Intensive care unit management of intra-abdominal infection

John C. Marshall, MD; Marilyn Innes, MD

Objective: **To review the biologic characteristics of, and management approaches to, intra-abdominal infection in the critically ill patient.**

Design: **Narrative review.**

Setting: **Medline review focussed on intra-abdominal infection in the critically ill patient.**

Patients and Subjects: **Restricted to studies involving human subjects.**

Interventions: **None.**

Results: **Intra-abdominal infections are an important cause of morbidity and mortality in the intensive care unit (ICU). Peritonitis can be classified as primary, secondary, or tertiary, the unique pathologic features reflecting the complex nature of the endogenous gut flora and the gut-associated immune system, and the alterations of these that occur in critical illness. Outcome is dependent on timely and accurate diagnosis, vigorous resuscitation and antibiotic support, and decisive implementation of optimal source control measures, specifically the drainage of abscesses and collections of infected fluid, the debridement of necrotic infected tissue, and the use of definitive measures to prevent further contamination and to restore anatomy and function.**

Conclusions: **Optimal management of intra-abdominal infection in the critically ill patient is based on the synthesis of evidence, an understanding of biologic principles, and clinical experience. An algorithm outlining a clinical approach to the ICU patient with complex intra-abdominal infection is presented. (Crit Care Med 2003; 31:2228–2237)**

KEY WORDS: intra-abdominal infections; morbidity; mortality; multiple organ dysfunction syndrome; peritonitis

Intra-abdominal infections are an important cause of intensive care unit (ICU) morbidity and mortality. Approximately 30% of patients admitted to an ICU with intra-abdominal infection succumb to their illness, and when peritonitis arises as a complication of a previous surgical procedure (1, 2), or recurs during ICU admission (3), mortality rates exceed 50%. Moreover, their morbidity is substantial. Multiple organ dysfunction syndrome was originally described as a complication of intra-abdominal infection (4, 5), and the association between occult intraperitoneal infection and organ dysfunction was deemed sufficiently strong to justify empiric laparotomy for the patient with worsening organ dysfunction but no defined focus of infection (6). The management of the critically ill patient with intra-abdominal infection can be alternatively gratifying and frustrating for the intensivist. We will review the biologic, clinical, diagnostic, and therapeutic features of this heterogeneous disorder.

From the Department of Surgery and the Interdepartmental Division of Critical Care Medicine, University of Toronto; and the Toronto General Hospital, University Health Network, Toronto, Canada.

Address requests for reprints to: John C. Marshall, MD, Eaton North 9-234, Toronto General Hospital, University Health Network, 200 Elizabeth Street, Toronto, Ontario, Canada M5G 2C4. E-mail: John.Marshall@uhn.on.ca

DOI: 10.1097/01.CCM.0000087326.59341.51

Biologic Considerations

The abdominal cavity is lined by a mesothelial membrane, the peritoneum, which covers the abdominal viscera and creates a potential space—the peritoneal cavity. The area posterior to the peritoneal cavity is known as the retroperitoneum; its anatomic contents include the kidneys, pancreas, great vessels, and the posterior aspects of portions of the gastrointestinal tract, specifically the duodenum, ascending and descending colons, and rectum. In health, the peritoneal cavity contains <100 mL of peritoneal fluid containing scattered macrophages and lymphocytes (7). This fluid circulates throughout the peritoneal cavity, drawn by the negative pressures generated by diaphragmatic contraction upward toward specialized fenestrae in the diaphragmatic peritoneum that, in turn, drain into the lymphatic system (8).

Inflammatory stimuli within the peritoneal cavity evoke a vigorous inflammatory response, with increased vascular permeability, outpouring of protein-rich fluid containing cytokines and chemokines (9, 10), and the influx of inflammatory cells, particularly monocytes and neutrophils (11, 12). The activation of an inflammatory response induces tissue factor expression on peritoneal macrophages, activating the coagulation cascade and resulting in accelerated generation of fibrin that polymerizes to form adhesions and the capsule of an abscess (13, 14). The peritoneum is richly endowed with somatic nerve fibers; thus, the onset of peritonitis invokes severe pain, localized to the anatomic site of maximal inflammation and aggravated by stimuli that result in movement of the peritoneum (the biologic basis for clinical tests to evoke rebound tenderness). The normal innate immune response of the peritoneal cavity is rapid and effective; however, there is evidence that the phagocytic capacity of the neutrophil is impaired in patients with complicated peritonitis (15) and that defense mechanisms such as fibrin deposition can impede microbial clearance (16).

Infections within the peritoneal cavity most typically arise as a consequence of disruption of the adjacent gastrointestinal tract, with spillage of the indigenous flora into the peritoneal space. This flora is enormously complex and variable throughout the gastrointestinal tract. In health, the stomach and duodenum are sterile or only sparsely populated with Gram-positive organisms, lactobacilli,

and, occasionally, *Candida* (17). Both the variety and the density of this flora increase more distally. Gram-negative organisms are encountered in the proximal small bowel, and anaerobes are encountered in the distal small bowel and colon. In total, as many as 600 separate microbial species comprise the indigenous flora of the healthy adult, and bacteria are so numerous that they outnumber human cells of the body by a factor of 10:1 (18). Despite the variety of organisms present within the lumen of the gastrointestinal tract, intraperitoneal infections arising as a result of a breach of gut integrity typically yield a mixed flora whose composition, though complex, is quite predictable (Table 1). Animal models have shown that differing groups of organisms make differential contributions to the outcome of infection: Gram-negative aerobic organisms are associated with acute lethality, whereas anaerobic flora contributes to abscess formation (19).

The anaerobic flora of the normal gut also plays an important role in the maintenance of stable patterns of intestinal microbial colonization, a phenomenon known as "colonization resistance" (20). In experimental animals, ablation of the anaerobic flora of the cecum by oral antibiotics such as clindamycin or penicillin results in a 5-log increase in numbers of cecal *Escherichia coli* and translocation of *E. coli* to adjacent mesenteric lymph nodes in essentially all animals (21). Studies in humans show that the use of antibiotics with anti-anaerobic activity can promote gut colonization with *Candida* (22, 23) and vancomycin-resistant *Enterococci* (24); these effects are particularly prominent when normal colonization resistance has been disrupted (23). Such changes in the composition of the normal intraluminal flora can occur over time in the critically ill patient (25) and explain the typical flora seen in cases of recurrent or tertiary peritonitis discussed in greater detail below.

Although intra-abdominal infections are typically polymicrobial, the composition of the infecting flora is influenced by the clinical setting. Enterococci are isolated more frequently in patients with postoperative peritonitis than in patients with intra-abdominal abscesses developing outside the hospital (26), and nasal colonization with methicillin-resistant *Staphylococcus aureus* is a risk factor for the acquisition of intra-abdominal methicillin-resistant *S. aureus* infection (27).

An acute loss of the integrity of the gut wall—for example, after perforation of an ulcer or an uninflamed diverticulum, disruption of an anastomosis, or traumatic perforation of the intestine—results in spillage of intestinal contents into the peritoneal cavity and produces generalized peritonitis. More commonly, however, the leakage of gut contents is a slow process, accompanied by an inflammatory response in the surrounding tissues, as encountered, for example, in perforated appendicitis or a postoperative abscess arising from residual intraperitoneal bacteria or a small anastomotic leak. The result of this interaction between the infecting bacteria and the defenses of the peritoneal cavity is the formation of an abscess that walls off the infectious insult. The abscess lies adjacent to the site of contamination or in a dependent location such as the pelvis or subhepatic space.

