



Current focus

## Intra-abdominal infections

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### Abstract

Intra-abdominal infections in the hospitalized patient differ from those arising in the community in their clinical presentation, sites of involvement, and characteristic microbiology. They are also associated with greater morbidity and mortality. New onset organ dysfunction, more than acute abdominal pain and tenderness, is the predominant clinical manifestation. Successful management depends on aggressive resuscitation and hemodynamic support, administration of adequate antimicrobial therapy, and the timely use of source control measures appropriate to the clinical situation.

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### 1. Introduction

Intra-abdominal infections comprise a heterogeneous group of conditions ranging from such relatively benign processes as acute appendicitis to conditions such as infected pancreatic necrosis, diffuse peritonitis, and intestinal infarction that are associated with substantial morbidity and mortality. They typically develop in the ambulatory patient who presents to the emergency department with abdominal pain, and the clinical manifestations of an acute abdomen. However, intra-abdominal infection can also develop in the hospitalized patient—most commonly as a complication of an antecedent disease process or invasive procedure. The presentation of these infections is often insidious and atypical, and their mortality and morbidity substantial.

### 2. The pathogenesis of intra-abdominal infection

Despite a variety of clinical presentations, intra-abdominal infections share important common features that reflect their distinctive microbiology and the unique defense mechanisms of the peritoneal cavity. They have been associated with substantial homeostatic derangements—

physiologic abnormalities that are sufficiently profound that early descriptions of the syndrome of multiple organ failure suggested that its occurrence could be considered a valid sign of occult intra-abdominal infection [1–3].

#### 2.1. Microbiologic considerations

The gastrointestinal (GI) tract of the normal healthy human being harbors a complex indigenous flora whose composition is remarkably stable over the lifetime of the individual [4]. The stomach and proximal small intestine are sparsely populated with a predominantly Gram-negative flora. Both the density and diversity of this flora increase as one proceeds distally. Upwards of 500–600 distinct microbial species can be cultured from normal stool, and the density of this flora is sufficiently great that microbial cells outnumber human cells by a factor of 10 to one. Stability of the GI flora is maintained by a number of factors including competition for nutrients and mucosal binding sites, gut motility, local pH, bile flow, and the production of antimicrobial substances by both the gut epithelium and other luminal organisms [5]. The normal flora plays a crucial role in the maintenance of normal metabolic and immunologic homeostasis. Anaerobes greatly outnumber aerobes within the colon; disruption of the anaerobic flora by the injudicious use of broad-spectrum antibiotics promotes pathologic gut colonization by resistant species, and has been shown to be an important factor contributing to gut colonization by vancomycin-resistant *Enterococci* [6].

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Table 1  
The microbial flora of secondary peritonitis

Type	Organism	Percent
Aerobic bacteria		
Gram-negatives	<i>E. coli</i>	60%
	<i>Enterobacter/Klebsiella</i>	26%
	<i>Proteus</i>	22%
	<i>Pseudomonas</i>	8%
Gram-positives	<i>Streptococci</i>	28%
	<i>Enterococci</i>	17%
	<i>Staphylococci</i>	7%
Anaerobic bacteria		
	<i>Bacteroides</i>	72%
	<i>Eubacteria</i>	24%
	<i>Clostridia</i>	17%
	<i>Peptostreptococci</i>	14%
	<i>Peptococci</i>	11%
Fungi	<i>Candida</i>	2%

From Hau et al. [7].

Although cultures of stool specimens grow a remarkably diverse flora, cultures of the peritoneal cavity of patients with peritonitis secondary to a colonic perforation yield a polymicrobial, but predictable group of organisms [7,8] (Table 1). Experimental studies suggest that the aerobic Gram-negative organisms are largely responsible for the lethality of peritonitis, whereas the anaerobes play an important role in the induction of abscess formation [9,10]. The clinical features of peritonitis, however, are dependent more on the response of the host than on the intrinsic virulence of the infecting flora.

### 2.2. The normal defenses of the peritoneal cavity

A single layer of mesothelial cells covers the abdominal viscera and is reflected onto the anterior abdominal wall, to create a closed potential space—the peritoneal cavity. Within this space is approximately 50–100 ml of peritoneal fluid and resident cells of the innate immune system, predominantly macrophages, mast cells, and lymphocytes. Peritoneal fluid is drawn cephalad by the negative pressure created by diaphragmatic contraction, and is absorbed into the lymphatics through special stomata that overlie the diaphragm [11,12].

The abdominal viscera are innervated by visceral nerves that respond primarily to stretch and that map to areas reflecting the embryologic development of the GI tract: pain arising from foregut structures including the stomach, pancreas, liver and biliary tree, and duodenum is perceived as arising in the epigastrium; pain from midgut structures from the proximal small bowel to the splenic flexure is perceived as arising in the periumbilical area, and pain from hindgut structures from the splenic flexure of the colon to the rectum is perceived as arising in the suprapubic region. Visceral pain is poorly localized, and perceived as non-lateralizing. The peritoneum, on the other hand, is innervated by somatic nerves, and pain arising from inflammation of the peritoneum is localized to the site of inflammation. An understanding of these principles is invaluable in establishing a precise anatomic and pathologic diagnosis in the patient with acute

abdominal pain. The pain of appendicitis, for example, starts as a colicky pain localized to the periumbilical region, reflecting the early stages of appendicitis as the obstruction of a midgut viscus—the appendix. As ischemia and inflammation progresses in the obstructed appendix, the overlying peritoneum becomes inflamed, and the patient experiences this pathologic evolution as a migration of the pain to the right lower quadrant at the anatomic site of the appendix.

