17 NOSOCOMIAL INFECTION

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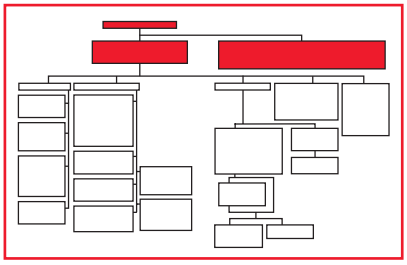
Approach to Postoperative Symptoms of Infection



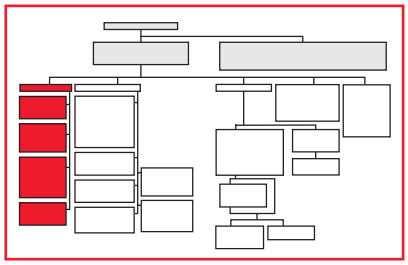
Nosocomial infections are a potential threat to all hospitalized patients. They increase morbidity and mortality, prolong hospital stay, increase patient care costs,[1-5] and occur in almost every body site.

At any time during hospitalization, but especially postoperatively, the onset of fever or an elevated white blood cell count may signal an infectious process. Fever that begins or persists after postoperative day 4 is more likely to represent true infection. Although an infection will not develop in many febrile postoperative patients [*see* Discussion, *below*], a careful, directed examination of the patient, guided by history and operative procedure, should be undertaken, including inspection of the ears and the pharynx. Laboratory tests and x-rays are complementary. The use of empirical antibiotics or the prolonged administration of perioperative prophylactic antibiotics in the absence of a specific diagnosis is rarely efficacious. In fact, either may confuse the clinical picture and may lead to separate toxic or allergic complications. Antibiotics alone rarely constitute an adequate response to infectious complications, especially in the early postoperative period.

Respiratory infections are the most common early infection, with most wound infections presenting between postoperative days 4 and 7 and urinary tract infections (UTIs) occurring throughout hospitalization. However, if a high fever (temperature > 38.9° C [102° F]) develops in a patient within 48 hours of an operation, three diagnoses are most likely: atelectasis [*see 8:5 Pulmonary Insufficiency*], peritonitis caused by a leaking viscus after intra-abdominal operation [*see 8:18 Intra-abdominal Infection*], and invasive wound infection. Of these, atelectasis is most often diagnosed. It is not serious if recognized and treated. It can be diagnosed on the basis of decreased breath sounds, rales, or both on physical examination and on the basis of platelike densities or volume loss on chest x-ray. Atelectasis may be accompanied by hypoxemia and usually responds to standard physical measures. However, many patients with x-ray evidence of atelectasis are not febrile, and more than one third of patients with fever and no other apparent cause have no evidence of atelectasis.[6,7]

Clues to the diagnosis of peritonitis caused by a leaking viscus are knowledge of problems in the conduct of the operative procedure, evidence of the hemodynamic and fluid balance changes that usually accompany a leaking viscus, and suggestive findings on abdominal examination. Technical difficulties with anastomoses, excessive operative blood loss, and multiple bowel injuries can all increase the risk of leakage. Diffuse abdominal tenderness away from the incision, excessive fluid requirements in the early postoperative interval, and tachycardia all suggest iatrogenic peritonitis. Treatment always involves operative intervention and antibiotics. The least common cause of early high postoperative fever is an invasive wound infection, either with β-hemolytic streptococci or with clostridia. Diagnosis is made by local inspection of the wound and by a Gram stain of the wound's contents; treatment requires operative intervention in addition to antibiotics [*see* Infection Related to Operative Site or Injury, *below*].

Respiratory Infection



Pneumonia is the third most common nosocomial infection on surgical services and is the one most commonly associated with death.[8] Diagnosis is not usually difficult in a patient without respiratory failure who is breathing spontaneously. In a patient with acute respiratory distress syndrome (ARDS) who is intubated and being ventilated, however, the diagnosis may be extremely difficult.[9] This is because ARDS is associated with markedly abnormal chest x-ray findings and gas exchange abnormalities and may also include an elevated temperature without infection. A number of techniques for diagnosis, including bronchoalveolar lavage both with and without a bronchoscope and protected specimen brush cultures, have been reported to increase the sensitivity and specificity of diagnosis of pneumonia in this setting but have not been widely adopted.[10,11]

The prevention of pneumonia in ventilated patients would be the best alternative, but there is not widespread agreement about the best means of prevention. Recommendations include standard infection control measures, elevation of the head of the bed, and possibly the use of endotracheal tubes that permit the aspiration of subglottic secretions.[10,12-14]

The diagnosis of pneumonitis or atelectasis (see above) is frequently entertained during the workup of postoperative fever. It is important to remember that a common cause of basilar atelectasis and pleural effusion in the postlaparotomy patient is an inflammatory process below the diaphragm. Tracheitis or bronchitis, as indicated by purulent sputum in the absence of pul-

Approach to Postoperative Symptoms of Infection

Fever or an elevated WBC develops postoperatively

Fever begins or persists after 4th postoperative day

Identify source of infection:
- Perform physical examination guided by history and prior operations.
- Inspect all intravascular devices and urinary catheters.
- Order appropriate x-rays and laboratory tests.

Respiratory infection

Pneumonia, as suggested by ↑ WBC, ↑ temperature, purulent sputum, and lung infiltrate

Give appropriate antibiotics; provide supportive care.