Infection within the peritoneal cavity or retroperitoneum evokes a vigorous systemic response, reflected in elevated levels of circulating inflammatory mediators such as tumor necrosis factor and interleukin-6 (28, 29) and the clinical sequelae of acute organ system dysfunction (30, 31).

Table 1. Microbiology of peritonitis

Primary Peritonitis	Secondary Peritonitis		Tertiary Peritonitis
Gram-negative bacteria	Gram-negative bacteria		Gram-negative bacteria
Eschecheri coli	*E. coli*	32–61%	*Pseudomonas*
Klebsiella	*Enterobacter*	8–26%	*Enterobacter*
	Klebsiella	6–26%	*Acinetobacter*
	Proteus	4–23%	
Gram-positive bacteria	Gram-positive bacteria		Gram-positive bacteria
S. aureus	*Enterococci*	18–24%	*Enterococci*
Enterococci	*Streptococci*	6–55%	Coagulase-negative
	Staphylococci	6–16%	*Staphylococci*
	Anerobic bacteria		
	Bacteroides	25–80%	
	Clostridium	5–18%	
	Fungi	2–15%	Fungi
			Candida

Classification and Clinical Features

Peritonitis can be classified as primary, secondary, and tertiary. Primary peritonitis, also known as spontaneous bacterial peritonitis, is peritonitis arising in the absence of a breach of the peritoneal cavity or gastrointestinal tract. Primary peritonitis can arise in otherwise healthy young girls, in whom the *Pneumococcus* is the typical infecting bacterium. In the critically ill patient, it is most commonly seen in the decompensated cirrhotic patient, and it often presents with an acute deterioration in otherwise stable advanced liver disease (32, 33). Infection is thought to reflect the translocation of enteric bacteria across an anatomically intact gut wall, promoted, perhaps, by abnormal overgrowth of organisms in the proximal small bowel (34, 35). The infection is characteristically monomicrobial, with enteric Gram-negatives and enterococci being the most common isolates; Gram-positive cocci are particularly prevalent when the infection arises in an ICU patient (36) (Table 1). Methicillin-resistant *S. aureus* is a common isolate when primary peritonitis occurs as a nosocomial infection in a hospitalized cirrhotic patient (37). Physical findings may be minimal; the diagnosis can be established by culture of an aspirate of the peritoneal fluid and is suggested by demonstration of >500 white cells/mm^3 of ascitic fluid, increased lactate, or a reduced glucose, and a decline in polymorphonuclear cell counts to <250 cells/mm^3 is associated with successful resolution (38). Primary peritonitis is treated with systemic antibiotics appropriate for the infecting flora, although there is no convincing evidence for the superiority of one regimen over another nor even for the utility of systemic antibiotics at all (39). Mortality is increased for patients admitted to an ICU (40).

Secondary peritonitis is peritonitis occurring as a consequence of egress of gut organisms through a physical hole in the gastrointestinal tract or through a necrotic gut wall (41, 42). Its flora is typically polymicrobial, including both aerobes and anaerobes when the distal gastrointestinal tract is the site of the

perforation (43). In contrast, anaerobes are unusual isolates from perforations of the stomach or duodenum. It is important to keep in mind that secondary peritonitis can occur in the cirrhotic patient: a polymicrobial culture, or the presence of anaerobes in the aspirate, suggest the diagnosis of secondary peritonitis (44).

The typical clinical presentation is with abdominal pain and tenderness with signs of peritoneal irritation on physical examination. Diffuse pain suggests generalized peritonitis, whereas localized pain suggests a walled-off process arising from an organ in the immediate anatomic vicinity. In the young, otherwise healthy patient, diagnosis is generally straightforward. However, in the elderly or medically compromised patient, the clinical presentation may be quite subtle. Corticosteroids can blunt the inflammatory response of the peritoneum and so mask the clinical signs. In the patient with an altered level of consciousness—the sedated patient receiving mechanical ventilation, for example—the only evidence of a treatable but life-threatening infection may be an unexplained septic response or an unanticipated deterioration of organ system function.

Tertiary peritonitis is peritonitis in the critically ill patient that persists or recurs at least 48 hrs after the apparently adequate management of primary or secondary peritonitis. Differentiation of this entity from secondary peritonitis underlines its strikingly different microbiologic features and its generally unsatisfying response to antibiotics and surgical source control measures (45, 46). The microbial flora isolated in tertiary peritonitis is dominated by organisms such as coagulase-negative *Staphylococci*, *Pseudomonas*, *Candida*, and the enterococcus (3, 47) (Table 1). These same species are the dominant floras of the upper gastrointestinal tract of the critically ill patient and common causes of nosocomial ICU-acquired infection (25, 48). Their preeminence in tertiary peritonitis suggests a role for bacterial translocation, aided by antibiotic pressures, in the pathogenesis of the disease. The mortality for patients with tertiary peritonitis is significant, typically in excess of 50%, and optimal therapeutic strategies are not well defined (49).

Diagnosis

Intra-abdominal infection can be particularly difficult to diagnose in the critically ill patient because an informative history is usually unobtainable, and findings on physical examination are masked by changes in level of consciousness. Thus, the diagnosis depends on consideration of the clinical setting, the development of otherwise unexplained signs of sepsis or organ dysfunction, and definitively on the results of radiographic examination (50).

The common causes of secondary bacterial peritonitis of sufficient severity to necessitate ICU admission are relatively few (Table 2). Perforation of the upper gastrointestinal tract secondary to ulcer disease or of the lower gastrointestinal tract secondary to diverticular disease or cancer are among the most common causes of severe intra-abdominal infection. In the trauma patient, occult injury to the gut can result in delayed onset of peritonitis. Gut ischemia secondary to arterial intrinsic vascular disease, a low-flow state, or strangulation of obstructed bowel is a relatively common and potentially devastating cause of intra-abdominal infection (51, 52). Mesenteric arterial embolism should be suspected in the patient with a potential source of emboli—for example, the patient with atrial fibrillation, a recent myocardial infarct, or a recent invasive vascular imaging procedure. Mesenteric arterial thrombosis typically occurs in the patient with evidence of peripheral vascular disease at other sites, whereas a history of thrombotic disorders should suggest the diagnosis of mesenteric venous thrombosis. Left-colon ischemia is a relatively common complication of emergency abdominal aortic aneurysm repair and occurs because the inferior mesenteric artery is ligated during repair of the aneurysm, rendering the left colon it supplies acutely ischemic. Previous abdominal surgery suggests the possibility of an anastomotic leak, an intra-abdominal abscess, or inadvertent and undetected injury to the bowel (e.g., caused during closure of the abdominal wall). Superinfection commonly complicates the course of severe necrotizing pancreatitis.