Inflammatory stimuli within the peritoneal cavity result in the exudation of a protein-rich fluid into the peritoneal space and in the release of chemoattractant factors from resident peritoneal macrophages that result in the recruitment of circulating neutrophils and monocytes [13]. The expression of tissue factor on the surface of peritoneal macrophages triggers local activation of the coagulation cascade, resulting in deposition of fibrin around the inflammatory focus, and producing the wall of an abscess—a process that serves to wall the infection from the rest of the peritoneal cavity.

Inflammation within the peritoneal cavity evokes a series of secondary changes that produce the clinical syndrome of peritonitis. The acute inflammatory process within the abdomen results in sympathetic activation, and suppression of intestinal peristalsis, or ileus. Fluid absorption through the wall of the bowel is impaired, and significant amounts of tissue fluid may be sequestered within the lumen of the gut, resulting in systemic hypovolemia. Moreover reduced intestinal peristalsis promotes microbial overgrowth, leading to the translocation of bacteria and their products from the gut lumen into regional nodes, the peritoneal cavity, and the portal circulation [14]. Host-derived mediators are disseminated from the peritoneal cavity through the mesenteric lymph [15], or through their release from hepatic Kupffer cells [16]. Shunting of gut blood flow away from the splanchnic circulation in response to a combination of relative hypovolemia, secondary to third space fluid sequestration, and peripheral vasodilatation in response to the inflammatory stimulus further compromises intestinal barrier function and promotes bacterial translocation and endotoxin absorption from the gut lumen.

### 3. Clinical presentation and diagnosis

The signs and symptoms of intra-abdominal infection in the hospitalized patient are frequently subtle, and the clinician must be alert to the possibility in order to make a timely diagnosis.

The clinical setting is commonly one of the most important clues. Primary peritonitis should be considered in the cirrhotic patient who deteriorates despite therapy. Prior abdominal surgery should raise the prospect of an unrecognized complication—either directly related to the procedure itself (for example, a leak from an intestinal anastomosis) or to the laparotomy undertaken to perform the procedure (for example, an unrecognized enterostomy, or the inadvertent incorporation of a loop of bowel into the abdominal wall

closure). An unrecognized injury in the trauma patient can also give rise to intra-abdominal infection. A history of hypotension raises the possibility of intestinal ischemia or infarction, particularly in the patient with co-existing peripheral vascular disease, while embolization of an atherosclerotic plaque should be suspected in the patient who deteriorates following aortography. Perforation of a duodenal ulcer is a not uncommon complication of major surgical intervention, particularly in the patient with known peptic ulcer disease [17]. Biliary stents placed for the relief of obstructive jaundice are prone to obstruction, causing cholangitis, and other invasive devices within the peritoneal cavity—peritoneal dialysis cannulae, for example—are prone to infection. Finally, infection may complicate the later course of a disease such as pancreatitis, which is initially a sterile process.

New and unanticipated organ dysfunction is a common presenting manifestation of intra-abdominal infection in the hospitalized patient. The physiologic response to the trauma of surgery causes increased levels of anti-diuretic hormone (ADH) and aldosterone, leading to fluid retention. In the absence of complications, this process usually resolves by the third day; a persistently positive fluid balance after this time should raise the possibility of unrecognized complications. Fluid retention is often manifested clinically by signs of organ dysfunction—tachypnea and hypoxemia, confusion, or the onset of a new supraventricular dysrhythmia, for example. For the non-surgeon, it is important to stress that major intra-abdominal surgical complications do not usually become manifest until several days after the operative procedure, typically becoming evident on the third post-operative day, but presenting up to 7–10 days after the surgical procedure.

While clinical examination may be all that is needed to establish a diagnosis of intra-abdominal infection, and to inform a decision for operative or conservative management, in the ambulatory patient presenting to the emergency department with abdominal pain, it is much less reliable in the diagnosis of nosocomial infection. Radiographic studies are the mainstay of the diagnosis of nosocomial intra-abdominal infection. Plain radiographs of the chest or abdomen may disclose intra-peritoneal free air, although air may normally be present for up to 7 days following a laparotomy. Other findings on plain films that may be of diagnostic use, are evidence of intestinal obstruction or abnormalities of the mucosal pattern, such as thumb-printing, that suggest ischemia. Contrast studies may demonstrate leaks or delineate the location of an obstruction. Ultrasonography is of particular use in assessing the liver and biliary tree. It has the advantage of being portable, inexpensive, and usually readily obtained; however, it is highly operator-dependent, and visualization may be impeded by intestinal gas or dressings on the abdominal wall. Computed tomography is the most reliable imaging modality for evaluating the abdomen [18]. Combined with oral and intravenous contrast, the CT scan can show intra- or retroperitoneal fluid collections, and suggest the diagnosis of an abscess by virtue of such features as

