents should be combined with a gram-negative agent such as ceftazidime or an aminoglycoside. If an aminoglycoside is used, it is preferred that it be given intraperitoneally via intermittent dosing (eg, gentamicin 0.6 mg/kg/day). Long durations of aminoglycoside therapy should be avoided if possible to mitigate the risk of ototoxicity and loss of residual renal function. Another option is monotherapy with cefepime or imipenem/cilastatin. If patients have significant residual renal function, increased antimicrobial doses may not be necessary.[60,83] As with other intra-abdominal infections, source control should be prioritized; in patients with an ongoing catheter exit site or tunnel infection, catheter removal with reinsertion should be strongly considered. If peritonitis relapses or recurs, the catheter should be promptly removed. Antimicrobial therapy should typically be continued for 14 to 21 days. The reader is referred to recent guidelines for additional information.[60,81]

After acute bacterial contamination, such as with abdominal trauma where GI contents spill into the peritoneum, antibiotics should be administered. If the patient is seen soon after injury (within 2 hours) and surgical measures are instituted promptly, an anti-anaerobic cephalosporin (such as cefoxitin), a third-generation cephalosporin (such as ceftriaxone) with metronidazole, or piperacillin/tazobactam is effective in preventing most infectious complications. Antimicrobials should be administered as soon as possible after injury.[84]

For appendicitis, the antimicrobial regimen used should depend on the appearance of the appendix at the time of operation, which may be normal, inflamed, gangrenous, or perforated. It is advisable to begin antimicrobial agents before the appendectomy is performed. Reasonable regimens would be antianaerobic cephalosporins or, if the patient is seriously ill, piperacillin/tazobactam, or an anti-pseudomonal carbapenem. If, at operation, the appendix is normal or inflamed, postoperative antimicrobials are not required. If the appendix is gangrenous or perforated, a treatment course of 3 to 4 days with the agents listed in Table 137-6 is appropriate.[11,85] For uncomplicated appendicitis (defined as the absence of perforation, abscess, appendicolith, CT consistent with possible tumor, peritonitis, severe systemic illness) confirmed by CT, a nonsurgical approach of antibiotic therapy alone may also be considered.[11,86,87] Patients who received initial appendectomy (mostly open procedures), instead of antibiotics alone, experienced greater pain, a longer duration of sick leave from work, and more complications such as surgical site infections and delayed healing.[11] In addition, 27% of patients managed nonsurgically required an appendectomy within 1 year of their index hospitalization. In over 1,500 adults with appendicitis, antibiotics were found to be non-inferior to appendectomy at 30 days based on a quality of life questionaire.[87] However, complications were more common in the antibiotics groups and 29% required an appendectomy within 90 days. Similarly, a smaller randomized study also demonstrated that 27.3% of adult patients receiving antibiotics alone required an appendectomy within 1 year,[11] and 39.1% were at an increased risk of late recurrence of uncomplicated acute appendicitis within 5 years.[88] Conversely, another smaller randomized study found that adult patients who received a supportive care only for CT-confirmed uncomplicated appendicitis experienced similar treatment failure rates within 19 months compared to those who received 4 days of antibiotic therapy.[89] In children, nonoperative management of uncomplicated appendicitis with 7 days of antibiotics had a success rate of 67.1% and had significantly fewer disability days at 1 year compared to those who underwent surgery.[90] Despite these limitations, the risks and benefits of surgery versus antibiotics alone should be considered along with the patient's own preferences.

Treatment of diverticulitis varies based on disease severity. For mild, acute uncomplicated diverticulitis, antibiotics are not necessary with appropriate follow-up in immunocompetent adults[91]; however, if antibiotics are prescribed, amoxicillin/clavulanate or an oral cephalosporin with metronidazole is recommended.[92] Oral antibiotics (ciprofloxacin with metronidazole) are as effective as intravenous antibiotics for uncomplicated diverticulitis.[93] In adults who present with complicated diverticulitis with an abscess, antibiotics that cover gram-negative aerobic bacilli and anaerobes should be combined with drainage of the abscess; however, once source control is achieved, antibiotics are no longer needed. In immunocompromised adults, early elective resectional surgery is recommended due to the risk for early, frequent, and severe relapses of complicated acute diverticulitis managed with antibiotics alone. In general, 15% to 30% of patients admitted for management of acute diverticulitis required surgery during that admission.[94] When surgery is required, laparoscopic surgery is preferred to open colectomy due to shorter lengths of hospital stay, fewer complications, and lower in-hospital mortality.[95]