The clinical manifestations of intra-abdominal infection include the otherwise unexplained development of organ system dysfunction. The differential diagnosis of unanticipated shortness of breath or new onset of a supraventricular dysrhythmia arising 3 or 4 days after an abdominal operation includes anastomotic leakage or other intra-abdominal infectious pathology, and the diagnosis should be excluded with the appropriate imaging procedures. New onset of renal dysfunction or elevation of the bilirubin and transaminase levels is also suggestive of occult intra-abdominal infection. Blood cultures are often negative; in fact, it has been suggested that the absence of bacteremia in a febrile surgical patient increases the likelihood of intra-abdominal infection (53). However, polymicrobial bacteremia (54) or anaerobic bacteremia should also raise the possibility of intraperitoneal infection.

Radiographic imaging is the definitive diagnostic approach to patients with suspected intra-abdominal infection and can usually characterize the problem before planned intervention (55). Plain films may reveal intraperitoneal free air, bowel obstruction, or subtle signs of intestinal ischemia. Contrast studies performed using water-soluble agents can disclose leaks; injection of contrast into drains, fistulas, or sinus tracts can aid in delineation of the anatomy of complex infections and help to monitor the adequacy of abscess drainage.

Ultrasonography performed in the ICU has the advantage of being portable, and it is an excellent technique for identifying

Table 2. Common causes of intra-abdominal infection in patients in the intensive care unit

Perforation of GI tract	Diverticular disease
	Peptic ulcer: duodenal, gastric
	Traumatic: penetrating or blunt
	Ischemic
	Malignant
Visceral ischemia	Small bowel, colon from embolism
	Thrombosis, low-flow state, strangulation
	Gall bladder cholecystitis
Postoperative complication	Anastomotic leak
	Intra-abdominal abscess
Solid organ abscess	Liver
	Spleen

GI, gastrointestinal.

intra-abdominal abscesses, detecting free fluid, and evaluating the biliary tree. However it is operator dependent and difficult to perform in patients who have abdominal dressings or paralytic ileus. Ultrasonography can also be used to aspirate or drain intra-abdominal fluid collections and to obtain fluid for culture and sensitivity.

The standard technique for the evaluation of the abdomen in the critically ill patient is computerized tomography (CT) (56, 57). With the combined use of intravenous and oral or rectal contrast, most causes of secondary peritonitis can be readily diagnosed. Abnormal collections in the peritoneal cavity or retroperitoneum are readily evident, and infection is suggested by demonstration of intracavitary air, inhomogeneity of contents, or the characteristic rim enhancement of an abscess capsule (Fig. 1, *top*); inflammation is further suggested by edema and stranding of the mesenteric fat. The CT scan may also show extraluminal passage of contrast medium, indicating a leak, or bowel distension and a point of narrowing, indicating an area of obstruction.

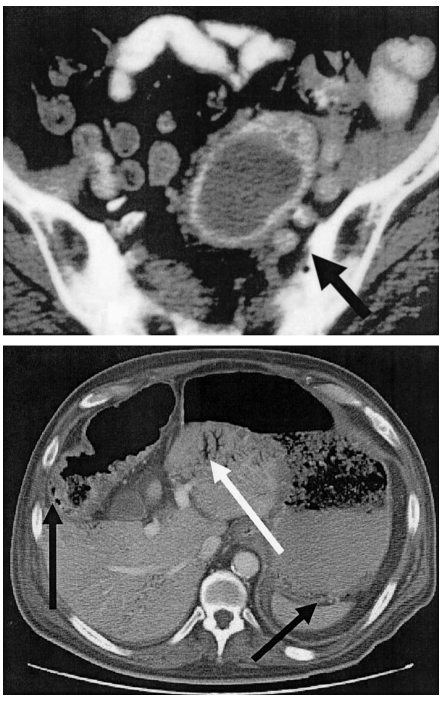

Figure 1. *Top panel*, localized diverticular abscess adjacent to the sigmoid colon; note the rim enhancement of the abscess capsule (*arrow*). *Bottom panel*, CT scan of a 62-yr-old man with intestinal ischemia secondary to low-flow state after coronary artery bypass surgery. Intestinal ischemia is suggested by evidence of pneumatosis in the intestinal wall (*black arrows*) and air in the intrahepatic portal vein (*white arrow*).

Ischemia is suggested by the presence of gas within the wall of the bowel (pneumatosis) or mesenteric vasculature (Fig. 1, *bottom*) or the absence of tissue perfusion; occasionally, an obstructing clot can be seen. The CT scan is an invaluable diagnostic tool, but it does necessitate transfer of a potentially unstable patient from the ICU. Moreover, radioiodinated contrast agents can aggravate renal dysfunction, although one report suggests that the severity of the injury can be attenuated by premedication with acetylcysteine (600 mg, twice daily) (58). Renal dysfunction or paralytic ileus are relative contraindications to CT scanning; the risks must be weighed against the potential benefits.

Radionuclide scans have only a very limited role in the diagnosis of intra-abdominal infection in the critically ill patient because they lack specificity and do not permit image-guided management of any collections that are found. The logistic challenges of transferring a critically ill patient to a magnetic resonance imaging facility render this test impractical in most circumstances.

Finally, intra-abdominal infection can often be demonstrated by more invasive interventions performed within the ICU. Judicious probing of surgical wounds with a sterile culture swab or a gloved finger can often identify collections of infected material immediately adjacent to the incision. Diagnostic peritoneal lavage performed in the ICU may reveal bacteria and white cells, bile, and intestinal contents (59); a bloody lavage return suggests the diagnosis of acute intestinal ischemia. Laparoscopic evaluation of the peritoneal cavity can be performed at the bedside in the ICU (40) and has been reported to reduce the need for unnecessary laparotomy (60). However laparoscopy also requires an adequately equipped operating suite, and it usually necessitates transfer of the patient from the ICU. Moreover, adhesions from previous surgery or infection may make visualization more difficult, and the pneumoperitoneum necessary for proper visualization of the peritoneal cavity can compromise venous return. Experience with diagnostic laparoscopy in critically ill patients is largely anecdotal (61), and although successful laparoscopic management of intra-abdominal abscesses has been reported (62), CT remains the most useful diagnostic and therapeutic modality in the contemporary ICU setting.

Management

The initial management of the patient with intra-abdominal infection is resuscitation and physiologic organ system support, combined with appropriate monitoring. Early fluid requirements may be substantial because of considerable third-space fluid loss into the peritoneal cavity, the retroperitoneum, and the lumen of the gastrointestinal tract. For patients with extensive intraperitoneal or retroperitoneal inflammation and significant early fluid requirements, monitoring of bladder pressures to detect an abdominal compartment syndrome should be performed (63).

Systemic antibiotics are administered based on knowledge of the probable composition of the infecting flora (Table 1). Coverage is directed against aerobic Gram-negative organisms and anaerobes when the source of contamination is unknown; however, if the infection is known to arise from the upper gastrointestinal tract (for example, as a result of a perforated ulcer), coverage directed against aerobes alone is adequate (64).

The selection of an empiric broad-spectrum antibiotic regimen is guided by considerations of patient-specific toxicity, cost, and local patterns of antimicrobial resistance; the many available regimens are of largely equivalent clinical efficacy (Table 3) (65). The optimal duration of therapy is unknown. When source control has been effective (see below), the role of antibiotics is a purely adjuvant one (66), and the course can be restricted to 5–7 days (67).

Although mortality rates are higher when the enterococcus is isolated from polymicrobial intra-abdominal infections (26), there is no compelling evidence that providing specific anti-enterococcal therapy improves the clinical outcome (68, 69). Similarly, although the isolation of *Candida* at the time of abdominal abscess drainage identifies a patient at increased risk of mortality (43, 70), there is no convincing evidence that antifungal therapy alters this risk (71).

