Intra-abdominal and Pelvic Emergencies

Sushma Singh, MDa, Nancy Misri Khardori, MD, PhDab,*

KEYWORDS
• Intra-abdominal emergencies • Pelvic emergencies • Intra-abdominal infections • Peritonitis

KEY POINTS
• The presence of peritoneal reflections and mesenteric attachments leads to compartmentalization of the intraperitoneal space and the potential of spreading exudates to sites distant from the source.
• Intra-abdominal infections can masquerade as a fever of obscure origin or as dysfunction of neighboring organs, such as lower lobe pneumonia related to a subphrenic abscess or an abscess causing small bowel obstruction.
• The most common features of an intra-abdominal infectious process are diffuse or localized pain and fever.

INTRA-ABDOMINAL INFECTIONS
Introduction
The abdominal/pelvic cavity has been labeled as a Pandora’s box. The diversity in intra-abdominal/pelvic infections is more than any other organ system. The peritoneal cavity has a large surface area extending from the undersurface of the diaphragm to the pelvic floor. The peritoneal cavity is a closed space in males. In females, the free ends of the fallopian tubes open into the peritoneal cavity. Because of the presence of many dependent recesses, pouches, and paracolic gutters in the peritoneal cavity, loculation followed by abscess formation is common. The presence of peritoneal reflections and mesenteric attachments leads to compartmentalization of the intraperitoneal space and the potential of spreading exudates to sites distant from the source. In addition, abscesses can form in the intra-abdominal/pelvic organs, such as the liver, spleen, pancreas, and ovaries/fallopian tubes.1

a Division of Infectious Diseases, Department of Internal Medicine, Eastern Virginia Medical School, 825 Fairfax Avenue, VA 23507, USA; b Department of Microbiology and Cell Biology, Eastern Virginia Medical School, 825 Fairfax Avenue, Norfolk, VA 23507, USA
* Corresponding author. Division of Infectious Diseases, Department of Internal Medicine, Eastern Virginia Medical School, 700 West Olney Road, Norfolk, VA 23507.
E-mail address: nkhardori@gmail.com

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Several clinical scenarios can end up in intra-abdominal abscesses. The common causes include penetrating abdominal trauma, abdominal surgery, diverticulitis, appendicitis, pancreatitis, biliary disease, perforated viscus, and primary peritonitis. Intra-abdominal infections can masquerade as fever of obscure origin or as dysfunction of neighboring organs, such as lower lobe pneumonia related to a subphrenic abscess or an abscess causing small bowel obstruction. An urgent surgical intervention is the mainstay of management of serious intra-abdominal infections.

The most common features of an intra-abdominal infectious process are diffuse or localized pain and fever. However, the presentation can be atypical in the elderly and in the immunocompromised host; therefore, the index of suspicion for a significant intra-abdominal process should be high in these patients even though they are afebrile. It is also important to remember that the pain from an abdominal process can be referred to a distant site, such as gall bladder pain referred to the right shoulder.

The causes of intra-abdominal pain are listed in Boxes 1 and 2 (reviewed from).

**SECTION A: PERITONITIS**

### Acute Peritonitis

Because of the large surface area, dependent recesses, pouches, and paracolic gutters created by reflections of the peritoneal membrane, it is highly likely to get infected from diverse sources. Inflammation of the peritoneum, diffuse or localized, can result from infections; irritating chemicals (like bile); carcinomatosis; foreign-body reaction, such as talc peritonitis; connective tissue disorders, such as systemic lupus erythematosus; and diseases of unknown cause, such as familial Mediterranean fever.

Infectious peritonitis is categorized as primary, secondary, or tertiary. In primary peritonitis, there is no known intra-abdominal or distant source. In secondary peritonitis, an intra-abdominal process, such as a ruptured appendix or a perforated peptic ulcer, is the cause. Tertiary peritonitis is defined as late-stage disease whereby the infection persists or recurs after treatment of secondary peritonitis. In such cases, microbiological diagnosis is difficult because it is usually associated with the presence of low-grade pathogens (e.g., coagulase-negative staphylococci) or nosocomial pathogens. The direct correlation of such culture results with the ongoing infectious process is difficult.

### Box 1

**Gastrointestinal causes**

1. Esophageal: gastroesophageal reflux disease, esophagitis (candida, herpes simplex virus, eosinophilic), perforation, spasm
2. Gastric: foreign-body ingestion, peptic ulcer disease, acute gastritis
3. Biliary: acute cholecystitis, cholangitis, gall bladder or common bile duct stone
4. Hepatic: hepatitis (viral, alcoholic, autoimmune), pyogenic liver abscess, hepatocellular carcinoma causing hemorrhage/infarct
5. Pancreatic: acute or chronic pancreatitis, pancreatic cancer
6. Small bowel: small bowel obstruction, mass, celiac disease
7. Large bowel: diverticulitis, acute appendicitis, inflammatory bowel disease, volvulus, obstruction either by malignancy or ileus, constipation
Primary Peritonitis/Spontaneous Bacterial Peritonitis

Spontaneous bacterial peritonitis (SBP) is the most frequent and life-threatening infection in patients with cirrhosis. It is defined by the presence of more than 250 polymorphonuclear cells (PMN) per microliter in ascitic fluid in the absence of an intra-abdominal focus of infection or malignancy. Among hospitalized patients with cirrhosis and ascites, SBP is diagnosed in 10% to 30%. The risk of SBP is increased in patients with cirrhosis with a low ascitic fluid protein level (1 g/dL or lower) and in patients with gastrointestinal hemorrhage. In a small number of patients, the ascitic fluid has bacteria but no PMN. Such cases may be an early stage peritonitis, with PMN appearing 2 to 3 days later, or bacteria may simply have translocated without causing infection. Cirrhosis complicated by SBP has a bad prognosis, with a 1-year mortality of 31% to 93%. The in-hospital mortality of a first episode is 10% to 50%.