Tracheitis or bronchitis, as suggested by purulent sputum, normal x-ray findings, and endotracheal or tracheostomy intubation

Give appropriate antibiotics if patient is febrile.

Paranasal sinusitis, as suggested by purulent nasal drainage, otitis media, and/or CT findings of fluid, air-fluid levels, and mucosal thickening

Identify pathogen via Gram stain and culture of sinus aspirate. Remove all nasal tubes; administer decongestants and appropriate antibiotics. Perform sinus irrigation or drainage for unresponsive cases.

Otitis media (associated with eustachian tube blockage from nasal tubes or inflammation)

Remove nasal tube, and give decongestants.

Infection related to operative site or injury

Wound infection (incisional SSI), as suggested by erythema, swelling, drainage, and increasing local pain and tenderness

Incise and drain. For minimal local soft tissue and systemic response, treat with dressing changes and no antibiotics. If antibiotics are required, give as follows. **Clean wounds:** Give cefazolin, 1 g I.V. q. 8 hr, or oxacillin, 1 g I.V. q. 6 hr. **Other wounds:** If infection is aggressive, give a third-generation cephalosporin or a quinolone plus clindamycin or metronidazole; or aztreonam plus clindamycin; or imipenem-cilastatin, meropenem, or piperacillin-tazobactam alone. If infection is less serious, give cefotetan, 1 g I.V. q. 12 hr, or cefoxitin, 1 g I.V. q. 6 hr. Invasive and necrotizing infection requires aggressive debridement. Stop antibiotics as soon as local inflammation and systemic signs of infection have resolved.

Intra-abdominal infection (organ/space SSI), as suggested by fever and abdominal tenderness

Confirm diagnosis by CT or ultrasonography. Perform appropriate operative or percutaneous procedure; give antibiotics.

Sternal and mediastinal infection, as suggested by sternal instability

Debride the sternum and affected mediastinal tissues. Consider transposition of viable soft tissue for wound closure.

Osteomyelitis (suggested by nonunion of a fracture, loosening of a prosthesis, or prolonged wound drainage)

Repeated operative debridement, prolonged use of antibiotics, and fracture stabilization may be required.

Empyema, as suggested by systemic signs and pleural effusion

Examine and culture pleural fluid. Drain pleural space. Give appropriate antibiotics. If empyema fails to resolve, consider thoracoscopy, thoracotomy, and decortication.

Posttraumatic meningitis (anticipate if there is a history of CSF rhinorrhea or otorrhea)

Perform lumbar puncture for examination and culture of CSF if unexplained fever, headache, spinal pain or stiffness, or changes in mental status develop. Give appropriate antibiotics.

High fever (> 38.9° C [102° F]) develops within 48 hr of operation

Consider:
- Atelectasis (suggested by decreased breath sounds or rales, or both, and by platelike densities or volume loss on x-ray): Manage via standard physical measures.
- Peritonitis from a leaking viscus (suggested by hemodynamic changes, diffuse abdominal tenderness, excessive early fluid requirements, and tachycardia): Treat with operative intervention and antibiotics.
- Invasive wound infection: Inspect wound and obtain Gram stain of wound contents; treat with operative intervention and antibiotics.

Infection related to intravascular devices

Systemic symptoms suggest catheter-related bacteremia

Peripheral catheters:
Remove and culture via semiquantitative technique.
Central venous catheters:
If local signs of infection are present, remove catheter and culture insertion site and catheter.
If local infection is not present:
- Consider placing a second catheter over a guide wire.
- Culture intracutaneous segment, or the intracutaneous segment and the distal tip, of first catheter semiquantitatively.

Culture results are not available, or empirical treatment is required

Include antibiotic effective against methicillin-resistant *Staphylococcus aureus* (e.g., vancomycin) in therapy.

Culture results are positive

Give appropriate antibiotics. Remove any second catheter placed by guide wire; place any new catheter in a different site.

Culture results are negative

Second catheter may be left in place.

Infection is localized

Remove catheter promptly, and culture via semiquantitative technique. Place any new catheter in a different site.

Infection progresses to septic thrombophlebitis

Correct surgically.

Catheter-associated urinary tract infection

Remove catheter as soon as possible.
Symptomatic bacteriuria:
Give appropriate antibiotics on the basis of culture and sensitivity results.
Asymptomatic bacteriuria: Treat with appropriate antibiotic for 1 day after catheter removal. Culture urine 1 wk later; if bacteriuria persists, give appropriate antibiotics for 7 to 10 days.

Enteric infection

Consider antibiotic-associated colitis in any patient with diarrhea.
Severe cases: Identify mucosal changes immediately via endoscopy.
All cases: Culture stool for *Clostridium difficile* and assay for *C. difficile* toxin.
Severe diarrhea with systemic manifestations: Discontinue antibiotics. Give metronidazole (500 mg p.o., t.i.d.); if unresponsive to metronidazole, give vancomycin (125 mg p.o., q.i.d.).
Mild cases: Discontinue antibiotics.

monary infiltrate, is often seen in modern ICUs, most commonly in association with an endotracheal or tracheostomy tube. Pneumonia may or may not follow. There is often a febrile response, in which case antibiotics may be appropriate on the basis of culture and sensitivity information. Sorting out the cause of purulent secretions in intubated patients is not easy but is important. Other causes of fever should be sought and an overall judgment rendered regarding the probable cause. If tracheitis or bronchitis is suspected, it can be treated with a brief course of antibiotics. A 2000 report described empirical treatment of patients for suspected pneumonia, followed by reevaluation at 3 days.[15] By stopping antibiotic treatment at 3 days for patients without a confirmed diagnosis, the investigators were able to reduce antibiotic use threefold in that group, lower costs by more than half, and decrease the frequency with which resistant bacteria were isolated by more than half.