For the patient with tertiary peritonitis, the role of systemic antimicrobial therapy is poorly defined. There is little evidence that antibiotics significantly alter the clinical course; moreover, the infecting organisms tend to be resistant to the commonly used empiric regimens (3, 47, 72). We favor the use of narrow-spectrum agents, selecting on the basis of the results of culture and sensitivity and

Table 3. Recommended antimicrobial regimens for high-risk patients with intra-abdominal infection

Single agents
Imipenem/cilastatin
Meropenem
Piperacillin/tazobactam
Combination therapy
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)

Adapted with permission from Mazuski et al (65).

avoiding antibiotics with anti-anaerobic activity.

The definitive management of intra-abdominal infection must include source control—those physical measures that are undertaken to eradicate a focus of infection, to prevent ongoing contamination, and ultimately to restore optimal anatomy and function (73–75). Source control measures are based on three principles—drainage, debridement, and definitive management. Because successful management of even the most complicated intra-abdominal infection depends on the optimal application of these principles, it is instructive to review them in greater detail (Table 4).

Drainage. The inflammatory response evoked by intra-abdominal infection (see above) results in the local activation of coagulation, with the deposition of fibrin and the formation of an abscess—a collection of tissue debris, bacteria, neutrophils and macrophages, and protein-rich exudative fluid enclosed within a fibrous capsule (Fig. 2). Formation of an abscess serves to isolate the infection from the surrounding sterile tissues but also prevents the influx of further host immune cells or antibiotics: the result is a biologic standoff. Drainage converts an abscess to a controlled sinus (an abnormal communication between a deep space and an epithelial surface) or fistula (an abnormal communication between two epithelially lined surfaces) and, in essence, externalizes the infectious process. Drainage can be accomplished by several different strategies. Open surgical drainage has been the classical treatment strategy, and it permits definition of the extent of the collection and immediate evacuation of its contents. Ideally, drainage is accomplished by the most direct route, minimizing contamination of the peritoneal cavity (76), although with the use of adjuvant antibiotics, the benefits of extraserous drainage are minimal and often offset by the advantage that wider exposure gives for full exploration and management of the inciting cause of the infection.

Table 4. Definitions and concepts in the management of intra-abdominal infection

Peritonitis	Inflammation of the peritoneal lining of the abdominal cavity
Abscess	Collection of tissue fluid, neutrophils, and bacteria enclosed in a fibrin capsule
Fistula	Abnormal communication between two epithelially lined surfaces
Sinus	Cavity communicating with an epithelially lined surface
Drainage	Conversion of an abscess to a controlled sinus or fistula
Debridement	Physical removal of infected or necrotic solid tissue

More recently, however, with the recognition that the biologic objectives of drainage can be accomplished without the need for operative intervention, percutaneous drainage guided by ultrasound or CT has become the initial intervention of choice in the management of a localized, radiologically defined infectious focus (77). Initial reports of the efficacy of percutaneous drainage for well-demarcated, unilocular collections (78) led to an expansion of its indications to include multiple collections, those in relatively inaccessible anatomic locations, and collections containing solid debris or communicating with the gastrointestinal tract (79). Moreover, percutaneous drainage can serve as a temporizing measure useful, for example, in decompressing infected retroperitoneal collections in the patient with necrotizing pancreatitis so that operative intervention can be deferred until it is safer (Fig. 3).

The relative merits of operative and percutaneous drainage have never been compared in a formal randomized trial, although case series with historical controls (80–82) and an expanding clinical experience point to the utility of an initial attempt at percutaneous drainage for most patients with intra-abdominal abscesses. Surgical drainage is indicated for failures of percutaneous drainage, for collections with a significant solid tissue component requiring debridement, for simultaneous management of a source of ongoing contamination, and when local peritoneal defenses have not contained the infectious focus, leading to generalized peritonitis (Fig. 4).

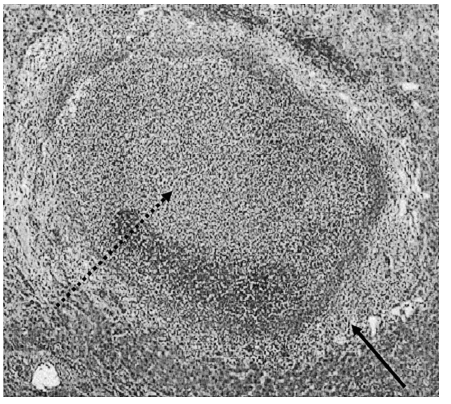

Figure 2. Photomicrograph of an intrahepatic abscess. Note dense accumulation of neutrophils (*dashed arrow*) and fibrous capsule (*solid arrow*) that walls off the abscess from surrounding normal liver tissue.

Debridement. In contrast to drainage, which eliminates the liquid component of an infection, debridement is the physical removal of infected or necrotic solid tissue. The term encompasses, for example, the excision of necrotic infected peripancreatic fat in patients with infected pancreatic necrosis, the removal of feces and intestinal contents from the peritoneal cavity of the patient with a perforation of the gastrointestinal tract, the excision of necrotic intestine in the patient with acute intestinal ischemia, or the excision of abdominal wall muscle in the patient

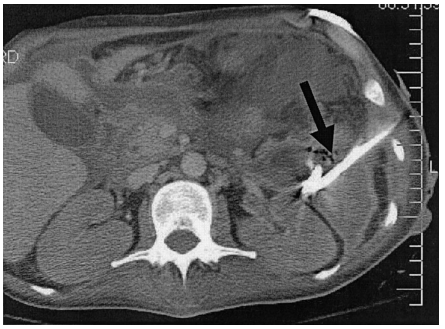

Figure 3. Percutaneous drainage of the fluid component of a peripancreatic abscess (*arrow*) facilitated a delay in surgical intervention until 5 wks after the onset of disease. Residual infected necrotic tissue was removed by laparoscopic debridement.

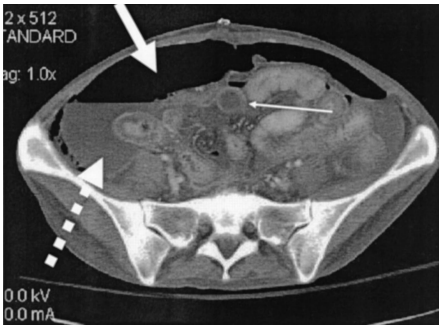

Figure 4. Diffuse peritonitis secondary to a leak from an unrecognized defect in the rectum after elective ileocolic resection for Crohn's disease. Peritoneal inflammation is suggested by enhancement of intestinal wall (*thin arrow*). Presence of fluid (*large dashed arrow*) and air (*large solid arrow*) throughout the peritoneal cavity renders percutaneous drainage ineffective.

with a secondary necrotizing soft-tissue infection. It also includes the removal of foreign bodies and such adjuvants for bacterial growth as blood clot and devitalized tissue.