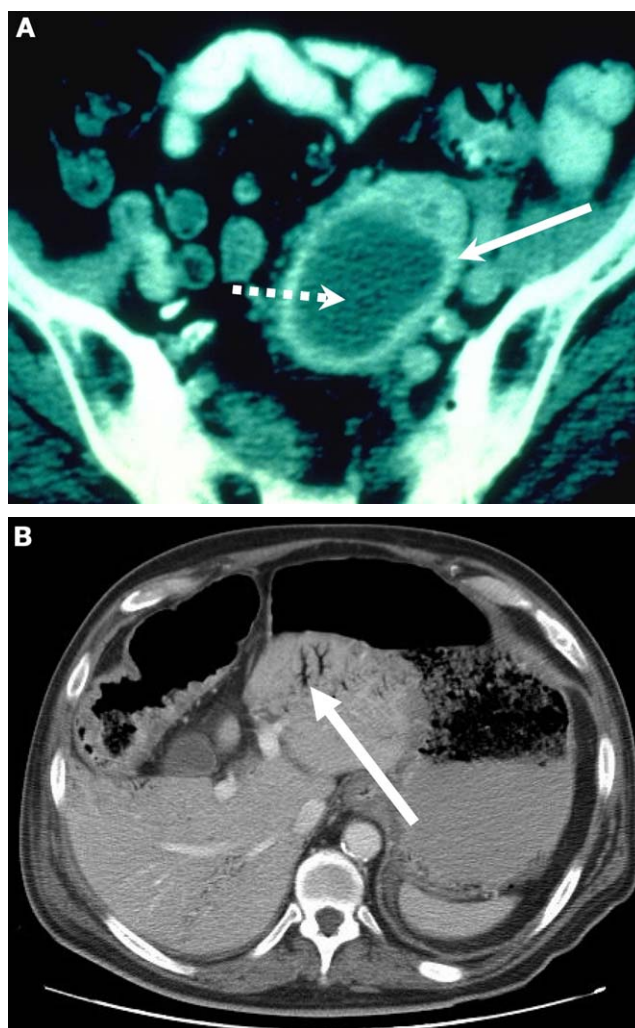


Fig. 1. CT findings in intra-abdominal infection. **1a**, CT scan showing a localized abscess secondary to perforated diverticulitis. Note rim enhancement of abscess wall (solid arrow) and inhomogeneity of abscess contents, with focal pockets of air (dashed arrow). **1b**, Intestinal ischemia secondary to a low flow state following complicated cardiac surgery; features of ischemia include pneumatosis (air in the gut wall) involving the stomach and transverse colon, and air in branches of the portal vein to the left lobe of the liver (white arrow).

rim enhancement, air fluid levels, or inhomogeneity (Fig. 1a). Ischemia can be demonstrated by the absence of flow, and clot may be visualized within larger vessels in the peritoneal cavity; gas in the wall of the intestine (pneumatosis) or within the portal vein also suggests intestinal ischemia (Fig. 1b). Magnetic resonance imaging has been used as an alternative diagnostic modality, but it is not clearly superior to CT scanning, with the possible exception of the evaluation of retroperitoneal pancreatic pathology [19].

As a general principle, it is desirable to establish an anatomic and pathologic diagnosis of the problem prior to undertaking intervention in the hospitalized patient. Not only does adequate imaging aid in planning the surgical procedure, but percutaneous, image-guided techniques are increasingly the preferred approach for achieving control of the source of the problem [20]. On the other hand, the necessary studies

should be performed expeditiously, and should not unduly delay operative intervention [21].

#### 4. Management principles

Successful management of the patient with intra-abdominal infection is dependent upon the optimal application of three principles:

1. timely hemodynamic resuscitation and support of vital organ function;
2. early administration of antimicrobial agents appropriate for the infectious problem;
3. rapid anatomic diagnosis and the institution of adequate source control measures.

Adjuvant therapies that target the biologic processes of acute inflammation hold promise for the future, but their role at present is limited.

#### 5. Hemodynamic resuscitation

The mainstay of resuscitation is the rapid administration of adequate amounts of fluid to restore adequate intravascular volume, and so to optimize oxygen delivery to the tissues. There is no compelling evidence of the superiority of one type of fluid over another. Resuscitation should be guided by frequent assessment of heart rate and blood pressure. Urinary output is a simple and sensitive measure of intravascular volume filling and organ function; an hourly output of 30–50 ml/kg should be the minimal objective of therapy. Patients who have significant co-morbidities, who present with more profound hemodynamic instability, or who fail to respond rapidly to fluid replacement should be managed in an ICU setting. The amount of fluid required to achieve hemodynamic stability is variable, and frequently substantial, because of unappreciated third space losses into the focus of infection and into the GI tract as a consequence of ileus [22].

#### 6. Antibiotics

Systemic antibiotics, whose spectrum of activity includes Gram-negative aerobic organisms and anaerobes, should be administered as soon as the diagnosis of intra-abdominal infection is suspected and without waiting for radiographic or microbiologic confirmation. A number of regimens are available, and are all of essentially comparable efficacy [23] (Table 2). While there is controversy regarding the utility of obtaining cultures in community-acquired peritonitis, cultures should be obtained from all patients with nosocomial intra-abdominal infection, since the GI flora of the hospitalized patient is profoundly altered, and overgrowth by resistant species is common. Once the results of culture and sensitivity testing are available, the antimicrobial regimen should be adjusted to narrow its spectrum to the documented

Table 2

Recommended antimicrobial regimens for high-risk patients with intra-abdominal infection

Regimen
<i>Single agents</i>
Imipenem/cilastatin
Meropenem
Piperacillin/tazobactam
<i>Combination therapy</i>
Aminoglycoside (amikacin, gentamicin, netilmicin, tobramycin) plus an anti-anaerobe (clindamycin or metronidazole)
Aztreonam plus clindamycin
Ciprofloxacin plus metronidazole
Third/fourth generation cephalosporin (cefepime, cefotaxime, ceftazidime, ceftizoxime, ceftriaxone) plus an anti-anaerobe (clindamycin or metronidazole)

From Mazuski et al. [23].

infecting species [24]. There is no compelling evidence to support the administration of specific treatment aimed at *Enterococci* or *Candida* isolated from a polymicrobial intra-abdominal infection [25,26], although the isolation of either species is associated with a higher risk of mortality [27,28].