Acute intra-abdominal contamination, such as after a traumatic injury, may be treated with a short antimicrobial course (24 hours).[84] For established infections (ie, peritonitis or intra-abdominal abscess), an antimicrobial course limited to 4 days after source control is appropriate.[16,54] This allows eradication of bacteria remaining in the peritoneum after a surgical procedure that may enter the peritoneum through healing suture lines. Under certain conditions, therapy for longer than 4 days would be justified (eg, when the focus of infection in the abdomen is still present). For some abscesses, such as pyogenic liver abscess, antimicrobials may be required for a month or longer. If definitive source control is not possible, then a duration of 5 to 7 days of antibiotic therapy may be considered based on the patient's clinical stability including resolution or improvement in leukocytosis, fever, GI function.[16] These patients should be closely monitored for clinical worsening after cessation of antibiotics; a source control intervention may need to be reconsidered or antibiotics may need to be reinitiated.

Intraperitoneal irrigation of antimicrobial agents for the prevention of surgical site infection, abscess development, and other complications in patients with peritonitis has been studied; however, the quality of the data is limited and precludes a definitive determination of efficacy.[96,97] Possibly the most important aspect of peritoneal irrigation is the dilutional effect on bacteria and adjuvants that promote infection (intestinal contents and hemoglobin), and elimination of debris and gross contamination. Most systemically administered antimicrobials easily cross the peritoneal membrane so that peritoneal fluid concentrations are similar to serum. Confined areas, such as an abscess, can be expected to attain much lower antimicrobial concentrations. Given the unclear benefit of antibiotic irrigation, irrigation with crystalloid fluid alone is recommended.[16]

## EVALUATION OF THERAPEUTIC OUTCOMES

Whichever antimicrobial regimen is chosen, the patient should be reassessed continually to determine the success or failure of therapies. The clinician should recognize that there are many reasons for poor patient outcomes with intra-abdominal infections, improper antimicrobial administration is only one. The patient may be immunocompromised, which decreases the likelihood of successful outcome with any regimen. There may be surgical reasons for poor patient outcome. Failure to identify all intra-abdominal foci of infection or leaks from a GI anastomosis may cause continued infection. Finally, antimicrobial resistance may contribute to treatment failure as isolates from intra-abdominal infections are increasingly drug resistant.[49,98]

The outcome from intra-abdominal infection is not determined solely by what transpires in the abdomen. Unsatisfactory outcomes in patients with intra-abdominal infections may result from complications that arise in other organ systems, including renal or respiratory failure. Furthermore, pneumonia is a complication that is commonly associated with mortality after intra-abdominal infection.[99] Other nosocomial infections including catheter-related bacteremia and urinary tract infection are also independent predictors of mortality in patients with intra-abdominal infections.[100]

9 Once antimicrobials are initiated and the other important therapies described earlier are used, most patients should show improvement within 2 to 3 days. Usually, temperature will return to near normal, vital signs should stabilize, and the patient should not appear in distress, with the exception of recognized discomfort and pain from incisions, drains, and the nasogastric tube. Within 24 to 72 hours, aerobic bacterial culture results should return. If a suspected pathogen is not sensitive to the antimicrobial agents being given, the regimen should be changed to active therapy. If the isolated pathogen is susceptible to a narrower spectrum agent, therapy should be de-escalated.

With anaerobic culturing techniques and the slow growth of these organisms, anaerobes are often not identified until 4 to 7 days after culture. A report indicating that anaerobes were not isolated should not be the sole justification for discontinuing antianaerobic drugs because anaerobic bacteria that were present in the infectious process may not have been collected or maintained in anaerobic conditions which can lead to cell death in vitro.