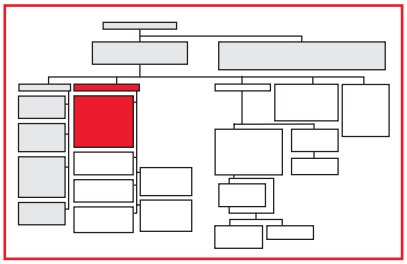
Paranasal sinusitis is a potentially lethal nosocomial infection, especially in ICU patients with nasogastric or nasotracheal tubes in place.[16-18] In one report, it accounted for 5% of all nosocomial infections.[16] The diagnosis of paranasal sinusitis should be considered in any febrile postoperative patient with nasal tubes or with facial fractures. Purulent nasal drainage is an important clue but may not be present. Plain films can be diagnostic but are often difficult to interpret in these patients because of superimposition of tubes, preexisting injuries, and suboptimal portable films. Fluid, air-fluid levels, and mucosal thickening are more easily detected by computed tomography. Diagnosis ultimately requires demonstration of white blood cells and bacteria on a Gram stain of sinus aspirate as well as culture for identification and sensitivity testing.

In one study of 67 patients with craniofacial injuries who underwent prospective otoscopy three times a week, 11 patients experienced either serous or purulent otitis media and were all found to have purulent paranasal sinusitis.[19] Eleven of 12 patients who were ultimately diagnosed as having purulent paranasal sinusitis had coexistent otitis media.

The spectrum of causative bacteria of paranasal sinusitis is similar to that of nosocomial pneumonia. Treatment includes removal of all nasal tubes and administration of decongestants and antibiotics. Occasionally, sinus irrigation, drainage, or both may be required. If empirical therapy must be initiated before specific culture results are known, the agents chosen should be effective against bacteria known to be present in sputum. The best method of prevention is to limit the number and the duration of use of nasal tubes.

Inflammation and infection of the nasopharyngeal mucosa can be significant in an ICU patient, though it is not often identified. Eustachian tube blockage, either from tubes or from inflammation, can be associated with either serous or infective otitis media. Prudent use of tubes is the most effective preventive measure. If clinical infection is recognized, tube removal and decongestants will usually provide adequate treatment.

Infection Related to Operative Site or Injury



SURGICAL SITE INFECTION

An infection of a surgical wound—that is, an incisional surgical site infection (SSI)—traditionally reflects on a surgeon's care and skill and is the classic surgical nosocomial infection [*see 1:1 Prevention of Postoperative Infection*] Such infections are diagnosed primarily on the basis of local findings. Erythema, swelling, and drainage, as well as increasing local pain and tenderness in a site at which pain should be decreasing, all suggest infection. Fever and an elevated white blood cell count may or may not be present. An incisional SSI develops most commonly in the subcutaneous layer, though animal studies fail to explain this observation.[20] In an obese patient, however, a thick, overlying layer of uninfected tissue may obscure evidence of infection and thus delay diagnosis. Presentation may also be delayed if the infection begins in anatomic layers below fascial and muscular barriers, as may be the case after a thoracotomy or an operation on the femur.

Whether an infection will occur in a wound is probably determined within the first few hours of wounding[21,22]; efforts to prevent wound infection are probably ineffective after this period.[23-27] The incidence of SSI is reduced with appropriate use of perioperative antibiotics.[28,29] However, there is no advantage to continuing prophylactic antibiotics beyond the perioperative period in response to fever or local wound erythema in the hope of preventing an overt SSI.[30-32]

The risk that an SSI will develop in an individual patient is best described by an index defined by the Centers for Disease Control and Prevention (CDC) in its National Nosocomial Infections Surveillance (NNIS) System. The index awards one point each for an American Society of Anesthesiologists (ASA) preoperative assessment score of III, IV, or V; an operation classified as either contaminated or dirty-infected; and an operation duration exceeding the 75th percentile for that procedure.[33,34] Examination of the NNIS data demonstrates that in patients undergoing procedures commonly performed laparoscopically, SSI rates are decreased to levels comparable to those reported in patients with a one point lower risk index who undergo equivalent open procedures.[35] The CDC definitions for SSI were agreed to by a consensus panel representing the CDC, the Society for Hospital Epidemiology of America, the Association for Practitioners in Infection Control, and the Surgical Infection Society.[34,36] In addition to appropriate use of prophylactic antibiotics, proper management of intraoperative temperature, oxygen concentrations, and blood glucose levels exerts a powerful influence on the risk of SSI and of other nosocomial infections.[37-41]