The optimal duration of antibiotic therapy is unknown, and when antibiotics are used in association with adequate source control, the duration of therapy can be short [29], and certainly no longer than 5–7 days.

#### 7. Source control

The term “source control” is used to encompass all physical measures undertaken to eradicate a focus of infection, to prevent ongoing microbial contamination, and to restore functional anatomy [20]. These involve one or more of three strategies:

- *drainage* of abscesses or infected fluid collections;
- *debridement* of necrotic infected tissue;
- *definitive measures* to control a source of ongoing microbial contamination and to restore anatomy and function.

##### 7.1. Drainage

Drainage converts an abscess to a controlled *sinus* (a cavity that communicates with an epithelially lined surface) or *fistula* (an abnormal communication between two epithelially lined surfaces) (Fig. 2). This objective can be accomplished operatively, but it can also be accomplished by percutaneous techniques, guided by radiographic imaging, or by other simple interventions such as opening an infected wound by removing sutures or staples. In general, the preferred approach is that which is the simplest, which results in the least physiologic upset for the patient and which best facilitates subsequent definitive or reconstructive measures. Although its use has not been evaluated by a randomized control trial, studies using historical or contemporaneous controls show percutaneous drainage to be as effective as operative drainage, and when percutaneous techniques are

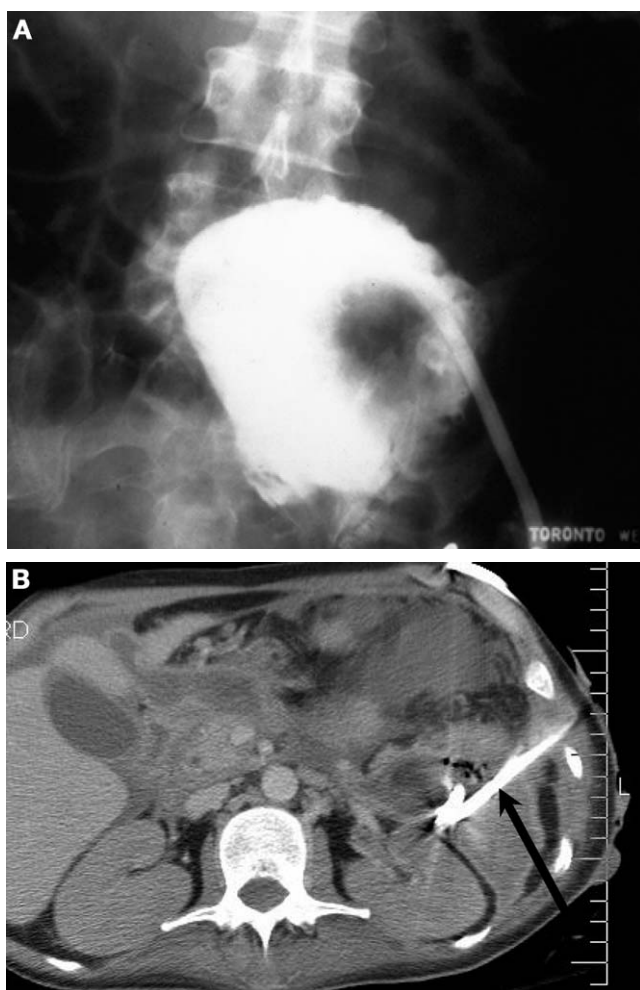


Fig. 2. **2a**, Percutaneous drainage of a diverticular abscess creates a controlled colcutaneous fistula, an abnormal communication between the sigmoid colon and the skin of the abdominal wall; the abscess cavity is outlined by contrast on this plain film of the abdomen. **2b**, Percutaneous drainage of a pancreatic abscess associated with infected peripancreatic necrosis in a patient with severe necrotizing pancreatitis. The drain, indicated by the solid arrow, serves to create a fistula between the disrupted pancreatic duct and the skin of the abdominal wall. Although there is residual necrotic infected tissue present following percutaneous drainage, the drainage procedure permitted temporization so that the residual necrosis could be debrided laparoscopically 5 weeks later.

feasible, they are the preferred initial approach [30,31]. Factors that preclude successful percutaneous drainage include diffuse peritonitis, with lack of localization of the infectious process (Fig. 3), multiple abscesses, anatomic inaccessibility, or the concomitant presence of a process requiring surgical debridement—for example, intestinal infarction.

### 7.2. Debridement

Debridement is the physical removal of necrotic or infected tissue. It can be accomplished surgically, but debridement of superficial tissues is also possible through the use of frequent dressing changes: fibrin and necrotic tissue adhere to the dressing, and are removed when the dressing is changed.

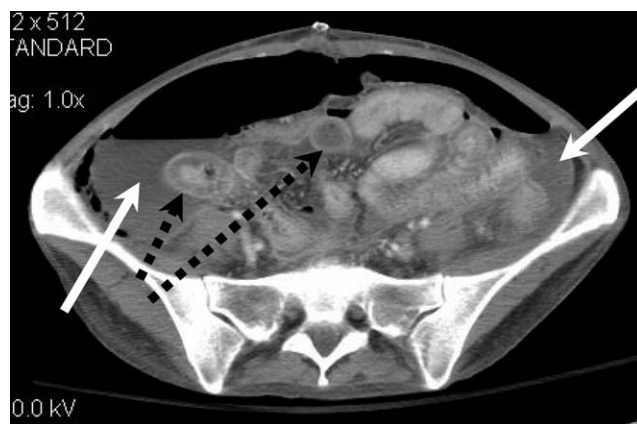


Fig. 3. CT scan of a 37-year-old woman, 4 days following an ileocecal resection for Crohn's disease. The CT findings of diffuse intra-peritoneal fluid and free air (white arrows) indicate a process that is not amenable to percutaneous drainage; operative exploration revealed an unrecognized defect in the rectum. Note enhancement of peritoneum overlying loops of small bowel, a further sign of diffuse peritonitis (dashed arrows).