Reasons for antimicrobial failure may not always be apparent. Even when antimicrobial susceptibility tests indicate that an organism is susceptible in vitro to the antimicrobial agent, therapeutic failures may occur. Possibly there is poor penetration of the antimicrobial agent into the focus of infection, or bacterial resistance may develop after initiation of antimicrobial therapy. In addition, it is possible that an antimicrobial regimen may encourage the development of infection by organisms not susceptible to the regimen being used. Superinfection in patients being treated for intra-abdominal infection can be caused by *Candida*; however, enterococci or opportunistic gram-negative bacilli such as *Pseudomonas* may be involved.

Treatment regimens for intra-abdominal infection can be judged as successful if the patient recovers from the infection without recurrent peritonitis or intra-abdominal abscess and without the need for additional antimicrobials. A regimen can be considered unsuccessful if a significant adverse drug reaction occurs, reoperation or percutaneous drainage is necessary, or patient improvement is delayed beyond 1 or 2 weeks. The costs of treatment can be significantly reduced if parenteral antimicrobials can be switched to oral agents for completion of therapy.[101]

## ABBREVIATIONS

| | |
|---|---|
| APACHE | acute physiology and chronic health evaluation |
| CAPD | chronic ambulatory peritoneal dialysis |
| CNS | central nervous system |
| CT | computed tomography |
| CVP | central venous pressure |
| ESBL | extended-spectrum β-lactamase |
| IDSA | Infectious Diseases Society of America |
| IL | interleukin |
| INF | interferon |
| KPC | *Klebsiella pneumoniae* carbapenemase |
| LD | loading dose |
| MAP | mean arterial pressure |
| MD | maintenance dose |
| MRSA | methicillin-resistant *Staphylococcus aureus* |
| SIS | Surgical Infection Society |
| TNF | tumor necrosis factor |
| WBC | white blood cell |

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## SELF-ASSESSMENT QUESTIONS

1. A patient presents with an abscess in the abdomen, most likely associated with a perforated diverticulum in the colon. Which of the following would be the most appropriate initial antimicrobial regimen?

   A. Ceftriaxone plus metronidazole

   B. Clindamycin

   C. Ampicillin–sulbactam

   D. Gentamicin plus metronidazole

2. Which of the following is the best choice for complicated intra-abdominal infections due to extended-spectrum β-lactamase-producing Enterobacterales?

   A. Tigecycline

   B. Sulfamethoxazole/trimethoprim

   C. Polymyxin B or Colistin

   D. Meropenem

3. The appropriate duration of antimicrobial treatment for acute contamination of the abdomen without established infection is:

   A. 24 hours or less

   B. 10 days

C. 3 days

D. 4-7 days

4. Which of the following would be considered optimal therapy for community-acquired acute cholecystitis?

A. Meropenem

B. Ciprofloxacin

C. Ceftriaxone

D. Cefepime

5. Identify the correct statement:

A. Mild-to-moderate community-acquired complicated intra-abdominal infections DO NOT require empiric coverage for *Enterococcus* spp.

B. Empiric coverage for methicillin-resistant *Staphylococcus aureus* is routinely required for healthcare-associated complicated intra-abdominal infections.

C. Empiric coverage for *Candida* spp. is routinely required for high-risk/severe community-acquired complicated intra-abdominal infections.

D. Empiric coverage for *Candida* spp. is routinely required for mild-to-moderate community-acquired complicated intra-abdominal infections.

6. In patients with primary peritonitis, bacteria may enter the abdomen via all of the following routes, except:

A. Through a cerebrospinal–peritoneal shunt

B. Through the damage done to the GI tract by blunt trauma

C. Through the bloodstream when there is no damage to the GI tract

D. Through a peritoneal dialysis catheter

7. Which of the following statements is false?

A. Antimicrobial regimens for secondary intra-abdominal infections should cover a broad spectrum of aerobic and anaerobic bacteria.

B. Antimicrobial treatment of acute bacterial contamination after trauma to the GI tract is adequately treated with an antianaerobic cephalosporin.

C. Most patients should not complete their antimicrobial regimen orally after an uncomplicated secondary intra-abdominal infection.