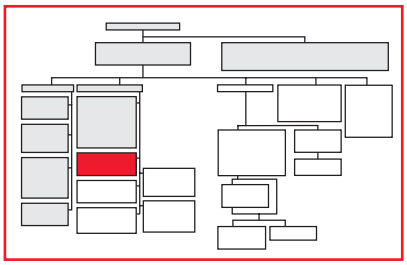
Primary treatment of an SSI consists of opening the wound. When an SSI is suspected, the patient should not be given antibiotics without the wound having been opened. In most cases, the infection is confined to the incision. If the infection is of a superficial wound and if no major systemic manifestations are present, antibiotic therapy is unnecessary. If the local reaction around an infected wound is severe or extensive, administration of antibiotics is advisable until the reaction subsides (which usually takes no more than 3 days). In clean wounds that are away from the perineum and that are not associated with an operation that entered the bowel, the likely pathogens are *Staphylococcus aureus*, streptococci, or both. In such cases, treatment with cefazolin, 1 g I.V. every 8 hours, or oxacillin, 1 g I.V. every 6 hours, is satisfactory. By contrast, SSIs in the perineum and those that occur after bowel operations often involve mixed aerobic and anaerobic bacterial flora. If the infection is not very serious, it can be treated with cefoxitin, 1 g I.V. every 6 hours, or with cefotetan, 1 g I.V. every 12 hours. For more aggressive infections accompanied by evidence of tissue invasion or necrosis beyond the immediate

wound or by a severe systemic reaction, more comprehensive antibiotic treatment is indicated—that is, a third-generation cephalosporin or a quinolone combined with clindamycin or metronidazole; aztreonam combined with clindamycin; or imipenem-cilastatin, meropenem, or piperacillin-tazobactam alone. Infection of an abdominal incision may be a superficial manifestation of an underlying intra-abdominal abscess or of peritonitis.

Occasionally, infection is invasive and necrotizing. In surgical wounds, such an infection is most common after a GI procedure in which the wound was exposed to colonic microflora and in which wound closure was difficult. Necrotizing infection is also more likely in a patient who is seriously ill or who has evidence of multiple organ failure. Such infection should be suspected if there is undermining of the wound edges, extensive fascial necrosis, distant signs of infection, or a marked systemic response. It requires aggressive operative debridement and administration of antibiotics [*see 3:2 Soft Tissue Infection*].

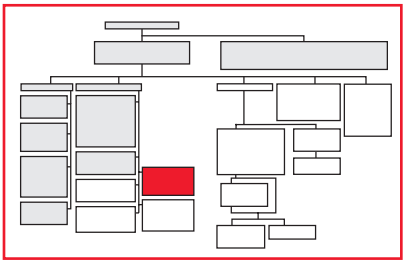
Clostridium species, which can cause life-threatening postoperative necrotizing SSI, can also cause routine postoperative incisional infection limited to the wound and without myonecrosis.[42] Such infection is marked by the absence of the systemic symptoms associated with clostridial myonecrosis and by the presence of intact white blood cells on a Gram stain of the wound contents. (Clostridial myonecrosis, on the other hand, is characterized by a Gram stain that shows gram-positive rods but few or no white blood cells [*see 3:2 Soft Tissue Infection*].)

INTRA-ABDOMINAL INFECTION



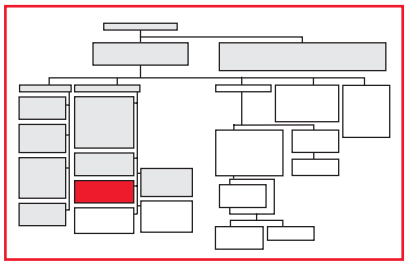
Intra-abdominal infections—that is, organ/space SSIs—are a major cause of postoperative morbidity and mortality, particularly when diagnosis is delayed.[43,44] Suspected intra-abdominal organ/space SSI in a patient with fever or abdominal tenderness, or both, after an abdominal procedure or injury should not be treated with antibiotics alone; after a specific diagnosis, the appropriate operative or percutaneous procedure must be performed [*see 8:18 Intra-abdominal Infection*].

EMPYEMA



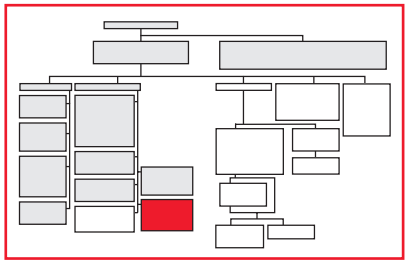
Empyema, which may follow thoracotomy or chest trauma necessitating tube thoracostomy, is a significant cause of posttraumatic infection.[45] Less commonly, empyema develops as a complication of pneumonia. Empyema should be suspected in any patient with systemic signs of infection, a pleural effusion, and no other obvious source of infection. Diagnosis requires thoracentesis of pleural fluid for a Gram stain and culture. The most common pathogen is *S. aureus,* though many other pathogens may be found as well. Initial treatment is by drainage with a chest tube and by administration of appropriate antibiotics based on the results of the Gram stain and culture. Because treatment is invasive, it should not be instituted until the diagnosis is confirmed. Cases that do not resolve promptly and completely may ultimately require thoracoscopy or thoracotomy and decortication. Empyema after pulmonary resection or esophageal operation raises the possibility of a leaking bronchial closure or esophageal anastomosis. A leak is almost certain if an air-fluid level is present on chest x-ray. An esophageal leak is treated with repair or diversion.