For the patient with intra-abdominal infection, debridement encompasses such interventions as the excision of necrotic intestine, the removal of feces or fibrin from the peritoneal cavity, and the excision of necrotic and infected retroperitoneal fat in the patient with infected pancreatic necrosis. Clear demarcation between viable and non-viable tissues is a prerequisite to successful debridement. In patients with pancreatitis, for example, a distinct plane between viable and necrotic retroperitoneal fat becomes apparent only 3–4 weeks after the onset of the inflammatory process; attempts at early debridement are commonly complicated by uncontrolled hemorrhage from the retroperitoneum. Thus it has been demonstrated in a randomized clinical trial that delayed surgical intervention in patients with pancreatic necrosis results in improved survival when compared to early intervention [32]. While abdominal infection is typically accompanied by a vigorous peritoneal response, leading to extensive fibrin deposition on the peritoneal surface of loops of bowel, there is no evidence that meticulous attempts to remove this fibrin improve the clinical course [33].

### 7.3. Definitive interventions

Definitive interventions are those that remove a source of ongoing microbial contamination, and correct the anatomic or functional disorder resulting in the infection, and from its treatment.

If a foreign body such as a peritoneal dialysis cannula is present, its removal will aid in the resolution of the infectious episode. Certain organisms such as coagulase-negative *Staphylococci* form biofilms on prosthetic surfaces, and the presence of these biofilms serves to sequester the organism from normal host defenses [34,35]. Moreover, the mere presence of a foreign body in an infected field significantly reduces the inoculum required to produce an established infection. Continuous ambulatory peritoneal dialysis (CAPD) peritonitis can be managed without catheter re-

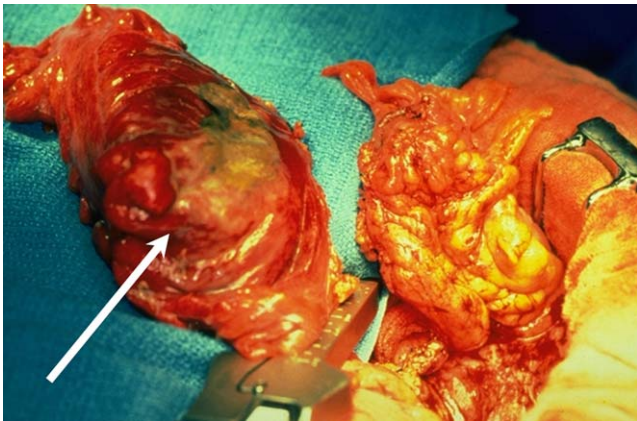


Fig. 4. Acute diverticulitis. A thickened and inflamed sigmoid colon is being resected; options for reconstruction are discussed in the text.

moval: the decision to treat with antibiotics alone or to remove the catheter, requires careful consideration of the probability of resolution by antibiotics alone, and the risks associated with alternate strategies for dialysis [36].

The evolution of approaches to the management of perforated diverticulitis provides an instructive example of the elements of the decision-making process for the definitive management of intra-abdominal infection (Fig. 4). In the past, patients with perforated diverticulitis were managed using a three-stage operative approach. The initial operative procedure involved laparotomy and drainage of the diverticular abscess, along with the creation of a proximal diverting colostomy to prevent further peritoneal contamination through the perforated diverticulum. Once the patient had convalesced, he or she underwent a second operation to resect the involved sigmoid colon and to anastomose the descending colon to the rectum. The third and final stage of the procedure, performed at a later date when healing of the colo-rectal anastomosis had been confirmed, involved closure of the protecting loop colostomy. An alternate two-stage approach is the Hartmann procedure. In the first stage, the abscess is drained, the involved sigmoid colon is resected and the rectum closed, and the descending colon is exteriorized as a colostomy. The second stage of the procedure, performed once the acute peritoneal inflammatory process has resolved, consists of a laparotomy to close the colostomy by anastomosing the descending colon to the rectal stump, a procedure that has been greatly facilitated by the widespread availability of surgical staplers.

While there has only been one randomized trial comparing the three-stage and two-stage approaches [37], both this small study and pooled data from case series [20] support the conclusion that the two-stage approach is superior to the traditional three-stage approach, particularly when the morbidity of each of the three operations is factored into the evaluation. Indeed, a number of recent trials suggest that primary resection and anastomosis [38,39] is the preferred approach, even in the presence of diffuse peritonitis [40,41]. Yet another alternative is percutaneous drainage of the abscess, followed by subsequent one-stage resection of the focus of diverticular disease.

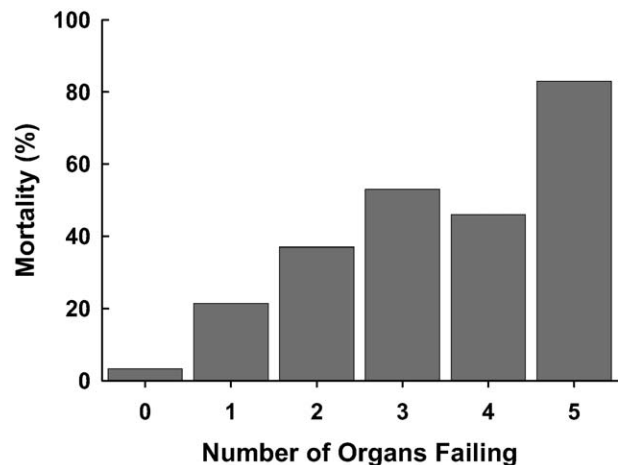


Fig. 5. Mortality for patients with secondary peritonitis is directly related to the number of failing organs at the time of diagnosis, in this large, population-based study. (From [43]).