Pathophysiology

Except for a small number of cases caused by transient bacteremia, most cases of SBP are caused by translocation of bacteria from the gastrointestinal tract. Bacterial translocation in cirrhosis occurs because of (1) alterations in gut microbiota, (2) increased intestinal permeability, and (3) impaired peritoneal immunity.

Microbiology

Most cases of SBP (>90%) are monomicrobial. Enteric organisms are the most common, accounting for 69% of pathogens. *Escherichia coli* is the most frequently recovered pathogen, followed by *Klebsiella pneumoniae*, *Streptococcus pneumoniae*, other streptococcal species, and enterococci. Peritonitis caused by *Mycobacterium tuberculosis*, *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, or *Coccidioides immitis* is uncommon and usually the result of a disseminated infection or sometimes spread from the adjacent foci of infection.

Recently, enterococci have been grown in 11% to 35% of cases of SBP. Prior antibiotic therapy and nosocomial acquisition were shown to be independent risk factors.
for enterococcal SBP. The 90-day survival was worse in enterococcal SBP (12%) compared with non- enterococcal (50%) infection.11

The frequent use of primary antibiotic prophylaxis and multiple hospitalizations and procedures has led to an increase in multiresistant organisms in SBP. Fig. 1A, B shows the distribution of pathogens in community-acquired and nosocomial SBP (see Fig. 1).12

Fig. 1. (A) Microorganisms seen in community acquired spontaneous bacterial peritonitis (SBP). (B) Microorganisms seen in hospital acquired SBP. TP, Treatment period; MRSA, Methicillin-resistant Staphylococcus aureus; ESBL, Extended-spectrum beta-lactamase. (Reproduced from Jafferbhoy HM et al. Spontaneous bacterial peritonitis prophylaxis in the era of healthcare associated infection. Gut. November 2012, Vol 61; No. 11: 1644–5; with permission.)
Clinical manifestations
Typically, patients present with fever, abdominal pain, nausea, vomiting, and diarrhea and have diffuse and rebound abdominal tenderness on examination. Bowel sounds are hypoactive or absent. However, atypical presentations are common with insidious onset and the absence of findings of peritoneal irritation. In stable patients with chronic liver disease, SBP should always be in the differential diagnosis when decompensation occurs.

Occasionally, gonococcal perihepatitis (Fitz-Hugh–Curtis syndrome) and tuberculous peritonitis present as insidious-onset primary peritonitis.

Diagnosis
Paracentesis is the diagnostic method of choice for SBP with the presence of PMN at greater than 250 PMN per microliter. However, a cutoff of 500 PMN per microliter is reported to have the best specificity. It is important to use a large volume (10–20 mL) of ascitic fluid for cultures and preferably inoculate them at the bedside. These fluids increase the yield of the cultures because the number of bacteria in the ascitic fluid is usually low.

In typical SBP, cultures are positive and the PMN count is greater than 250/μL. When the cultures are positive and the PMN count is less than 250/μL, the syndrome is called bacterascites. In contrast, ascitic fluid with negative culture but a higher PMN of 500/μL or more is called culture negative neutrophilic ascites (CNNA). CNNA and SBP are managed identically. Bacterascites formed of SBP can be self-limited and managed with careful observation and repeat paracentesis after 48 hours.

Treatment
Cefotaxime and similar third-generation cephalosporin antibiotics are as efficacious as the combination of ampicillin plus an aminoglycoside for presumptive therapy for primary bacterial peritonitis. Alternate choices include broad-spectrum penicillins (eg, ticarcillin and piperacillin); carbapenems (eg, imipenem, meropenem, doripenem, and ertapenem); β-lactam/β-lactamase combinations (eg, piperacillin-tazobactam, ticarcillin-clavulanate, and ampicillin-sulbactam); and the newer fluoroquinolones, such as levofloxacin and moxifloxacin. A 5-day therapy has been shown to be effective; however, most patients are treated for 10 to 14 days.

Prevention
Primary prophylaxis using trimethoprim-sulfamethoxazole (TMP-SMX) or oral fluoroquinolones has been commonly used in recent years. The recurrence rate after the first episode of SBP is 43% in 6 months and 69% in 1 year. Primary prophylaxis is recommended in patients with cirrhosis who have had upper gastrointestinal bleeding and/or have ascitic fluid albumin less than 1.5 g/L. Norfloxacin 400 mg/d, ciprofloxacin 750 mg/wk, and TMP-SMX (one double-strength dose given once daily for 5 days each week) are the agents used commonly and are equally efficacious.

Of note is the finding that a Clostridium difficile infection is more common in patients receiving quinolones for prophylaxis. A retrospective review of 404 patients with cirrhosis and ascites showed that rifaximin caused a 72% reduction in SBP compared with no antibiotic prophylaxis. Rifaximin also increased the time to transplant survival.

Secondary Peritonitis
Secondary peritonitis is caused by spillage of a gastrointestinal or genitourinary microorganism in to the peritoneal cavity because of a breach in the mucosal barrier, such
as perforated appendicitis, perforated diverticulitis, cholecystitis, and perforated peptic ulcer.

**Microbiology**
In contrast to primary peritonitis, most cases of secondary peritonitis are polymicrobial. The pathogens in secondary peritonitis are a reflection of existing gastrointestinal flora. The common pathogens are members of Enterobacteriaceae (*E. coli*, *Proteus mirabilis*, *K. pneumoniae*); various streptococci and enterococci; and anaerobic organisms, such as the *Bacteroides fragilis* group, *Peptococci*, and *Peptostreptococci*. Bacteremia commonly caused by *E. coli*, *Bacteroides* spp, or both occurs in 20% to 30% of patients.\(^\text{16}\)

**Clinical manifestation and diagnosis**
Clinical manifestations include fever, abdominal pain and tenderness, abdominal distention, and leukocytosis. Free air under the diaphragm may be seen on a plain radiograph of the abdomen in the presence of a perforated viscus. A computed tomography (CT) scan usually shows free fluid or gas in the peritoneum, which, in association with a compatible clinical picture, confirms the diagnosis.