STERNAL AND MEDIASTINAL INFECTION



Sternal and mediastinal infections are the most serious infectious complications of operations that involve a median sternotomy.[46] The risk that a superficial infection will spread to involve the sternum and mediastinum is high because there is little soft tissue between the skin and the sternum. Infection may also start deep to the sternum without early superficial evidence. Sternal instability is an important indication of sternal infection. Computed tomography of the chest is sensitive and specific for the diagnosis of sternal osteomyelitis and mediastinitis.[47] All such infections require operative debridement of the sternum and of affected mediastinal tissues. Some wounds can then be closed. Many wounds require closure of the mediastinal space by transposition of viable soft tissue. Pectoralis or rectus muscle flaps, omental flaps, or both are commonly used.[48]

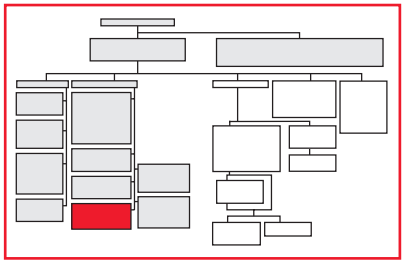
POSTTRAUMATIC MENINGITIS



A basilar skull fracture with a cerebrospinal leak increases the risk of posttraumatic meningitis.[49] The most common pathogens are *Streptococcus pneumoniae, S. aureus,* other streptococcal species, and *Haemophilus influenzae,* but any oropharyngeal organism can be responsible.[50] Since the association between trauma and meningitis was first reported in 1970,[49] the appropriate use of antibiotics in these patients has been debated. Some researchers advocate prophylactic administration of antibiotics until any CSF leakage ceases,[51] whereas others advocate them for an arbitrary period after injury (usually 5 days); however, controlled studies have failed to support a specific protocol.[50] Furthermore, experience in other clinical settings suggests that prophylactic antibiotics would be as likely to promote the development of resistant oropharyngeal flora and subsequent meningitis as they are to prevent it.[52,53]

The ideal approach to patients with CSF rhinorrhea or otorrhea is to maintain a high index of suspicion for the development of meningitis. Fever not clearly attributable to another source or not immediately responsive to specific treatment for its presumed cause should prompt a lumbar puncture for examination and culture of spinal fluid. Lumbar puncture should also be performed to investigate headache, spinal pain or stiffness, or unexplained changes in mental status. Such an approach should result in a prompt diagnosis and permit early specific treatment of the responsible pathogen if meningitis is diagnosed.

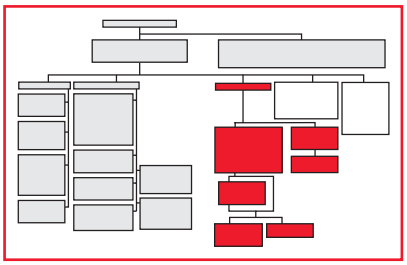
OSTEOMYELITIS



Osteomyelitis is a relatively rare complication after elective orthopedic procedures. Its diagnosis and management are similar to those of infections involving other operative sites, but because the infection is deep and covered by muscular and fascial planes, diagnosis may be delayed. Nonunion of a fracture or loosening of a prosthesis may be the first sign of infection. Infection after open fractures is common; rates range from 5% to 50%.[54-56] The primary determinants of infection after open fracture are the degree of soft tissue damage surrounding the fracture and the surgeon's ability to stabilize the fracture fragments.[55] Other important factors include the patient's age and overall condition, the severity of other injuries, the interval between injury and definitive management, and the use of prophylactic antibiotics. A brief course of perioperative antibiotics may prevent subsequent infection as effectively as a more prolonged course.[30,57]

Treatment of osteomyelitis may require repeated operative debridement, prolonged use of specific antibiotics, and fracture stabilization. Pathogens include *S. aureus* for all grades of open fracture and, increasingly, gram-negative bacteria (e.g., *Pseudomonas aeruginosa* and *Klebsiella* and *Enterobacter* species) for grade III fractures.[57]

Infection Associated with Intravascular Devices



Every type and location of intravascular device has been associated with clinically significant nosocomial bloodstream infection. The incidence of infection is highest with central venous catheters used for monitoring purposes.[58,59]

It is important to specify the different definitions of catheter infection and catheter-related bloodstream infection (CRBSI). Infection at the catheter site is commonly defined as the presence of lymphangitis, purulence, or at least two of the following: erythema, tenderness, increased warmth, and a palpable thrombosed vein. However, many cases of phlebitis with no evidence of bacterial infection present with erythema and with tenderness, a palpable thrombosed vein, or both.[60] Few or no premonitory signs occur before phlebitis is obvious, and the first evidence of as many as 45% of phlebitis cases appears more than 24 hours after catheter removal. If a functional catheter remains in place for 12 hours after the onset of phlebitis symptoms, the duration and severity of symptoms increase markedly.[61]

CRBSI is characterized by (1) isolation of the same organism from the catheter and the blood, (2) clinical (or autopsy) and microbiologic data disclosing no other source of the bloodstream infection, and (3) clinical features of bloodstream infection (e.g., fever and leukocytosis).[62] For indwelling, long-term central venous catheters (e.g., Hickman, Broviac, and Groshong), infections have been classified as exit-site and tunnel infections. Infections at the exit site are defined as the presence of erythema, tenderness, induration, or purulence within 2 cm of the skin around the exit site. They are presumably confined to the portion of the catheter external to the subcutaneous Dacron cuff. Tunnel infections are defined as the presence of the same signs along the subcutaneous tract, at a distance more than 2 cm from the tract.[63,64] The importance of this distinction is that many infections at the exit site are successfully treated with antibiotic therapy and local wound care, whereas tunnel infections usually necessitate removal of the catheter.[63,64]