The need for debridement is encountered less frequently in patients with intra-abdominal infection, exceptions including the patient with intestinal infarction or infected peripancreatic necrosis. Intestinal infarction is a catastrophic complication, having a prohibitively high mortality rate unless the necrotic bowel is rapidly excised (83). In contrast, although infected peripancreatic necrosis is associated with a significant rate of mortality and major morbidity, prognosis is improved if operative intervention is delayed (84). The reason for this discrepancy underlines a fundamental principle in the source control management of intra-abdominal infection—that the benefits of intervention must be balanced against the risks associated with intervention. In the case of intestinal ischemia, leakage of bacteria through the necrotic bowel wall is considerable, whereas surgical intervention to excise the necrotic bowel is a relatively straightforward undertaking. The bacterial burden in infected retroperitoneal necrosis, on the other hand, is lower, and organisms sequestered in the necrotic tissue are less able to gain access to the circulation. At the same time, early surgical exploration of the retroperitoneum is fraught with hazard because the demarcation between viable and nonviable tissue is poor, leading to a significant risk of major hemorrhage, and operative exposure of this area is difficult (85). Thus, evolving approaches to the management of infected pancreatic necrosis emphasize the importance of delayed, rather than immediate, intervention (86, 87).

Irrigation of the peritoneal cavity to remove bacteria, devitalized tissue, and fibrin can also be considered a form of debridement. Although the practice is popular with many surgeons, there is no convincing evidence of its utility (88). Similarly, a randomized trial of peritoneal debridement to remove fibrin attached to loops of bowel also failed to show any evidence of benefit (89).

Definitive Measures. The definitive management of intra-abdominal infection includes measures to remove foci of ongoing contamination and to restore, as much as possible, normal structure and function. Such measures include, for example, the excision of an area of diverticular disease containing a perforation in the patient with diverticulitis and restoring function either by the creation of an end colostomy of the descending colon (when the distal rectal stump is closed and left in the abdomen, this is known as a Hartmann procedure) or by creating an anastomosis between the two ends of the remaining colon (primary anastomosis). Pooled data from case series indicate that in patients with perforated diverticulitis, outcomes are improved by excising the involved colon (73) and perhaps even by undertaking a primary anastomosis (90–93). The benefits of more extensive intervention must be weighed against the risks of that intervention. For the patient with a contained diverticular abscess, it may well be preferable to drain the abscess percutaneously and to plan an elective sigmoid resection with primary anastomosis at a later date. For the critically ill patient with cholecystitis or even an empyema of the gall bladder, percutaneous cholecystostomy may be the safer option to surgical cholecystectomy (94–97).

The approach to the patient with suspected intra-abdominal infection must be based on a combination of evidence from the literature and inference from basic biologic principles, interpreted through a combination of experience and the ability to adapt one's approach to a changing situation.

It is important to consider the options for future reconstructive procedures at the time of the initial source control intervention (98). Incisions should be chosen to permit maximal flexibility at the time of re-operation: a midline abdominal incision probably represents the most versatile approach. Stomas should be planned and sited to accommodate the demands of the management of an open wound and to minimize the magnitude of surgery required for their subsequent closure. Rather than creating multiple stomas, for example, it is generally preferable to reconstruct the distal gastrointestinal tract but to protect potentially tenuous anastomoses with a proximal loop enterostomy: subsequent reconstruction will simply require local closure of the loop enterostomy.

Occasionally, circumstances are such that even the most basic of definitive procedures—abdominal wall closure, for example—are hazardous. In the patient with loss of the abdominal wall from associated soft-tissue infection or extensive edema of the viscera and abdominal wall, closure will result in increased intra-abdominal pressure, resulting in abdominal compartment syndrome. Open management of the abdomen is advisable, using absorbable mesh or a nonadhering prosthesis to prevent evisceration of the

intestinal contents. Beyond circumstances of necessity, however, there is little evidence that approaches such as scheduled re-laparotomy or an open-abdomen approach improve patient outcome (99–102). Rather, these are associated with worsening of organ dysfunction, amplification and persistence of inflammation, and greater use of blood component therapy (103, 104).

Successful source control and antibiotic management of intra-abdominal infection is associated with resolution of systemic signs and symptoms of acute inflammation (105) and reversal of organ dysfunction. Conversely, progression or failure of resolution of organ dysfunction suggests persistence of the disease and the need for further intervention (106).

Although the management of the critically ill patient with peritonitis is commonly challenging, often frustrating, and invariably costly, long-term quality of life in survivors is very good (107, 108), and cost-utility ratios are favorable, with a cost per quality-adjusted life years of less than $3000 (109), thus, fully justifying the efforts expended in this complex patient population.

Approach to the Patient with Suspected Intra-abdominal Infection

The antecedents of intra-abdominal infection in the critically ill patient are many, the clinical presentations highly varied, and the associated factors that complicate one approach or another in the individual patient are numerous. It is, therefore, neither possible nor advisable to present a simple management algorithm that is likely to define the best specific option in a particular patient. Rather, the decision of how to manage a problem must be individualized and based on the principles articulated above and on the unique features of the particular patient. Nonetheless, it is entirely possible to outline the elements of the decision-making process without anticipating the final decision, and Figure 5 provides an algorithm for an approach to the management of suspected intra-abdominal infection in the critically ill patient.

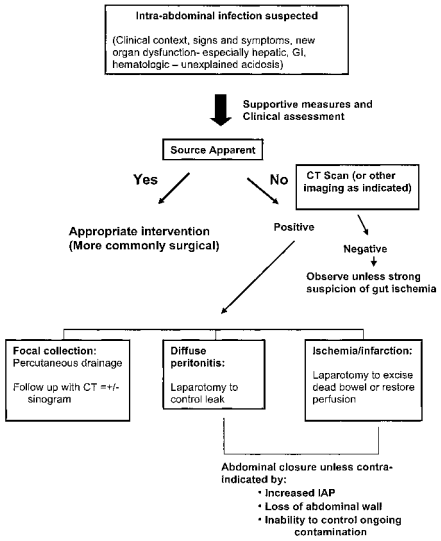

Figure 5. An approach to the management of a critically ill patient with suspected intra-abdominal infection. *GI*, gastrointestinal; *CT*, computerized tomography; *IAP*, intraabdominal pressure.

The suspicion that something is amiss within the peritoneal cavity arises because of characteristic signs and symptoms that, however, are often difficult to interpret in the ICU setting. The development of new organ dysfunction, particularly that involving the gastrointestinal system, liver, or hematologic system, raises the possibility of intra-abdominal infection, as does the development of unexplained metabolic acidosis. However, the paramount consideration is the clinical setting. Is the patient at risk for infection because of recent abdominal surgery? Is there a source of arterial emboli, evidence of peripheral vascular disease, a thrombotic disorder, a history of recent arteriography, or a history of reduced splanchnic flow as a result of the use of vasopressors or prolonged shock? The absence of such risk factors makes the abdomen much less likely to be the source of an explanation for unexplained clinical deterioration.

If a source is readily apparent, for example, pus or gastrointestinal content is leaking from an abdominal wound, or intraperitoneal free air is demonstrated on a chest radiograph, then intervention should be undertaken without delay. Typically, this will entail operation rather than image-guided therapy. If no source is seen, then CT with oral, rectal, and intravenous contrast enhancement should be performed. The accuracy of the CT scan is such that further decisions are made on the basis of its findings. A focal or contained collection can be drained percutaneously, with a follow-up CT scan or sinogram, injecting water-soluble contrast medium into the drain, to confirm resolution. If there is evidence of a diffuse and nonlocalized process, then operative intervention is indicated. Similarly, if there is evidence of ischemia or infarction, then operation should be undertaken, unless there are compelling grounds for an alternative approach. The indication for surgery in the patient with gut ischemia is to restore flow or to resect dead bowel; for the patient with ischemia as a result of venous thrombosis or a low-flow state, neither of these options may be possible, and it may be preferable to observe the patient while maximizing splanchnic flow with anti-coagulants and hemodynamic support.