**Management**
Prompt surgical intervention is required in patients with a perforated viscus or intra-abdominal abscess for source control, debridement, and the prevention of recurrent soilage.

Table 1 lists the likely pathogens, first-line agents, and alternate agents for the antimicrobial therapy for secondary peritonitis and other intra-abdominal infections. The spectrum of activity should include aerobic and anaerobic gram-negative bacilli as well as gram-positive pathogens, like enterococci.\(^\text{17}\)

**SECTION B: INTRA-ABDOMINAL ABSCESSES**

**Intraperitoneal Abscess**

**Anatomy**
Intraperitoneal abscesses locate themselves to the site of the primary disease and progress in the direction of dependent peritoneal drainage. Appendicitis is associated with right lower quadrant and pelvic abscesses, and colonic diverticulitis is associated with left lower quadrant and pelvic abscesses. Pancreatitis causes abscesses within the lesser sac.

A case series of 267 patients with intra-abdominal abscesses revealed the location to be in the subphrenic space in about 50%, more than half of which were in the left perihepatic space.\(^\text{18,19}\)

**Microbiology**
The predominant bacteria in intra-abdominal infections are gram-negative aerobic and anaerobic bacilli, streptococci, and enterococci. The most common isolates in most series are the *B. fragilis* group and *E. coli*.\(^\text{20,21}\)

Intra-abdominal abscesses are often polymicrobial, with at least 5 to 6 organisms isolated in most series. The presence of anaerobic bacteria is assumed even though they may not grow in culture.\(^\text{22}\) The presence of certain organisms in abscesses can indicate the area of origin of infection; for example, *Citrobacter* species strongly suggests a biliary or upper gastrointestinal source; *Staphylococcus aureus* suggests hematogenous source. An *S. aureus* intra-abdominal abscess, particularly in retroperitoneal or perinephric locations, is also associated with vertebral osteomyelitis.
A perforation of the colon is likely to lead to the presence of Candida species in the abscess in addition to bacteria.

In patients who have received prior antibiotic therapy, the changed enteric flora to the selection processes can be seen in abscesses. In such situations, more resistant enteric bacteria, Enterococcus faecium, are more likely. This phenomenon is clearly demonstrated by a case report of abdominal abscess caused by recently described NDM-1–producing K pneumoniae in Spain after receiving treatment of appendicitis in India.

Pathogenesis
A breach in the normal gastrointestinal mucosal defense barrier is the initial event that allows entry of the gastrointestinal flora into the peritoneal cavity. This breach can be macroscopic, such as perforations, or microscopic, leading to transmigration of microorganisms. A diffuse peritonitis is followed by localization, usually in the pelvis, perihepatic spaces, and paracolic gutters. In addition, abscesses may develop around diseased organs, such as peripendiceal, pericholecystic, and perinephric abscesses. Penetrating trauma caused by stabbing, gunshots, motor vehicular accidents, other trauma, or surgical interventions also leads to intra-abdominal/pelvic abscess formation.

Clinical manifestation and diagnosis
The general clinical features of an intra-abdominal abscess include those seen in other acute infectious processes, such as intermittent high-grade fever, shaking, and chills, with abdominal pain and tenderness over the involved area. In undiagnosed patients, hypotension and septic shock may be presenting features. Unfortunately, this acute course is modified by prior antibiotics and may lead to misdiagnosis. The presence of leukocytosis with or without left shift is common; however, in the elderly, left shift may be present without the leukocytosis.

Plain radiography is helpful in locating the abscess in about 50% of patients. The findings include free air in the peritoneal cavity, air-fluid levels caused by loculated abscess, displaced loops of bowel by an abscess, and the so-called soap-bubble appearance, loss of the normal psoas shadow.

Ultrasound and CT are much more sensitive and specific than plain radiography. Ultrasonography is a noninvasive and readily available technique that is helpful in determining the size, shape, consistency, and anatomic relationship of intra-abdominal abscesses. The limitations of ultrasound are interference by overlying gas-filled viscera, ileus, postoperative wounds, and the presence of drains. The CT scan is now considered the radiographic method of choice for the evaluation of intra-abdominal abscesses, with specificity and sensitivity exceeding 90%. Contrast material is commonly administered orally and intravenously to better define the size and location of the abscess. The superiority of the CT scan lies in its ability to detect extraluminal gas, which is highly suggestive of an abscess.

At this point, magnetic resonance imaging has not been shown to add significantly to the diagnostic value of the CT scan.

Treatment
The mainstay of treatment of any intra-abdominal abscess is drainage either surgical or percutaneous. The mortality rate in undrained abdominal abscesses ranges between 45% and 100%. The advantage of percutaneous drainage lies in its noninvasive nature compared with surgical intervention. Ultrasound- or CT-guided drainage makes it even safer.
### Table 1
Antimicrobial treatment of various intra-abdominal infections