D. Four to 7 days of antimicrobial treatment is typically adequate for intra-abdominal infections with adequate source control.

8. The polymorphonuclear (PMN) leukocyte count from ascitic fluid consistent with bacterial peritonitis is:

A. >100 PMN/$mm^3$ ($0.1 \times 10^9$/L)

B. >250 PMN/$mm^3$ ($0.25 \times 10^9$/L)

C. >500 PMN/$mm^3$ ($0.5 \times 10^9$/L)

D. >1,000 PMN/$mm^3$ ($1.0 \times 10^9$/L)

9. Which of the following requires the empiric coverage of anaerobes?

A. Primary (spontaneous) bacterial peritonitis

B. Community-acquired acute cholecystitis

C. Mild-to-moderate community-acquired complicated intra-abdominal infection

D. Peritoneal dialysis-associated peritonitis

10. Which of the following regimens is reliably active against both Enterobacterales such as *E. coli* AND anaerobes such as *Bacteroides fragilis*?

A. Levofloxacin

B. Ceftriaxone plus metronidazole

C. Cefepime plus clindamycin

D. Ampicillin/sulbactam

11. Identify the incorrect statement regarding complicated healthcare-associated intra-abdominal infections in adults.

A. Microbiologic results and the patient's history of infecting organisms should guide empiric antibiotic therapy.

B. Ampicillin–sulbactam is appropriate for the treatment of complicated healthcare-associated, complicated intra-abdominal infections.

C. Piperacillin–tazobactam is appropriate for the treatment of healthcare-associated complicated intra-abdominal infections.

D. Ertapenem is appropriate for the treatment of complicated healthcare-associated intra-abdominal infections.

12. Which of the following organisms should be routinely treated empirically in patients with high-risk/severe community-acquired complicated intra-abdominal infection?

A. Vancomycin-resistant *Enterococcus* spp.

B. Methicillin-resistant *Staphylococcus aureus*

C. *Pseudomonas aeruginosa*

D. *Acinetobacter baumannii*

13. The most reasonable initial intraperitoneal empiric antimicrobial therapy for a 46-year-old male patient with peritoneal dialysis-associated peritonitis and a history of immediate hypersensitivity reaction (reaction occurred within the last year) to penicillin is:

A. Cefazolin plus ceftazidime (LD 500 mg/L, MD 125 mg/L for each)

B. Cefepime (LD 500 mg/L, MD 125 mg/L)

C. Vancomycin (LD 1,000 mg/L, MD 25 mg/L) plus tobramycin (LD 8 mg/L, MD 4 mg/L)

D. Metronidazole (LD 250 mg/L, MD 50 mg/L)

14. A 23-year-old woman who is not severely ill and is otherwise in good health is determined to have a perforated appendix. Which of the following is the best antimicrobial regimen for this patient?

A. Cefazolin plus vancomycin

B. Ceftriaxone plus metronidazole

C. Aztreonam plus vancomycin

D. Cefazolin plus gentamicin

15. The most important component of treatment of a perforated appendix is:

A. Using the best antimicrobial regimen

B. Aggressive IV fluid therapy

C. A surgical procedure, including drainage and repair

D. Enteral nutrition supplementation

## SELF-ASSESSMENT QUESTION-ANSWERS

1. **A.** Explanation: This patient presents with a community-acquired intra-abdominal infection and abscess. The most likely pathogens based on anatomical location, nature of infection are *Streptococcus*, anaerobes such as *Bacteroides*, and Enterobacterales. The only regimen that provides adequate empiric coverage for these is A. B is incorrect because it lacks both Enterobacterales and adequate *Bacteroide*s coverage. C is incorrect due to increasing rates of resistance among Enterobacterales. An aminoglycoside is unnecessary for this patient and carries significant toxicity risk, so D is incorrect.

2. **D.** Explanation: The drug of choice for extended-spectrum β-lactamase-producing Enterobacterales is typically carbapenems (D is correct). Tigecycline may be active; however, it should be reserved for patients who have no other therapeutic options given the potential for increased risk of toxicity and mortality with tigecycline. The polymyxins should also be reserved for patients with multidrug-resistant pathogens where no other agents are active. Sulfamethoxazole/trimethoprim is unlikely to be active given ESBL-containing plasmids usually display additional resistant genotypes including to sulfamethoxazole/trimethoprim and fluoroquinolones.