A semiquantitative technique for culturing intravascular catheters has been shown to distinguish between infection and contamination of the catheter and is more specific in the diagnosis of CRBSI than is broth culture of the catheter.[62] The catheter is removed from the patient after antiseptic cleansing of the insertion site to prevent contamination from surrounding skin. A 5 to 6 cm segment of the catheter is aseptically removed; transported to the laboratory in a dry, sterile tube; placed on the surface of an agar culture plate; and rolled at least four times across the surface of the plate [*see Figure 1*]. If the plate grows at least 15 colonies, the culture is positive. Most catheters associated with bloodstream infection actually grow more than 1,000 colonies [*see Figure 1*]. For peripheral catheters, the entire catheter is cultured. For central catheters that are longer than 6 cm, either the distal tip or both the intracutaneous segment and the distal tip should be cultured [*see Figure 2*].

The most common source of bacteria involved in catheter infection is the skin around the insertion site.[65,66] Patients who have a skin colonization at the insertion site of greater than 10^3 colony-forming units/25 cm^2 are 10 times more likely to have a catheter infection than those whose skin colonization is less. Of catheters that test positive with the semiquantitative culture technique, 16% to 44% appear to be primary sources of septicemia.[62,67-69]

The catheter hub and lumen are recognized as important routes of infection. Colonization at these sites is detected not by roll-plate cultures but by sonication culture of catheter segments or by simultaneous cultures of blood drawn through the suspect catheter and from a distant site. Either sonication cultures recovering more than 10^2 colonies or catheter cultures more than five times the number recovered from distant sites are sensitive and specific indicators of catheter infection.[70,71]

For catheters that are only locally infected and not responsible for CRBSI, removal is adequate treatment; the same is true for most catheters that cause bloodstream infection. If the patient's temperature and white blood cell (WBC) count return to normal within 24 hours after removal of the catheter and if local signs of inflammation at the catheter insertion site resolve within that period, antibiotics are not necessary. However, if the patient continues to show clinical signs of infection or has a documented bacteremia, a brief course of specific antibiotic therapy is indicated. Specific antibiotic therapy is also indicated if semiquantitative catheter culture reveals a large number of *S. aureus* organisms in conjunction with systemic signs of infection. If empirical therapy for CRBSI is undertaken before culture and sensitivity results are available, the antibiotic regimen should include vancomycin or another antibiotic known to be effective against methicillin-resistant *S. aureus* (MRSA): coagulase-negative staphylococci are the most commonly implicated pathogens,[58,70,72] and there is a high rate of methicillin resistance among these organisms. In candidemic patients with I.V. catheters in place, candidemia resolves an average of 3 days earlier if the catheters are removed at the time of diagnosis and initiation of antifungal therapy.[73]

For patients with documented catheter-associated bacteremia, treatment depends on the organism or organisms present. The available data on the necessary duration of treatment for coagulase-negative staphylococci are inconclusive. Often, good results

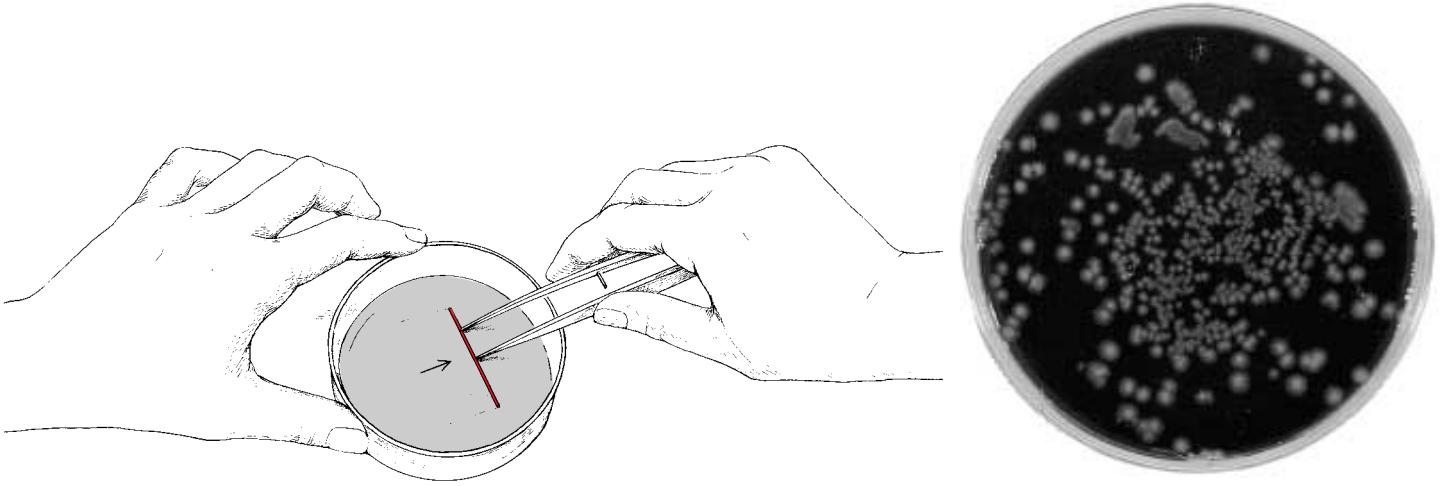


Figure 1 **In a semiquantitative technique used to distinguish between infection and contamination of intravascular catheters, a 5 to 6 cm segment of the catheter is rolled at least four times across the surface of an agar culture plate (left). Typically, a positive culture grows far more than 15 colonies (right).**

are achieved with catheter removal and either no antibiotics or a short course (1 to 3 days) of antibiotics; some experts recommend a 5- to 7-day course, but there is no compelling evidence that this is necessary. For *S. aureus* bacteremia, a 10- to 14-day antibiotic course is recommended if the infection is uncomplicated and a 4- to 6-week course if the infection is complicated. The relevant data on CRBSI caused by gram-negative bacilli or *Candida* are even sparser. Current recommendations call for antibiotic treatment lasting 10 to 14 days for gram-negative pathogens and 14 days or longer for *Candida*.[74]