<table>
<thead>
<tr>
<th>Infections</th>
<th>Common Microorganism</th>
<th>First-Line Antimicrobial Therapy</th>
<th>Second-Line Antimicrobial Therapy in Case of Allergy/Intolerance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Intra-abdominal abscesses and secondary peritonitis^a</td>
<td>Gram negative aerobic and anaerobic bacilli, streptococci, enterococci (most common <em>E. coli</em> and <em>B. fragilis</em> group)</td>
<td>β-lactam/β-lactamase inhibitor combinations, like ampicillin-sulbactam, ticarcillin-clavulanic acid, piperacillin-tazobactam or Carbapenem, like imipenem, meropenem, doripenem or Tigecycline</td>
<td>Fluoroquinolones, like moxifloxacin, levofloxacin, and ciprofloxacin, plus metronidazole or Aztreonam plus metronidazole</td>
</tr>
<tr>
<td>2. Intra-abdominal infection/secondary peritonitis with history of previous hospitalization or antibiotic exposure^a</td>
<td>Aforementioned organisms plus <em>Pseudomonas aeruginosa</em>, <em>S. aureus</em>, vancomycin-resistant enterococci</td>
<td>Carbapenems plus aminoglycoside plus vancomycin or linezolid</td>
<td>Aforementioned agents plus aminoglycoside and vancomycin or linezolid</td>
</tr>
<tr>
<td>3. Cholecystitis and cholangitis</td>
<td>Gram-negative aerobic and anaerobic bacilli, streptococci, <em>Enterococci</em>, salmonella</td>
<td>β-lactam/β-lactamase inhibitor combinations, like ampicillin-sulbactam, ticarcillin-clavulanic acid, piperacillin-tazobactam or Carbapenem, like imipenem, meropenem, doripenem or Tigecycline</td>
<td>Fluoroquinolones plus metronidazole</td>
</tr>
</tbody>
</table>

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| 4. Pyelonephritis and perinephric abscesses | Enteric gram-negative bacteria, including, \textit{E coli}, \textit{K pneumonia}, \textit{P mirabilis} | Fluoroquinolones, like levofloxacin, ciprofloxacin or \(\beta\)-lactam/\(\beta\)-lactamase inhibitor combinations, like piperacillin-tazobactam or Third-generation cephalosporin, like ceftriaxone | Aminoglycoside, like gentamycin, tobramycin or Trimethoprim/sulfamethoxazole |

| 5. Infectious colitis | \textit{C difficile} | Oral metronidazole or Oral vancomycin (in severe cases can use oral vancomycin with IV metronidazole) | Fidaxomicin (recently FDA approved) or Rifaximin or Fecal transplant |
| | \textit{Salmonella} (non-typhi) | Fluoroquinolones, like ciprofloxacin, levofloxacin, moxifloxacin or Third-generation cephalosporins, like ceftriaxone | Trimethoprim/sulfamethoxazole or Macrolide, like azithromycin |
| | \textit{Campylobacter} | Macrolides like erythromycin | Fluoroquinolones like ciprofloxacin (increasing resistance documented) |
| | \textit{Entamoeba histolytica} | Metronidazole or tinidazole followed by paromomycin or diloxanide furoate or iodoquinol |

\textit{Abbreviation:} FDA, Food and Drug Administration.

\(^a\) In case of perforated viscus antifungal therapy with either fluconazole or echinocandins should be considered for \textit{Candida} spp.
Ultrasound provides real-time imaging and it is the method of choice for the relatively superficially located and unilocular abscesses, where there is little risk of transgressing a vascular structure, bowel, or pleural cavity. The combined use of fluoroscopy and ultrasound allows precise positioning of the drainage catheter with an increase in both the safety and effectiveness of the procedure. Ultrasound is particularly useful for transrectal or transvaginal drainage procedures.\(^{31}\) Successful drainage is indicated by improvement in the clinical picture and collapse of the abscess cavity on repeat scanning. However, complications can occur, such as hemorrhage, spillage, fistula formation, and inadequate drainage of the abscess through the catheter caused by viscosity of the pus. Surgical intervention is indicated for these complications.

The concomitant use of early, aggressive, and appropriate antimicrobial therapy, after taking initial blood cultures, improves the outcome in abdominal abscesses, especially in patients who present with sepsis syndrome. While awaiting culture results, the presumptive antibiotic choices are the same as for acute peritonitis (ie, polymicrobial coverage for aerobic and anaerobic gram negative bacilli [see Table 1]). Several recent randomized controlled trials have shown that conservative antibiotic treatment of acute appendicitis without abscess formation is comparable with early surgical intervention. However, a recurrence rate of 14% within 12 months was observed.\(^{32,33}\)

**RETROPERITONEAL ABSCESSES**

The source of retroperitoneal infections is either an organ contained outside the peritoneum or retroperitoneal extension, such as in retrocecal appendicitis, perforated duodenal ulcers, pancreatitis, and diverticulitis. The large area and rather nondiscrete boundaries of the retroperitoneum allow some retroperitoneal abscesses to become large before being recognized.\(^{34}\)

In addition to systemic signs of infection and pain, erythema may be observed around the umbilicus (similar to the Cullen sign seen in retroperitoneal hemorrhage) or flank (Gray Turner sign seen in retroperitoneal hemorrhage). The diagnostic imaging modality of choice is the CT scan, which may demonstrate stranding of the retroperitoneal soft tissues and/or unilocular or multilocular collections.\(^{34}\) Treatment is usually percutaneous drainage and broad-spectrum antimicrobial therapy, as in the case of intra-abdominal abscesses (see Table 1).

**VISCERAL ABSCESSES**

**Liver Abscess**

Pyogenic liver abscess can develop by the extension of biliary tract infection, portal bacteremia from intra-abdominal septic foci, and systemic bacteremia. Less common causes include direct extension from a contiguous site of infection, complication of abdominal surgery, trauma, complication of hepatocellular carcinoma, or percutaneous transhepatic biliary drainage procedures in patients with cancer and obstructive jaundice.\(^{35-37}\)

Like the intra-abdominal abscesses, liver abscesses are usually polymicrobial. A liver abscess caused by \textit{S} aureus is usually associated with bacteremia.

Fever, chills, abdominal pain, and leukocytosis are common in patients with liver abscesses. A liver abscess can rupture and cause acute peritonitis and sepsis syndrome. A CT scan is the most optimal diagnosis modality. In the presence of epidemiologic risk factors, an amoebic liver abscess caused by \textit{Entamoeba histolytica} should be included in the differential diagnosis. Amoebic liver abscess is usually
solitary and confined to the right lobe of the liver. Serologic studies are highly sensitive and specific.