A negative abdominal CT scan generally indicates a very low probability of a process that can be reversed through surgical intervention, and if no treatable pathologic process is seen, then continued observation is appropriate. With advances in imaging technology, the era of blind surgical exploration to diagnose occult infection has almost ended (110).

Conclusions

Intra-abdominal infection is a common indication for ICU admission and an important cause of preventable morbidity and mortality after ICU admission. The disorders responsible for these infections are numerous, and their clinical presentation and optimal management are highly variable. The approach to the patient with suspected intra-abdominal infection must be based on a combination of evidence from the literature and inference from basic biologic principles, interpreted through a combination of experience and the ability to adapt one's approach to a changing situation. Even with optimal management, the short- and long-term morbidity can be substantial: close collaboration between surgeon, radiologist, and intensivist holds the key to minimizing these.

REFERENCES

1. Evans HL, Raymond DP, Pelletier SJ, et al: Diagnosis of intra-abdominal infection in the critically ill patient. *Curr Opin Crit Care* 2001; 7:117–121
2. Bohnen J, Boulanger M, Meakins JL, et al: Prognosis in generalized peritonitis: Relation to cause and risk factors. *Arch Surg* 1983; 118:285–290
3. Nathens AB, Rotstein OD, Marshall JC: Tertiary peritonitis: Clinical features of a complex nosocomial infection. *World J Surg* 1998; 22:158–163
4. Skillman JJ, Bushnell LS, Goldman H, et al:

Respiratory failure, hypotension, sepsis, and jaundice: A clinical syndrome associated with lethal hemorrhage and acute stress ulceration in the stomach. *Am J Surg* 1969; 117:523–530
5. Fry DE, Garrison RN, Heitsch RC, et al: Determinants of death in patients with intraabdominal abscess. *Surgery* 1980; 88: 517–523
6. Polk HC, Shields CL: Remote organ failure: A valid sign of occult intraabdominal infection. *Surgery* 1977; 81:310–313
7. Heemken R, Gandawidjaja L, Hau T: Peritonitis: Pathophysiology and local defense mechanisms. *Hepatogastroenterology* 1997; 44:927–936
8. Hall JC, Heel KA, Papadimitriou JM, et al: The pathobiology of peritonitis. *Gastroenterology* 1998; 114:185–196
9. Holzheimer RG, Schein M, Wittmann DH: Inflammatory response in peritoneal exudate and plasma of patients undergoing planned relaparotomy for severe secondary peritonitis. *Arch Surg* 1995; 130:1314–1320
10. Riese J, Schoolmann S, Denzel C, et al: Effect of abdominal infections on peritoneal and systemic production of interleukin 6 and monocyte chemoattractant protein-1. *Shock* 2002; 17:361–364
11. Broche A, Tellado J: Defense mechanisms of the peritoneal cavity. *Curr Opin Crit Care* 2001; 7:105–116
12. Finlay-Jones JJ, Davies KV, Sturm LP, et al: Inflammatory processes in a murine model of intra-abdominal abscess formation. *J Leuk Biol* 1999; 66:583–587
13. McRitchie DI, Girotti MJ, Glynn MFX, et al: Effect of systemic fibrinogen depletion on intraabdominal abscess formation. *J Lab Clin Med* 1991; 118:48–55
14. Hau T, Simmons RL: Heparin in the treatment of experimental peritonitis. *Ann Surg* 1978; 187:294–298
15. Holzer K, Konietzny P, Wilhelm K, et al: Phagocytosis by emigrated, intra-abdominal neutrophils is depressed during human secondary peritonitis. *Eur Surg Res* 2002; 34:275–284
16. Rotstein OD, Pruett TL, Simmons RL: Fibrin in peritonitis: V. Fibrin inhibits phagocytic killing of *Escherichia coli* by human polymorphonuclear leukocytes. *Ann Surg* 1986; 203:413–419
17. Lee A: Neglected niches: The microbial ecology of the gastrointestinal tract. *Adv Microb Ecol* 1985; 8:115–162
18. Savage DC: Microbial ecology of the gastrointestinal tract. *Annu Rev Med* 1977; 31: 107–133
19. Onderdonk AB, Bartlett JG, Louie T, et al: Microbial synergy in experimental intraabdominal abscess. *Infect Immun* 1997; 13: 22–26
20. Van Der Waaij D: The ecology of the human intestine and its consequences for overgrowth by pathogens such as *Clostridium difficile*. *Annu Rev Microbiol* 1989; 43: 69–87
21. Berg RD: Promotion of the translocation of enteric bacteria from the gastrointestinal tracts of mice by oral treatment with penicillin, clindamycin, or metronidazole. *Infect Immun* 1981; 33:854–861
22. Thomakos N, Maraki S, Liakakos T, et al: Effect of cefamandole, cefuroxime and cefoxitin on yeast fecal flora of surgical patients. *Chemotherapy* 2003; 44:324–327
23. Van der Leur JJ, Thunnissen PL, Clasener HA, et al: Effects of imipenem, cefotaxime and cotrimoxazole on aerobic microbial colonization of the digestive tract. *Scand J Infect Dis* 1993; 25:473–478
24. Donskey CJ, Chowdhry TK, Hecker MT, et al: Effect of antibiotic therapy on the density of vancomycin-resistant enterococci in the stool of colonized patients. *N Engl J Med* 2000; 343:1925–1932
25. Marshall JC, Christou NV, Meakins JL: The gastrointestinal tract: The "undrained abscess" of multiple organ failure. *Ann Surg* 1993; 218:111–119
26. Sitges-Serra A, Lopez MJ, Girvent M, et al: Postoperative enterococcal infection after treatment of complicated intra-abdominal sepsis. *Br J Surg* 2002; 89:361–367
27. Fierobe L, Decre D, Muller C, et al: Methicillin-resistant *Staphylococcus aureus* as a causative agent of post-operative intra-abdominal infection: Relation to nasal colonization. *Clin Infect Dis* 1999; 29: 1231–1238
28. Riche FC, Cholley BP, Panis YH, et al: Inflammatory cytokine response in patients with septic shock secondary to generalized peritonitis. *Crit Care Med* 2000; 28: 433–437
29. Hynninen M, Valtonen M, Markkanen H, et al: Intramucosal pH and endotoxin and cytokine release in severe acute pancreatitis. *Shock* 2000; 13:79–82
30. Fry DE, Pearlstein L, Fulton RL, et al: Multiple system organ failure: The role of uncontrolled infection. *Arch Surg* 1980; 115: 136–140
31. Tran DD, Groeneveld ABJ, Van der Meulen J, et al: Age, chronic disease, sepsis, organ system failure, and mortality in a medical intensive care unit. *Crit Care Med* 1990; 18:474–479
32. Conn HO: Spontaneous peritonitis and bacteremia in Laennec's cirrhosis caused by enteric organisms. *Ann Intern Med* 1964; 60:568–580
33. Guarner C, Soriano G: Spontaneous bacterial peritonitis. *Semin Liver Dis* 1997; 17: 203–217
34. Sola R, Soriano G: Why do bacteria reach ascitic fluid? *Eur J Gastroenterol Hepatol* 2002; 14:351–354
35. Cirera I, Bauer TM, Navasa M, et al: Bacterial translocation of enteric organisms in patients with cirrhosis. *J Hepatol* 2001; 34: 150–155
36. Fernandez J, Navasa M, Gomez J, et al: Bacterial infections in cirrhosis: epidemiological changes with invasive procedures and norfloxacin prophylaxis. *Hepatology* 2002; 35:140–148
37. Campillo B, Richardet JP, Kheo T, et al: Nosocomial spontaneous bacterial peritonitis and bacteremia in cirrhotic patients: Impact of isolate type on prognosis and characteristics of infection. *Clin Infect Dis* 2002; 35:1–10
38. Ljubcic N, Spajic D, Vrkljan MMM, et al: The value of ascitic fluid polymorphonuclear cell count determination during therapy of spontaneous bacterial peritonitis in patients with liver cirrhosis. *Hepatogastroenterology* 2000; 47:1360–1363
39. Soares-Weiser K, Brezis M, Leibovici L: Antibiotics for spontaneous bacterial peritonitis in cirrhotics. *Cochrane Database Syst Rev* 2001; 3:CD002232
40. Thuluvath PJ, Morss S, Thompson R: Spontaneous bacterial peritonitis: In-hospital mortality, predictors of survival, and health care costs from 1988 to 1998. *Am J Gastroenterol* 2001; 96:1232–1236
41. Marshall JC, Spencer-Netto F: Secondary bacterial peritonitis. *Prob Gen Surg* 2002; 19:53–64
42. Laroche M, Harding G: Primary and secondary peritonitis: An update. *Eur J Clin Biol Microbiol Infect Dis* 1998; 17:542–550
43. Hoerauf A, Hammer S, Muller-Myhsok B, et al: Intra-abdominal *Candida* infection during acute necrotizing pancreatitis has a high prevalence and is associated with increased mortality. *Crit Care Med* 1998; 26: 2010–2015
44. Akriviadis EA, Runyon BA: Utility of an algorithm in differentiating spontaneous from secondary bacterial peritonitis. *Gastroenterology* 1990; 98:127–133
45. Buijk SE, Bruining HA: Future directions in the management of tertiary peritonitis. *Intensive Care Med* 2002; 28:1024–1029
46. Malangoni MA: Evaluation and management of tertiary peritonitis. *Am Surg* 2000; 66:157–161
47. Rotstein OD, Pruett TL, Simmons RL: Microbiologic features and treatment of persistent peritonitis in patients in the intensive care unit. *Can J Surg* 1986; 29:247–250
48. Marshall JC, Christou NV, Horn R, et al: The microbiology of multiple organ failure: The proximal GI tract as an occult reservoir of pathogens. *Arch Surg* 1988; 123:309–315
49. Sawyer RG, Rosenlof LK, Adams RB, et al: Peritonitis into the 1990's: Changing pathogens and changing strategies in the critically ill. *Am Surg* 1992; 58:82–87
50. Johnson CC, Baldessarre J, Levison ME: Peritonitis: Update on pathophysiology, clinical manifestations, and management. *Clin Infect Dis* 1997; 24:1035–1047
51. Kaleya RN, Boley SJ: Acute mesenteric ischemia. *Crit Care Clin* 1995; 11:479–512
52. Stoney RJ, Cunningham CG: Acute mesenteric ischemia. *Surgery* 1993; 114:489–490
53. Le Gall JR, Fagniez PL, Meakins JL, et al: Diagnostic features of early high post-