In a small proportion of patients, local catheter-related infection may progress to a life-threatening condition characterized by the formation of microabscesses within the cannulated vein and by persistent bacteremia after catheter removal. Septic thrombophlebitis can occur in a broad range of hospitalized patients and should be suspected when clinical signs of systemic sepsis, local signs of inflammation, and positive blood cultures persist after removal of the catheter. A surgical approach to the affected vein is required. When possible, the vein should be excised over the affected area and the wound left open. The presence of gross pus within the vein wall is not necessary for the diagnosis. The wall of the affected vein may simply appear thickened, with inflammation surrounding it and an edematous, pale thrombus enclosed within it. Fungal peripheral thrombophlebitis may be especially difficult to diagnose because the local site often does not appear infected. In the presence of continued candidemia without an obvious source, any palpably thrombosed vein near a site of present or previous catheterization must be suspected. Gram staining and hematoxylin-eosin staining of the vein contents or the vein wall are significantly less sensitive than silver staining and culture.[59]

Even more rare is catheter-related septic central venous thrombosis. The diagnosis is made by the occurrence of (1) thrombosis of the internal jugular, subclavian, or brachiocephalic vein proved by venography or duplex Doppler examination; (2) central venous catheter infection with positive catheter tip culture and positive peripheral blood cultures; and (3) persistent bacteremia or candidemia after catheter removal.[75,76] Initial therapy consists of catheter removal, systemic antibiotics based on sensitivity testing and administered in a quantity and duration appropriate to treatment of endocarditis, and systemic anticoagulation during the same period. Surgical excision or drainage is reserved for failure of nonoperative measures.

At one time, it was common practice for both central and peripheral venous catheters to be either completely changed or exchanged over a guide wire at fixed intervals to reduce the risk of infection. Data from randomized, controlled, prospective trials did not demonstrate any advantage to this policy.[60,70,77,78] These trials demonstrated that the risk of infection is linear, increasing with the duration of I.V. catheterization, whether one or multiple catheters are used.

Current practice is to change catheters when infection is suspected when the catheters are not working or not needed.[60,70,77,79,80] Clearly, any catheter that is a cause of bloodstream infection must be removed, as should infected catheters that may not yet have caused such infection. The practical problem is that not all infected catheters show external evidence of infection. In addition, catheter culture and the subsequent clinical course confirm infection in only a small proportion of patients with central venous catheters or pulmonary artery catheters in place who are suspected on clinical grounds of having CRBSI.[81] Changing central venous catheters over a guide wire circumvents most of the mechanical complications associated with central venous catheterization, saves time, and is more comfortable for the patient.[82] However, if a culture of the first catheter is positive, the second catheter should be removed immediately, and any new

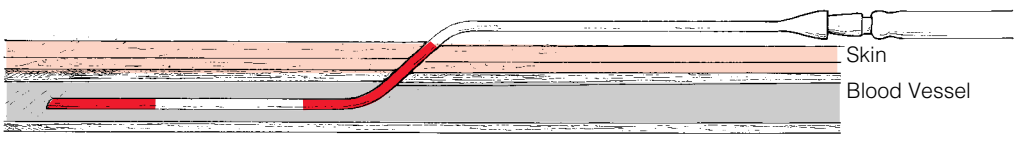


Figure 2 **When a catheter is longer than 6 cm, either 5 to 6 cm of the catheter tip or both this segment and a 5 to 6 cm intracutaneous segment (red) can be cultured.**

catheter should be placed in a different location.[60,70,77,79-81]

Recommendations for changing central venous and pulmonary artery catheters are as follows:

1. Signs of inflammation, skin irritation, or purulence at the insertion site should prompt immediate removal of the catheter. Any new catheter should be inserted in a different site. In a patient with systemic signs of infection (fever, leukocytosis, malaise), culture of the insertion site or of the catheter, or both, is indicated to identify potential pathogens and to direct therapy. In a patient without systemic signs of infection, culture is not necessary.
2. If a patient with a catheter experiences systemic signs and symptoms of infection without a readily apparent source, the catheter should be removed even in the absence of inflammation at the insertion site. In this setting, however, approximately 75% of catheters are not infected, and a new catheter can be inserted at the same site over a guide wire placed through the first catheter.[81,83-85] However, a catheter exchange places the new catheter in the old subcutaneous tunnel, which would be the most likely origin of catheter infection. The first catheter should be cultured semiquantitatively. If the culture is negative (i.e., < 15 colonies), the second catheter can be left in place. If the culture is positive (i.e., ≥ 15 colonies), the second catheter should be removed immediately, and any new catheter should be placed at a different site.