Treatment is usually percutaneous drainage along with broad-spectrum antibiotic therapy, as in acute peritonitis and intra-abdominal abscess (see Table 1). If metronidazole is not a part of the chosen regimen, it should be added in patients with suspicion of amoebic liver abscess.

**Splenic Abscess**

Splenic abscesses are often a result of bacteremia. The risk factors include hemoglobinopathy, splenic infarction, trauma, and immunosuppression. Fever and chills and left upper quadrant pain are common manifestations. CT scan and ultrasonography are equally useful. Percutaneous drainage and antimicrobial therapy should both be used unless drainage is considered unsafe. Initial antibiotic therapy should include vancomycin for *S aureus* (both methicillin susceptible and resistant) and broad-spectrum gram-negative agents, like piperacillin plus tazobactam, meropenem, and doripenem. Once the organism causing bacteremia is identified, therapy should be directed to the pathogen based on susceptibility result.

**SECTION C: GALL BLADDER AND BILIARY TRACT INFECTION**

**Acute Cholecystitis**

Acute inflammation of the gallbladder is most commonly caused by the obstruction of the cystic duct from gallstones or biliary sludge and occurs in 1% to 3% of people with symptomatic gallstones.

**Pathogenesis**

Obstruction leads to increased intraluminal pressure with compromise of blood supply and lymphatic drainage, which, along with the presence of supersaturated bile lead, to acute inflammation. Infection complicates 20% to 50% of acute cholecystitis cases. Complications that follow infection include gangrenous cholecystitis, emphysematous cholecystitis (a life-threatening complication in elderly patients with diabetes), gallbladder empyema, pyogenic liver abscess, and bacteremia.

Acalculous cholecystitis accounts for a minority (<15%) of patients with acute cholecystitis. It is usually seen in critically ill patients, such as severe trauma, burns, sepsis syndrome, immunosuppression, extensive surgery, and human immunodeficiency virus infection. It is difficult to diagnose, and the mortality rate is high. Acute gangrenous cholecystitis is a medical and surgical emergency estimated to complicate about a fourth of cases of acute cholecystitis. The mortality rate for this complication is 15% to 40%. Gangrenous cholecystitis occurs in elderly men with cardiovascular disease, patients with diabetes, those with multiple medical comorbidities, and trauma. It is thought to arise from acute cholecystitis complicated by infection, inflammation, bile stasis, and ischemia leading to gallbladder necrosis and perforation. Asymmetric gallbladder wall thickening, absence of gallbladder stones, impairment of gallbladder wall perfusion on color Doppler, and air within the gallbladder wall are all suggestive of acute gangrenous cholecystitis. The treatment is urgent cholecystectomy. Percutaneous cholecystostomy is an alternative in severely ill patients with significant surgical risk.

**Clinical manifestation and diagnosis**

The most common presentation is pain in the right upper quadrant with or without radiation to the infrascapular region, which is continuous in nature as compared with biliary colic. The presence of a Murphy sign (tenderness on palpation of gallbladder
fossa exacerbated by deep inspiration), with or without a palpable mass, is highly suggestive of biliary tract disease. In addition, systemic signs of infection, fever, tachycardia, and leukocytosis are common. Alkaline phosphatase and bilirubin are only elevated when common bile duct is obstructed.44

**Imaging studies**
Cholescintigraphy (hepatobiliary iminodiacetic acid [HIDA] scanning) has a sensitivity of 96% for the diagnosis of acute cholecystitis compared with 81% for ultrasonography and 85% for magnetic resonance imaging. The specificity for the 3 diagnostic modalities is 90%, 83%, and 81%, respectively. The CT scan has a sensitivity of 94% and specificity of 59%. These data make the HIDA scan the imaging modality of choice for acute cholecystitis.45

**Microbiology**
Bacterial cultures from the bile and surgical sites in patients with acute cholecystitis and acute cholangitis typically yield the members of the normal intestinal flora, which include aerobic and anaerobic gram-negative bacilli and enterococci. Parasites can cause relapsing cholangitis in Asia.46

**Treatment**
Treatment is aimed at the removal of obstruction, either surgically or endoscopically, such as endoscopic retrograde cholangiopancreatography (ERCP). Percutaneous drainage is used for patients who are not stable for a surgical or endoscopic approach. The presumptive antimicrobial therapy is directed against polymicrobial enteric flora and is similar to that in peritonitis and intra-abdominal abscess (see **Table 1**).

**Acute Cholangitis**
Cholangitis refers to inflammation and/or infection of the common bile duct. Obstruction of the common bile duct leads to biliary stasis, which favors the growth of bacteria and increased pressure predisposes to bacteremia. Bacteria may then ascend along the biliary tract (hence, the terms ascending and suppurative cholangitis).

Acute cholangitis is suggested by Charcot triad of the right upper quadrant or epigastric abdominal pain, fever or chills (or both), and jaundice, which is reported in 50% to 70% of patients. The addition of hypotension and altered mental status to Charcot triad constitute Reynolds pentad, which is seen in less than 14% of patients with ascending cholangitis.47

In addition to leukocytosis, routine laboratory studies show cholestatic liver function tests with elevations in alkaline phosphatase, $\gamma$-glutamyl transpeptidase, and bilirubin (particularly conjugated bilirubin). Amylase and transaminases may also be elevated. Treatment consists of the decompression of the biliary tract and antibiotic therapy in addition to supportive measures. Antibiotic choices are the same as for other intra-abdominal infections (see **Table 1**). ERCP is the procedure of choice for biliary decompression and is successful in 90% of the cases. Despite the advances in diagnosis and management, acute cholangitis continues to be associated with high mortality.48

**SECTION D: INFECTIOUS COLITIS**

**Infectious Colitis**
Inflammation of colonic mucosa can be caused by inflammatory bowel disease (IBD), ischemia/necrosis, irradiation, or infection. Infectious causes of colitis are diverse. A recent study from the National Commission for Digestive Diseases reported that the rate of age-adjusted hospitalizations from gastrointestinal infections increased by 92.8% between 1979 (76.1 per 100 000) and 2004 (146.7 per 100 000).49 Infectious
colitis is defined as bacterial invasion and infiltration into the mucosa resulting in an acute inflammation leading to the disruption of the mucosal barrier. The presence of mucus, red blood cells, and white blood cells in the stool is a correlate of mucosal inflammation.