3. **A.** Explanation: For acute stomach and proximal jejunum perforations, in the absence of acid-reducing therapy or malignancy and when source control is achieved within 24 hours, prophylactic anti-infective therapy directed at aerobic gram-positive cocci for 24 hours is adequate. Furthermore, bowel injuries attributable to penetrating, blunt, or iatrogenic trauma that are repaired within 12 hours and any other intraoperative contamination of the operative field by enteric contents should be treated with antibiotics for ≤24 hours.

4. **C.** Explanation: *Streptococcus* and Enterobacterales coverage is required for this indication, ceftriaxone provides good coverage for both. Cefepime and meropenem are incorrect because *Pseudomonas* coverage is not needed. Ciprofloxacin is not ideal given a significant risk of Enterobacterales resistance and poor *Streptococcus* coverage.

5. **A.** Explanation: Answer B is incorrect, MRSA is an unlikely cause of complicated intra-abdominal infections thus should be only used in healthcare-associated, complicated intra-abdominal infections where specific MRSA risk factors are present. C and D are incorrect because empiric coverage for *Candida* should not routinely be used for complicated intra-abdominal infections. However, if *Candida* is isolated in appropriate culture, typically it should be treated.

6. **B.** Explanation: Peritonitis resulting from damage done to the GI tract from blunt trauma would be classified as secondary peritonitis.

7. **C.** Explanation: Oral therapy is reasonable for patients with uncomplicated secondary intra-abdominal infection as long as the regiment is likely or confirmed to be active.

8. **B.** Explanation: Ascitic fluid with >250/$mm^3$ ($0.25 \times 10^9$/L) PMN is suggestive of spontaneous bacterial peritonitis.

9. **C.** Explanation: Of the infections listed, only patients with complicated intra-abdominal infections require anaerobic coverage.

10. **B.** Explanation: Levofloxacin and ampicillin/sulbactam are less likely to be active empirically for Enterobacterales relative to ceftriaxone or cefepime. Levofloxacin also lacks significant *Bacteroides* coverage. Clindamycin does not have reliable *Bacteroides* coverage.

11. **B.** Explanation: Ampicillin/sulbactam lacks *Pseudomonas* coverage which is required in healthcare-associated complicated intra-abdominal infections. Ampicillin/sulbactam also has poor empiric activity for Enterobacterales.

12. **C.** Explanation: *Pseudomonas* should be routinely covered empirically in patients with high-risk/severe, community-acquired complicated intra-abdominal infection. VRE, MRSA, and *Acinetobacter* coverage is not routinely needed given the infrequency of those organisms in community-acquired disease.

13. **C.** Explanation: Initial empiric regimens for peritoneal dialysis-associated peritonitis should be active against both gram-positive (including *S. aureus*) and gram-negative pathogens including Enterobacterales and *Pseudomonas.* Cefepime monotherapy is reasonable empiric therapy; however, the patient's immediate hypersensitivity reaction to penicillin precludes cefepime use. Response A is also incorrect for the same reason and furthermore using two cephalosporins at the same time is suboptimal. Metronidazole only covers anaerobes which are not likely to be causative of this syndrome. The only other option that has the required spectrum and is safe given the patient's allergy history is response C.

14. **B.** Explanation: Patients presenting from the community with perforated appendix where antibiotic therapy is used can receive the same treatment as those complicated intra-abdominal infection (in her case mild/moderate severity, answer B is correct).

15. **C.** Explanation: Uncomplicated appendicitis (defined as the absence of perforation, abscess, appendicolith, CT consistent with possible tumor, peritonitis, severe systemic illness) may be treated nonsurgically, with antibiotics alone. However, if perforated, drainage and repair is required to decrease morbidity (answer C is correct). Fluids, enteral nutrition, and even antibiotic therapy are less important relative to source control in patients with perforated appendicitis.