It is particularly the case in nosocomial intra-abdominal infection, that the approach employed to treat the immediate problem must take into consideration the consequences of that decision for later reconstruction. Open abdomen approaches, for example, commit the patient to a series of reconstructive procedures to repair abdominal wall hernias or to close enterocutaneous fistulae. The creation of a stoma requires a subsequent procedure if the stoma is to be closed, and the morbidity associated with such procedures can be substantial [42]. Moreover, if a stoma is created, a loop enterostomy or colostomy is easier to close than an end stoma, for it can be accomplished locally without the need for a full laparotomy.

## 8. Classification and clinical features

Infections within the abdomen can arise within the peritoneal cavity or in the retroperitoneal area, and can be further classified on the basis of the anatomic structure involved.

Infections within the peritoneal cavity induce inflammation of the peritoneum, resulting in primary, secondary, or tertiary peritonitis. Depending on the degree of localization of the infectious process, peritonitis is typically, but somewhat arbitrarily, characterized as localized (intra-peritoneal abscess) or diffuse; appendicitis and diverticulitis are the most common causes of a localized intra-peritoneal abscess, whereas small bowel and gastroduodenal perforations are the most common cause of diffuse peritonitis [43]. The mortality risk is directly related to the extent of organ dysfunction (Fig. 5).

## 9. Intra-peritoneal infections

### 9.1. Primary peritonitis

Primary peritonitis is peritonitis that develops spontaneously, rather than as a consequence of a local infectious

process. It is most commonly seen in cirrhotic patients, in whom peritoneal infection occurs because of translocation of organisms from the gut lumen into the peritoneal cavity, a process facilitated by microbial overgrowth in the intestinal lumen and reduced antimicrobial activity of the ascitic fluid [44–46].

Primary peritonitis characteristically presents as acute deterioration in a previously stable cirrhotic patient with ascites. The diagnosis is established by aspiration and culture of the ascitic fluid. In the hospitalized patient, Gram-positive organisms, including methicillin-resistant *Staphylococcus aureus* have emerged as the predominant infecting pathogens, likely as a consequence of increased use of antibiotic prophylaxis and an increased frequency of invasive investigative procedures [47,48].

The management of primary peritonitis is supportive, including systemic antibiotics directed against the microflora most commonly encountered in the particular center; there is no evidence for the superiority of one antibiotic regimen over another [49]. A reduction in the ascitic fluid polymorphonuclear leukocyte count to less than 250 cells per ml by 48 h has been found to predict a successful response to antibiotic therapy [50]. Despite optimal therapy, the prognosis of patients with nosocomial primary peritonitis is poor, and the hospital mortality exceeds 30% [47,51].

### 9.2. Secondary peritonitis

Secondary peritonitis is peritonitis arising as a consequence of a mechanical breach of the GI tract. The microbial species isolated reflect the patterns of colonization of the involved level of the GI tract: perforation of the stomach or duodenum results in an inflammatory process that is primarily chemical, whereas perforations of the colon create polymicrobial infections. The hallmark of secondary peritonitis is abdominal pain, with clinical manifestations of peritoneal irritation on physical examination; however, these features may be less apparent in the hospitalized patient in whom concomitant illnesses, and the effects of analgesic or sedative medications may obscure clinical findings. While community-acquired infection such as appendicitis or diverticulitis may occur in the hospitalized patient, certain nosocomial causes of secondary peritonitis are sufficiently common that they merit special mention (Table 3).

### 9.3. Post-operative complications and anastomotic leaks

The most common cause of peritonitis in the hospitalized patient is intra-peritoneal infection as a consequence of prior abdominal surgery, both elective laparotomy and emergent abdominal procedures. Its causes are several, and usually can be inferred from knowledge of the prior abdominal procedure.

Peritonitis as a consequence of colonization of the exposed peritoneum at the time of surgery is uncommon in the absence of mechanical complications, or the presence of

Table 3  
Causes of secondary bacterial peritonitis in the hospitalized patient

Type	Cause
Post-operative peritonitis	Anastomotic leak
Procedural complications	Inadvertent or missed intestinal injury
	Infected hematoma, biloma
	Perforation secondary to GI endoscopy
	Intestinal injury secondary to laparoscopic trocar or abdominal paracentesis
	Displacement of gastrostomy or jejunostomy tube
	Intestinal ischemia secondary to angiography
Spontaneous GI perforation	Perforation of gastric or duodenal ulcer
Intestinal ischemia	Delayed ischemia secondary to low-flow
	Mesenteric venous thrombosis
	Secondary to abdominal aortic surgery
	Acalculous cholecystitis
Device-related infection	CAPD peritonitis
	Infected ventriculoperitoneal shunt
Community-acquired infection	Appendicitis
	Diverticulitis

adjuvants such as blood, bile, or a foreign body. If the GI tract has been entered, then the possibility of an anastomotic leak should be considered. Risk factors for this complication include excessive tension on the suture line, hematoma at the suture line, ischemia related to underlying vascular disease, excessive devascularization of the intestine at the site of the anastomosis, or intestinal distension at the suture line, and technical errors in the creation of the anastomosis. Review of the operative records may provide clues to the probability of such a complication.