Common causes of infectious colitis include nontyphoid *Salmonella* (NTS), *Shigella*, *Campylobacter*, enterohemorrhagic *E coli* (EHEC), *E histolytica*, *C difficile*, and *Cytomegalovirus*.50

**Salmonella**

*Salmonella* enterocolitis is characterized by fever, cramping, abdominal pain, and diarrhea that start 8 to 48 hours after ingestion of an infectious dose. Symptoms generally last for 3 to 5 days. The source of infection is usually contaminated food. In addition to colitis, ulcerations of the colonic mucosa with erosion and crypt abscess formation can occur. *Salmonella* usually involves the small bowel. Colonic involvement results in blood and white blood cells in the stool. *Salmonella enterica* serovar typhi-murium is the most common serotype causing food-borne gastroenteritis in the United States.50

Major food sources are contaminated meat and poultry products. In 2 recent foodborne outbreaks of NTS reported in the United States, contaminated imported jalo-peno and serrano peppers from Mexico in 2008 and peanut butter in 2009 were the source.51 IBD, as a late complication following Salmonella or Campylobacter infection, is reported in a population-based cohort study.52 Most cases of salmonella enteritis/colitis do not require antimicrobial therapy. Severely ill patients and those with risk factors for developing extraintestinal spread should be treated with fluoroquinolones or third-generation cephalosporins.

**Shigella**

Shigellosis as a cause of infectious colitis is responsible for 10% to 20% of cases worldwide. More than 200 million infections and 650 000 deaths are reported each year are.53 *Shigella* species produce a potent toxin (Shiga toxin) with enterotoxic, cytotoxic, and neurotoxic properties. They are invasive pathogens causing acute bloody dysentery with abdominal pain and systemic manifestations of fever, malaise, and headache. The incubation period is usually less than 72 hours but may range from 6 hours to 9 days.

Antibiotic treatment of shigella infections is recommended for most cases. It causes marked symptomatic improvement within 48 hours and reduces the average duration of illness to 3 days. Consequently, antibiotic treatment also reduces the period of presence of *Shigella* in the stool and, therefore, secondary transmission.54

Shigella dysentery is complicated by Reiter syndrome after 2 to 5 weeks of illness in up to 10% of patients. Patients with histocompatibility antigen HLA-B27 are at the highest risk.

**Campylobacter**

*Campylobacter* causes 14% of infectious diarrhea worldwide. In a recent study from Sweden, *Campylobacter jejuni* was isolated in 56% patients with colitis.55 *C jejuni* and *Campylobacter coli* are the most prevalent species causing enteric infections. The sources of infection include contaminated water, raw milk, and uncooked meat and poultry. In contrast to *Salmonella* and *Shigella*, *Campylobacter* lacks plasmid-promoting bacterial invasion and classical enterotoxins. *C jejuni* disrupts the mucosal barrier by invading and replicating in infected epithelial cells via Toll-like receptors (TLR-2 and TLR-4). *Campylobacter* infection increases the risk of postinfectious
irritable bowel syndrome and is associated with IBD. The sequelae of Campylobacter infection also include reactive arthritis and Guillain-Barré syndrome. Most patients with mild to moderate C jejuni enterocolitis do not need antibiotic treatment. Antibiotic therapy is beneficial for severely ill patients. Macrolides and fluoroquinolones are the antibiotics of choice. However, increasing resistance to fluoroquinolones is being reported.

**EHEC**

EHEC is one of the common causes of infectious colitis in the Western world, including the United States. EHEC (serotype O157) producing a Shiga-like toxin is estimated to account for 15% to 36% of bloody diarrhea and 75% to 90% of hemolytic uremic syndrome (HUS) in North America. HUS develops in 8% of EHEC infections.

The usual incubation period after ingestion of contaminated food or water is 3 to 4 days. The common sources of infection include undercooked beef, raw milk, or other products contaminated by the intestinal contents of cattle. Contaminated water is a less likely source of infection. The symptoms are abdominal cramps and watery diarrhea followed by bloody diarrhea. HUS and thrombocytopenia can occur 2 to 4 days after the onset of diarrhea, especially in children younger than 5 years and in older adults, respectively. Antibiotic therapy has not been shown to be effective for disease caused by EHEC and may increase the frequency of HUS.

**E histolytica**

E histolytica causes diarrhea/dysentery in developing countries of Central and South America, Africa, and the Indian subcontinent. An estimated 40 000 to 100 000 people die annually of amebiasis, making this disease only second to malaria as a cause of death from parasitic diseases.

E histolytica cysts are ingested, resist the gastric acid pH, and undergo digestion of the capsule in the small bowel. The released trophozoites cause invasion of the colonic mucosa and produce shallow, flask-shaped, undermining ulcers. The trophozoites may then seed the liver via the portal vein with possible extension to the diaphragm, lung, or pericardium. Dissemination is more common in patients with malnutrition, during late pregnancy, and patients on steroid and cytotoxic medications. Asymptomatic cyst carriage has been reported in 1% to 5% of the population in the Southern United States. The presence of trophozoites in the stool is diagnostic of infection.

A commercially available enzyme-linked immunosorbent assay (ELISA) is able to identify E histolytica antigens in stool. Serologic methods are also available for diagnosis. The molecular diagnostic techniques are in research at this time.

The mainstay of treatment is nitroimidazole derivatives, such as metronidazole, tinidazole, and ornidazole, for amoebic colitis as well as amoebic liver abscess. Surgical drainage is avoided in uncomplicated cases. A luminal active agent, such as diloxanide furoate, paromomycin, and iodoquinol, is used to eradicate colonization by the cysts.