laparotomy fever: A prospective study of 100 patients. *Br J Surg* 1982; 69:452–455
54. Ing AFM, Mclean APH, Meakins JL: Multiple organism bacteremia in the surgical intensive care unit: A sign of intraperitoneal sepsis. *Surgery* 1981; 90:779–786
55. Adam EJ, Page JE: Intra-abdominal sepsis: The role of radiology: *Baillieres Clin Gastroenterol* 1991; 5(3Pt1):587–609
56. Fry DE: Noninvasive imaging tests in the diagnosis and treatment of intra-abdominal abscess in the postoperative patient. *Surg Clin North Am* 1994; 74:693–709
57. Velmahos GC, Kamel E, Berne TV, et al: Abdominal computed tomography for the diagnosis of intra-abdominal sepsis in critically injured patients: Fishing in murky waters. *Arch Surg* 1999; 134:831–838
58. Tepel M, van der Giet M, Schwarzfeld C, et al: Prevention of radiographic contrast agent-induced reductions in renal function by acetylcysteine. *N Engl J Med* 2000; 343: 180–184
59. Alverdy JC, Saunders J, Chamberlin WH, et al: Diagnostic peritoneal lavage in intra-abdominal sepsis. *Am Surg* 1988; 54: 456–459
60. Gagne DJ, Malay MB, Hogle NJ, et al: Bedside diagnostic minilaparoscopy in the intensive care patient. *Surgery* 2003; 131: 491–496
61. Gorecki P: The role of laparoscopy. *In:* Source Control: A Guide to the Management of Surgical Infections. Schein M, Marshall JC (Eds). Berlin, Springer-Verlag, 2002, pp 350–357
62. Kok KY, Yapp SK: Laparoscopic drainage of postoperative complicated intra-abdominal abscesses. *Surg Laparosc Endosc Percutan Tech* 2000; 10:311–313
63. Schein M, Wittmann DH, Aprahamian CC, et al: The abdominal compartment syndrome: The physiological and clinical consequences of elevated intra-abdominal pressure. *J Am Coll Surg* 1995; 180:745–753
64. Nathens AB, Rotstein OD: Therapeutic options in peritonitis. *Surg Clin North Am* 1997; 74:677–692
65. Mazuski JE, Sawyer RG, Nathens AB, et al: The Surgical Infection Society guidelines on antimicrobial therapy for intra-abdominal infections: An executive summary. *Surg Infect* 2002; 3:161–173
66. Sotto A, Lefrant JY, Fabbro-Peray P, et al: Evaluation of antimicrobial therapy management of 120 consecutive patients with secondary peritonitis. *J Antimicrob Chemother* 2002; 50:569–576
67. Wittmann DH, Schein M: Let us shorten antibiotic prophylaxis and therapy in surgery. *Am J Surg* 1996; 172:26S–32S
68. Barie PS, Christou NV, Dellinger EP, et al: Pathogenicity of the enterococcus in surgical infections. *Ann Surg* 1990; 212:155–159
69. Röhrborn A, Wacha H, Schöffel U, et al: Coverage of enterococci in community acquired secondary peritonitis: Results of a randomized trial. *Surg Infect* 2000; 1:95–107
70. Calandra T, Bille J, Schneider R, et al: Clinical significance of *Candida* isolated from peritoneum in surgical patients. *Lancet* 1989; 2:1437–1440
71. Sandven P, Qvist H, Skovlund P, et al: Significance of *Candida* recovered from intraoperative specimens in patients with intra-abdominal perforations. *Crit Care Med* 2002; 30:541–547
72. Roehrborn A, Thomas L, Potreck O, et al: The microbiology of postoperative peritonitis. *Clin Infect Dis* 2001; 33:1513–1519
73. Jimenez MF, Marshall JC: Source control in the management of sepsis. *Intensive Care Med* 2001; 27:S49–S62
74. Grunau G, Heemken R, Hau T: Predictors of outcome in patients with post-operative intra-abdominal infection. *Eur J Surg* 2002; 162:619–625
75. Seiler CA, Brugger L, Forssmann U, et al: Conservative surgical treatment of diffuse peritonitis. *Surgery* 2000; 127:178–184
76. Spain DA, Martin RC, Carrillo EH, et al: Twelfth rib resection: Preferred therapy for subphrenic abscess in selected surgical patients. *Arch Surg* 1997; 132:1203–1206
77. van Sonnenberg E, Wittich GR, Goodacre BW, et al: Percutaneous abscess drainage: Update. *World J Surg* 2001; 25:362–372
78. Gerzof SG, Robbins AH, Johnson WC, et al: Percutaneous catheter drainage of abdominal abscesses: A five-year experience. *N Engl J Med* 1981; 305:653–657
79. Gerzof SG, Robbins AH, Johnson WC, et al: Expanded criteria for percutaneous abscess drainage. *Arch Surg* 1985; 120:227
80. Olak JO, Christou NV, Stein LA, et al: Operative versus percutaneous drainage of intra-abdominal abscesses. *Arch Surg* 1986; 121:141
81. Hemming A, Davis NL, Robins RE: Surgical versus percutaneous drainage of intra-abdominal abscesses. *Am J Surg* 1991; 161: 593–595
82. Bufalari A, Giustozzi G, Moggi L: Postoperative intraabdominal abscesses: Percutaneous versus surgical treatment. *Acta Chir Belg* 1996; 96:197–200
83. Raymond DP, May AK: Acute mesenteric ischemia. *In:* Source Control: A Guide to the Management of Surgical Infections. Schein M, Marshall JC (Eds). Berlin, Springer-Verlag, 2003, pp 178–190
84. Mier J, Leon EL, Castillo A, et al: Early versus late necrosectomy in severe necrotizing pancreatitis. *Am J Surg* 1997; 173: 71–75
85. Urbach DR, Marshall JC: Pancreatic abscess and infected pancreatic necrosis. *Curr Opin Surg Infect* 1996; 4:57–66
86. Dellinger P: Pancreatic infection. *In:* Source Control: A Guide to the Management of Surgical Infections. Schein M, Marshall JC (Eds). Berlin, Springer-Verlag, 2003, pp 154–166
87. Fernandez-del Castillo C, Rattner DW, Makary MA, et al: Debridement and closed packing for the treatment of necrotizing pancreatitis. *Ann Surg* 1998; 228:676–684
88. Platell C, Papadimitriou JM, Hall JC: The influence of lavage on peritonitis. *J Am Coll Surg* 2000; 191:672–680
89. Hudspeth AS: Radical surgical debridement in the treatment of advanced generalized bacterial peritonitis. *Arch Surg* 1975; 110: 1233–1236
90. Schilling MK, Maurer CA, Kollmar O, et al: Primary vs. secondary anastomosis after sigmoid colon resection for perforated diverticulitis (Hinchey Stage III and IV): A prospective outcome and cost analysis. *Dis Col Rect* 2001; 44:699–703
91. Gooszen AW, Tollenaar RA, Geelkerken RH, et al: Prospective study of primary anastomosis following sigmoid resection for suspected acute complicated diverticular disease. *Br J Surg* 2001; 88:693–697
92. Biondo S, Jaurrieta E, Marti Rague J, et al: Role of resection and primary anastomosis of the left colon in the presence of peritonitis. *Br J Surg* 2000; 87:1580–1584
93. Zeitoun G, Laurent A, Rouffet F, et al: Multicentre, randomized clinical trial of primary versus secondary sigmoid resection in generalized peritonitis complicating sigmoid diverticulitis. *Br J Surg* 2000; 87: 1366–1374
94. Hamy A, Visset J, Likholatnikov D, et al: Percutaneous cholecystostomy for acute cholecystitis in critically ill patients. *Surgery* 1997; 121:398–401
95. Boggi U, Candio G, Campatelli A, et al: Percutaneous cholecystostomy for acute cholecystitis in critically ill patients. *Hepatogastroenterology* 1999; 46:121–125
96. Melin MM, Sarr MG, Bender CE, et al: Percutaneous cholecystostomy: A valuable technique in high-risk patients with presumed acute cholecystitis. *Br J Surg* 1995; 82:1274–1277
97. Boland G, Lee MJ, Mueller PR: Acute cholecystitis in the intensive care unit. *Crit Care Med* 1993; 1:246–250
98. Rotstein OD: Reoperation after source control surgery for intra-abdominal infection. *In:* Source Control: A Guide to the Management of Surgical Infections. Schein M, Marshall JC (Eds). Berlin, Springer-Verlag, 2003, pp 300–311
99. Christou NV, Barie PS, Dellinger EP, et al: Surgical Infection Society intra-abdominal infection study: Prospective evaluation of management techniques and outcome. *Arch Surg* 1993; 128:193–198
100. Schein M, Hirshberg A, Hashmonai M: Current surgical management of severe intra-abdominal infection. *Surgery* 1992; 112: 489–496
101. Hau T, Ohmann C, Wolmershauser A, et al: Planned relaparotomy versus relaparotomy on demand in the treatment of intra-abdominal infections. *Arch Surg* 1995; 130: 1193–1197
102. Lamme B, Boermeester MA, Reitsma JB, et