Collections of bile or blood within the peritoneal cavity support the proliferation of bacteria shed at the time of surgery, and are the most common predisposing factor to post-operative abscesses. Their anatomic location reflects the preceding operative procedure: following cholecystectomy, for example, post-operative abscesses are typically found in the subhepatic or right subphrenic spaces, whereas an abscess developing following an anterior resection of the rectum most commonly occurs in the pelvis. Unrecognized intra-operative complications—an unrecognized tear of a segment of bowel, or the inadvertent incorporation of a loop of bowel into the abdominal wall closure, for example—may also give rise to post-operative peritonitis. Such complications are more frequent in re-operative surgery, since scarring and adhesions distort the intra-abdominal anatomy and necessitate a more extensive dissection. Less common complications should also be considered: trocar injury following laparoscopic surgery, inadvertent passage of a drain through a loop of intestine, etc. the possibilities are, unfortunately,

numerous; however, they can usually be deduced through a careful review of the clinical situation.

The presenting manifestations of post-operative peritonitis are variable and often quite subtle. Infections typically do not become apparent before the third post-operative day, and then, commonly present as new onset organ dysfunction. Under normal circumstances, the acute stress response to trauma or major surgery results in fluid retention as a consequence of increased secretion of aldosterone and ADH. In the absence of complications, this process resolves within 72 h, and a net negative fluid balance at this time is suggestive of an uncomplicated post-operative course. On the other hand, fluid retention beyond 3 days suggests an unanticipated complication and commonly manifests as increasing dyspnea, the new onset of a supraventricular dysrhythmia, or alterations in level of consciousness. Expedient diagnosis is critically dependent upon a high index of suspicion and the liberal use of appropriate imaging techniques.

While the clinical presentation of post-operative peritonitis may be variable, a definitive diagnosis can usually be made by computed tomography. Management is guided by the principles outlined above, and re-operation is only necessary when percutaneous techniques are ineffective.

The morbidity and mortality of post-operative peritonitis is substantial, with mortality rates of up to 60% for patients having diffuse peritonitis [52].

#### 9.4. Intestinal ischemia

Intestinal ischemia is an uncommon, but devastating, cause of secondary bacterial peritonitis; its causes in the hospitalized patient differ from those encountered in the patient presenting de novo to the emergency department. Intestinal ischemia in the ambulatory patient is usually a consequence of acute disruption of the vascular supply to a segment of the GI as a result of thrombosis or embolus to the superior mesenteric artery, or occlusion of segmental branches secondary to volvulus or small bowel obstruction. Its diagnostic hallmark is severe constant abdominal pain, out of proportion to the physical findings, and unless blood flow is rapidly restored, necrosis of the ischemic segment results.

In the hospitalized patient, the presentation of intestinal ischemia is usually less dramatic, reflecting a different group of causes. Acute obstruction of the superior mesenteric artery may occur as a result of embolization of atherosclerotic plaque or dissection of the aortic wall at the time of angiography. More commonly, however, intestinal ischemia in the hospitalized patient is a delayed consequence of reduced splanchnic blood flow, with progressive small vessel thrombosis leading to trans-mural ischemia; a preceding history of hypotension or use of vasopressors is characteristic. Mesenteric venous thrombosis may also occur in the hospitalized patient, secondary to low flow or a hypercoagulable state. Left colon ischemia is relatively common following emergency repair of an abdominal aortic aneurysm, since the

inferior mesenteric artery must be sacrificed, and collateral blood flow may be inadequate. As is the case with other nosocomial causes of intestinal ischemia, the clinical presentation is typically delayed, and new or evolving organ dysfunction is an important clinical sign.

Intestinal ischemia is suggested by the presence of “thumb-printing” on plain films of the abdomen or pneumatosis of the intestinal wall on a CT scan (Fig. 1b). However, the radiographic findings of intestinal ischemia are non-specific [53], and it is difficult to differentiate mucosal ischemia—a problem that can resolve with expectant observation—from trans-mural infarction—a condition in which urgent surgery is mandated. Indeed, even the more ominous finding of gas in the portal vein is associated with pathology that can be managed non-operatively in many patients in whom it is encountered [54]. Treatment of trans-mural ischemia invariably necessitates resection of the ischemic segment, often using the staged approach of a second-look laparotomy, as the extent of the ischemic process may not be evident at the time of the initial abdominal exploration. Experienced surgical judgment is critical to accomplish expeditious resection of gangrenous bowel, while minimizing the excision of potentially viable intestine.

#### 9.5. Tertiary peritonitis

Tertiary peritonitis—defined as peritonitis arising at least 48 h following the apparently successful treatment of primary or secondary bacterial peritonitis—is largely a disorder of the critically ill patient in an intensive care unit. It is differentiated from primary or secondary peritonitis because of its strikingly different microbial flora, its association with organ dysfunction, and its significant mortality, despite apparently effective antibiotic and source control management [55,56].

The development of tertiary peritonitis is suggested by persistent or worsening organ dysfunction following treatment of an episode of peritonitis [57]. The microbial flora of tertiary peritonitis—dominated by such organisms as coagulase-negative *Staphylococci*, *Enterococci*, *Candida*, *Pseudomonas*, and *Enterobacter*—mirrors the altered microbial ecology of the stomach and small bowel of the critically ill patient [58]. Despite the relatively low level of virulence of these organisms, the mortality of tertiary peritonitis is high, exceeding 50% in most series [55,59], and is attributable less to the pathologic process itself than to the compromised nature of the patients who develop it [60].