**C difficile**

C difficile is an anaerobic spore forming gram-positive bacillus commonly found in the environment. C difficile infection (CDI) is defined as the presence of diarrhea (≥3 unformed stools in a 24-hour period) and toxin A or B (or both) or toxigenic C difficile in the stool. Pseudomembranous colitis associated with CDI is defined by characteristic colonoscopic and/or histopathologic findings. CDI is now the most common cause of hospital-acquired diarrhea in industrialized countries. Antibiotic use is a major contributing factor to the increased incidence of CDI.
The source of infection is person-to-person fecal-oral transmission. Transmission is enhanced by environmental contamination, infected fomites, and carriage on the hands of health care workers. Disruption of the normal bowel flora with overgrowth of *C. difficile* and toxin production is responsible for the pathogenesis of CDI. The two potent toxins, toxin A (enterotoxin) and toxin B (cytotoxin), lead to colonic mucosal disruption, inflammation, and CDI. In addition to antibiotics, chemotherapeutic agents, solid-organ or bone marrow transplantation, inflammatory bowel disease (IBD) leads to increased colonization by *C. difficile* spores. Prolonged hospitalization, advanced age, and immunosuppression are other risk factor for CDI.

Historically, use of lincosamides (clindamycin) has been associated with CDI. However, most antibiotics, except vancomycin, have been reported as the agents used before the development of CDI. Cephalosporins that have no antimicrobial activity against *C. difficile* and newer fluoroquinolones with a broader spectrum of activity against gastrointestinal flora are now commonly associated with CDI. In addition, the newer strain of *C. difficile*, North American pulsed-field gel electrophoresis type 1 (designated as NAP1), is resistant to fluoroquinolones. The extensive use of fluoroquinolones in the community is thought to have contributed to the emergence of this hypervirulent strain producing the binary toxin.

Most patients with CDI have a history of antibiotic exposure in the preceding 8 weeks and/or the presence of other risk factors. Clinical illness ranges from mild to moderate diarrhea to fulminant pseudomembranous colitis and toxic megacolon, which could be fatal. The usual symptoms are watery diarrhea with mucus and abdominal cramping. More severe illness causes high-grade fever, nausea, and dehydration. Leukocytosis and leukemoid reaction are commonly seen and may be the only clues to the presence of CDI. Recurrences of CDI are common and may be caused by relapse or reinfection.

The diagnosis of CDI is confirmed by the detection of toxin A and/or B in the stool. This test should be performed only on diarrheal stool. The sensitivity of currently available ELISA ranges from 63% to 94%, but positive predictive value is low. Stool culture for *C. difficile* is cumbersome, has a long turnaround time, and may be positive even in the absence of toxin production. Glutamine dehydrogenase is present in both toxigenic and nontoxigenic *C. difficile*. Enzyme immunoassay for glutamine dehydrogenase has a sensitivity of 85% to 95% and a specificity of 89% to 99%. However, the test does not differentiate between toxigenic and nontoxigenic strains, as is true for the culture. Because of the high negative predictive value, this test is used in a 2-step algorithm in conjunction with an enzyme immunoassay that detects toxins.

The recent Food and Drug Administration (FDA) approval of a polymerase chain reaction (PCR) for toxigenic *C. difficile* has a rapid turnaround time and sensitivity of about 94%. It may be positive in asymptomatic patients colonized with toxigenic *C. difficile* strains.

Oral metronidazole and oral vancomycin have been the mainstay of therapy for CDI. Although there is no difference in cure rates between oral metronidazole and oral vancomycin in patients with mild disease, oral vancomycin demonstrated superiority in patients with severe disease. The likely explanation is that the secretion of metronidazole into the colonic mucosa and lumen is impaired in severe disease because of poor blood flow. Hence, the Infectious Diseases Society of America’s (IDSA) guidelines recommend the use of oral vancomycin as the first-line therapy in patients with severe disease, defined as those with a white blood cell count of more than 15 000 per micro-liter, serum creatinine level more than 1.5 times the premorbid level, hypotension, shock, ileus, and toxic megacolon. Fecal transplant has been shown to be effective for treating recurrent CDI. Recently, Fidaxomicin, a macrocyclic antibiotic, has been
approved by the FDA for the treatment of CDI. Louie and colleagues conducted a randomized double-blind trial comparing the efficacy of oral Fidaxomicin 200 mg 3 times daily for 10 days with oral vancomycin 125 mg 4 times a day for 10 days in the treatment of CDI. Cure rates of CDI with Fidaxomicin were noninferior to those achieved with oral vancomycin. However, Fidaxomicin (7.8%) significantly decreased the recurrence rate of CDI compared with vancomycin (25.5%) in patients with non-BI/NAP1/PCR ribotype 027 strains. Emergent colectomy may be life saving in patients with fulminant CDI, including toxic megacolon, peritonitis, and colonic perforation.

SECTION E: PYELONEPHRITIS AND PERINEPHRIC ABSCESS

Acute Pyelonephritis

Acute pyelonephritis is a clinical syndrome characterized by flank pain and/or tenderness and fever, often associated with dysuria, urgency, and frequency of urination. These symptoms can also be seen with renal calculi or renal infarction. However, acute pyelonephritis is differentiated by pyuria and significant bacteriuria.

Pathogenesis

Ascending infection from the urethra to the bladder and up the ureter to the kidney allows the bacteria to establish infection. The mucosa of the bladder has antibacterial properties that eliminate organisms through mucus trapping and a polymorphonuclear leukocyte response. In addition, the normal urine has a low pH, low osmolarity, high urea concentration, and high organic acid content, all of which inhibit bacterial growth. Obstructive uropathy from many causes promote the bacterial growth and infection. A silent infection of the kidney is present in 30% of patients with lower urinary tract infection (UTIs) symptoms. Hematogenous infections may produce focal abscesses or areas of pyelonephritis within a kidney with positive urine cultures. Hematogenous spread is usually seen with relatively virulent organisms, like S aureus or S typhi.