al: Meta-analysis of relaparotomy for secondary peritonitis. *Br J Surg* 2002; 89: 1516–1524
103. Zugel N, Siebeck M, Geissler B, et al: Circulating mediators and organ function in patients undergoing planned relaparotomy vs conventional surgical therapy in severe secondary peritonitis. *Arch Surg* 2002; 137: 590–599
104. van Goor H, Hulsebos RG, Bleichrodt RP: Complications of planned relaparotomy in patients with severe general peritonitis. *Eur J Surg* 1997; 163:61–66
105. Stone HH, Bourneuf AA, Stinson LD: Reliability of criteria for predicting persistent or recurrent sepsis. *Arch Surg* 1985; 120: 17–20
106. Paugam-Burtz C, Dupont H, Marmuse JP, et al: Daily organ-system failure for diagnosis of persistent intra-abdominal sepsis after postoperative peritonitis. *Intensive Care Med* 2002; 28:594–598
107. Scheingraber S, Kurz T, Dralle H: Short- and long-term outcome and health-related quality of life after severe peritonitis. *World J Surg* 2002; 26:667–671
108. Bosscha K, Reijnders K, Jacobs MH, et al: Quality of life after severe bacterial peritonitis and infected necrotizing pancreatitis treated with open management of the abdomen and planned re-operations. *Crit Care Med* 2001; 29:1539–1543
109. Welcker K, Lederle J, Schorr M, et al: Surgery and adjuvant therapy in patients with diffuse peritonitis: Cost analysis. *World J Surg* 2002; 26:307–313
110. Bunt TJ: Non-directed relaparotomy for intraabdominal sepsis: A futile procedure. *Am Surg* 1986; 52:294