Radiographic evaluation of the patient with recurrent peritonitis often reveals the presence of multiple, poorly localized collections of intra-peritoneal fluid. Treatment is frustrating: the process responds poorly to systemic antibiotics, and neither recurrent percutaneous drainage procedures nor aggressive attempts at open abdomen management have a significant impact on clinical course [55]. Indeed, published reports of the excessive mortality associated with isolation of *Candida* [26,61] or *Enterococcus* [27] from patients with

peritonitis likely reflect the sequelae of advanced organ dysfunction in the critically ill patient.

## 10. Retroperitoneal infections

The retroperitoneum lies posterior and inferior to the space delineated by the peritoneal membrane; its structures include the kidneys, pancreas, and pelvic viscera. Of these, infections arising in the patient with acute pancreatitis present the greatest diagnostic and therapeutic challenges.

### 10.1. Pancreatic infection and infected peripancreatic necrosis

Infection is a common complication of severe necrotizing pancreatitis, its prevalence increasing with the severity of the initial episode. Its mechanism appears to be the translocation of bacteria from the adjacent gut lumen into the devitalized tissues and fluid collections that are a consequence of acute pancreatic inflammation [62]. The result is a complex infectious process that involves necrotic pancreatic and peripancreatic tissues or fluid collections, and so typically includes, to varying degrees, both abscess (from infection of loculated collections of pancreatic fluid) and infected necrosis (from infection of retroperitoneal fat devitalized through the activity of pancreatic lipases).

Approximately one-third of patients with necrotizing pancreatitis develop infection in the necrotic peripancreatic tissues [63]. Infection is a delayed and progressive process, with the majority of infections becoming microbiologically evident 2–3 weeks after the onset of the disease. While conventional clinical criteria such as fever, evolving organ dysfunction, leukocytosis, and elevation of circulating levels of diagnostic biomarkers such as procalcitonin are commonly evident in patients with infected pancreatic necrosis, they tend to be evident early in the course of the disease, before significant infection can be documented bacteriologically [64], and so are of less utility in clinical decision-making. A diagnosis of infected pancreatic necrosis can be inferred from the presence of clinical manifestations of sepsis in association with supportive CT findings, and established definitively by image-guided fine-needle aspiration. However, changing approaches to source control management have rendered a definitive diagnosis less urgent.

Approaches to the source control management of patients with necrotizing pancreatitis have shifted towards conservatism in both the timing and the extent of surgery. The leakage of enzyme-rich pancreatic juice into the pancreatic parenchyma and surrounding tissues leads to cellular necrosis and small vessel thrombosis, resulting in soft tissue necrosis that becomes secondarily infected. Initially the necrotic process is patchy, with areas of viable tissue interspersed with areas of non-viable tissue. As the process evolves, the areas of necrosis coalesce, and the demarcation between viable and non-viable tissue becomes more distinct, as granulation tis-



Fig. 6. Operative findings in a patient with severe, alcohol-related necrotizing pancreatitis, who underwent surgical exploration 2 weeks following the onset of the disease. The arrow indicates hemorrhagic fluid overlying the pancreas. Even at this time after the onset of symptoms, a clear demarcation between viable and non-viable tissues is not apparent, and repeat operative intervention was needed to achieve control of the area of infected necrosis.

sue forms at the margins of the viable tissue. Before this has happened, surgical intervention to debride non-viable tissue inevitably results in entry into viable tissues and bleeding (Fig. 6); bleeding can be catastrophic if vessels such as the splenic vein are injured, and surgical access in the retroperitoneum is limited. Once complete demarcation has occurred, however, necrotic debris can be removed with minimal trauma to viable tissues. Thus the decision on the timing of source control intervention hinges on weighing the risks of early intervention against the risks of leaving infected, necrotic tissue in situ.

Evidence from a single randomized trial [32], as well as from recent case series, suggests that mortality and morbidity can be reduced by a strategy of delaying surgical intervention for at least 3–4 weeks, even in the face of infected necrosis [65]. Although percutaneous drainage techniques are ineffective in evacuating infected necrotic tissue, they can temporize, by decompressing the liquid component of the infection, and so convert an emergency procedure into one that can be performed later under more controlled circumstances (Fig. 2b). Minimally invasive techniques are assuming a greater role, for they provide excellent visualization within the retroperitoneum, and minimize the trauma of surgical intervention [66].

## 11. Conclusions

Intra-abdominal infection in the hospitalized patient presents unique challenges in diagnosis and management. The

clinical presentation is often subtle, and the clinician must be particularly alert to the diagnostic implications of new onset organ dysfunction. Careful attention to earlier events during the hospital stay, such as hemodynamic instability, prior surgery, or invasive angiographic procedures may suggest an etiology. An anatomic and pathologic diagnosis using computed tomography or ultrasonography is desirable, and usually readily accomplished. Source control procedures are the mainstay of management. The widespread availability of percutaneous techniques has led to a clearer understanding of the biologic principles involved in source control and to the recognition that, in general, the best approach is the one that accomplishes source control with the least degree of anatomic and physiologic upset. Antibiotics are important as adjuvant therapy when source control can be accomplished and as front-line therapy when, as is the case in primary peritonitis, it cannot. However, antibiotics should never be used as an alternative to effective source control. The mortality and morbidity of nosocomial intra-abdominal infection is substantial, reflecting, in part, the compromised nature of the patients afflicted. Nonetheless, since the severity of organ dysfunction is the major determinant of outcome, diagnostic vigilance, and a high index of suspicion can prevent at least some of the toll of these infections.

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