In severe pyelonephritis, the kidney is enlarged with raised yellowish abscesses on the surfaces.

Clinical manifestations and diagnosis

Symptoms of pyelonephritis range from mild (ie, low-grade fever with low backache and costovertebral angle tenderness) to severe (ie, high-grade fever, shaking chills, nausea, vomiting, and dehydration). Leukocytosis is seen in both mild and severe forms. Pyuria and bacteriuria are easily demonstrable on urine microscopy and gram stain. Blood stream infection may complicate the course of acute pyelonephritis. Bacteremia from pyelonephritis is seldom associated with the more serious sequelae of gram-negative infections, which lead to septic shock, disseminated intravascular coagulation, or both. Emphysematous pyelonephritis is a particularly severe form of pyelonephritis associated with production of gas in renal and perinephric tissues and is seen exclusively in patients with diabetes. Acute papillary necrosis resulting in obstructive uropathy can lead to severe pyelonephritis, which is also seen in patients with diabetes.

Ultrasound and CT scan of the abdomen demonstrate perinephric stranding or intrarenal abscesses. Urine and blood cultures guide definitive antimicrobial therapy.

Microbiology

More than 95% of UTIs including pyelonephritis are caused by a single bacterial species. E coli is the most common infecting organism in acute pyelonephritis. Obstructive uropathy caused by structural abnormalities or neurogenic bladder is associated with infections caused by other gram-negative bacteria (Proteus, Pseudomonas, Klebsiella, Enterobacter spp), enterococci, and staphylococci. Repeated
courses of antimicrobial therapy and frequent instrumentation ultimately contribute to the infection by bacteria resistant to multiple antibiotics. *Corynebacterium urealyticum*, a gram-positive, urea-splitting, slow-growing bacillus, is an important nosocomial pathogen causing complications, like mucosal encrustations and struvite stones, especially in renal transplant recipients. It is highly resistant to antimicrobials, although usually sensitive to glycopeptides.\(^6^8\) In patients with indwelling catheters, *Candida* spp often colonize the catheter, which sometimes leads to true infection.

**Treatment**

Mild to moderate illness responds well to orally administered antimicrobial agents. Intravenous antimicrobial therapy becomes necessary in patients who do not tolerate oral therapy. Gram stain of the urine, especially with the predominant organism, may help choose presumptive antimicrobial therapy.

Oral ciprofloxacin (500 mg twice daily) for 7 days (or levofloxacin 750 mg daily for 5 days), with or without an initial 400-mg dose of intravenous ciprofloxacin, is often used as a first-line therapy. This practice may not be safe in communities where the resistance of community-acquired uropathogens to fluoroquinolones exceeds 10%.\(^6^9\)

Multiple studies, including a prospective multicenter trial conducted in Sweden, have demonstrated that the 7-day regimen of ciprofloxacin is successful and safer than the 14-day regimen.\(^7^0\) IDSA guidelines recommend an initial intravenous dose of a long-acting parenteral antimicrobial, such as 1 g of ceftriaxone, or a consolidated 24-hour dose of an aminoglycoside for a front-line therapy for pyelonephritis if the prevalence of fluoroquinolones resistance in the community exceeds 10%.

Patients requiring hospitalization are treated initially with an intravenous antimicrobial regimen, such as a fluoroquinolone; an aminoglycoside, with or without ampicillin; an extended-spectrum cephalosporin or extended-spectrum penicillin, with or without an aminoglycoside; or a carbapenem. The choice between these agents should be based on local resistance surveillance data. Definitive therapy is guided by and tailored from susceptibility results.\(^6^9\)

**Perinephric Abscess**

Perinephric abscess is an uncommon complication of acute pyelonephritis. The most common predisposing factors are urinary tract calculi/obstruction and diabetes mellitus. Most of them are caused by ascending UTI with the usual uropathogenic organisms. Occasionally, bacteremia, especially caused by *S. aureus*, can lead to a hematogenous perinephric abscess. Rarely contiguous spread from a neighboring site of infection, such as the colon or overlying rib, can lead to perinephric abscess. The usual presentation is insidious, with fever, weight loss, night sweats, and anorexia associated with flank or back pain. Symptoms referring to the urinary tract are often lacking. Physical examination reveals costovertebral angle tenderness and sometimes the abscess can be palpable.\(^2\) The index of suspicion for perinephric abscess should be high in patients with a febrile illness and unilateral flank pain who have not responded to appropriate therapy for acute pyelonephritis.

In addition to leukocytosis and anemia, signs of renal inflammation, such as pyuria or proteinuria, are seen on urinalysis. Abdominal ultrasound and CT scan are very helpful for early diagnosis. The most common CT scan findings include thickening of the Gerota fascia, renal enlargement, focal parenchymal inflammation, and fluid and/or gas in and around the kidney.

In patients with a clinical or radiographic suspicion of perinephric abscess, needle aspiration under ultrasonographic or CT guidance is safe and diagnostic. A percutaneously introduced small catheter provides immediate decompression and continuous
Early recognition of perinephric abscess by abdominal ultrasound or CT scan followed by prompt percutaneous drainage and antimicrobial therapy has significantly improved the prognosis. Surgical intervention is indicated only when percutaneous drainage is contraindicated or fails. Presumptive broad-spectrum parenteral antimicrobial therapy, as discussed earlier in acute pyelonephritis, should be started before or immediately after drainage. The results of blood, urine, and drainage cultures should be used to determine definitive antimicrobial therapy. It is important to treat the underlying cause for obstruction and to intensively manage diabetes. Nephrectomy is reserved for emphysematous pyelonephritis, patients with diffusely damaged renal parenchyma, or patients with refractory sepsis as an urgent intervention for survival.

REFERENCES