Sterile technique is always required for catheter insertion. However, most authorities advocate a surgical approach to preparation of the insertion site, with the operator wearing gown, gloves, mask, and hat for the procedure, if any of the following risk factors is present[70,86]: (1) the location is central, (2) catheterization will probably be long term, (3) the patient is seriously ill, or (4) parenteral nutrition is to be employed. Educational efforts to reinforce these guidelines in the hospital setting can reduce the incidence of catheter-related infections.[87]

Traditionally, central venous catheters have been inserted most commonly via either the subclavian or the internal jugular route. There is a well-demonstrated increase in infection risk when catheters are inserted by the jugular route instead of the subclavian.[69,80,88] The infection rate for the femoral route of insertion appears to be higher than that for the subclavian route and possibly higher than that for the internal jugular route[89]; however, it can be reduced by tunneling.[90] The femoral route can be used if other access routes are not available, but at the cost of a higher rate of thrombotic complications.[91]

A promising approach to prevention of catheter infection is antibiotic bonding of the entire catheter surface. Two trials reported fewer catheter and bloodstream infections in patients with antimicrobial-bonded catheters than in patients with unbonded catheters,[92,93] and one trial reported a lower infection rate with a catheter coated on both internal and external surfaces with minocycline and rifampin than with a catheter coated only on the external surface with chlorhexidine and silver sulfadiazine.[94]

The ideal method of caring for intravascular catheters after insertion is not firmly established. Sterile dressings of gauze and tape, as well as a variety of commercially available transparent dressings, have been advocated. The transparent dressings appear to save nursing time and permit the insertion site to be inspected without changing the dressing, but they promote bacterial growth on the underlying skin, as compared with gauze and tape dressings.[95] Transparent dressings have also been associated with an increased number of cases of catheter infection and CRBSI in patients with central venous catheters.[96] Thus, use of transparent dressings is not recommended, at least for central lines.

In addition, there is no firm evidence that the use of polyantibiotic ointments or iodophor ointments at the insertion site prevents infection, though such ointments have not been associated with an increase in infections with resistant organisms. Catheter teams are recommended to care for vascular catheters. Regular inspection of insertion sites and adherence to a specific protocol for catheter care can result in acceptably low infection rates.[70]

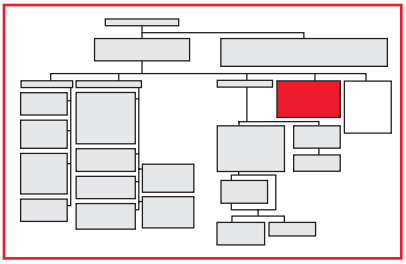
Catheters with two or three internal lumina have become widely available and are often sold in kits that include equipment for guide-wire insertion. These catheters are more convenient when a patient requires multiple lines for monitoring and for delivery of intravenous medications and parenteral nutrition. However, these multiple-lumen lines may be associated with a higher incidence of catheter-associated bloodstream infection than are single-lumen catheters[97,98]; the data are inconclusive.[85,99] In one small study, the insertion of two single-lumen catheters did not result in a lower complication rate than the insertion of one double-lumen catheter.[100] A catheter with multiple infusion ports is likely to be manipulated more often than a single-lumen catheter, but it is unclear whether the extra manipulation results in a higher infection rate. In situations in which one lumen would suffice, the temptation to insert a multiple-lumen line in case additional lumina are needed later should be resisted. One study showed that 53% of all triple-lumen lines observed had only one lumen in use, indicating that multiple-lumen lines are often used unnecessarily.[97]

When long-term use of catheters is required, insertion of a Silastic catheter with a subcutaneous Dacron cuff (e.g., Broviac, Hickman, or Groshong) is associated with the lowest rate of catheter-associated infection and the longest useful catheter life.[63] In the largest reported study of these catheters, the incidence of infection was only 0.14 infection per 100 catheter-days (range, 0.0 to 0.8).[63] The study also showed that double-lumen catheters did not have a higher rate of infection than single-lumen catheters, but the rate of catheter infections was increased 10-fold in patients who had catheter-related thrombosis. The mean catheter life span in this report was greater than 120 days.

Very low infection rates and long catheter life are also reported with nontunneled Silastic catheters and with peripherally inserted central catheters (PICC).[70,101] The lowest infection rates are associated with totally implantable devices with subcutaneous reservoirs.[102]

Use of warfarin to prevent thrombosis may result in a reduced rate of catheter infection. A prospective trial found a clinically and statistically significant reduction in the incidence of catheter-associated thrombosis (from 38% to 10%) over 90 days with the administration of 1 mg of warfarin daily, beginning 3 days before catheter insertion.[103] Measured prothrombin times did not increase, and no bleeding complications occurred.

Urinary Tract Infection



The traditional definition of urinary tract infection in patients without urinary catheters specifies the presence of at least 10^5 organisms/ml, but this criterion is probably not appropriate for catheterized patients. Research has

shown that of catheterized patients who have any detectable organisms in their urine (even < 10^2/ml), whose catheters remain in place, and who receive no specific antimicrobial therapy, 96% have organism counts higher than 10^5/ml within 3 days.[104] (By comparison, 27% of patients with sterile urine subsequently have colony counts higher than 10^5/ml before catheter removal.)

Although a catheter-associated UTI is a significant nosocomial infection with measurable morbidity and mortality [*see* Discussion, *below*], not all cases of bacteriuria should be treated with antibiotics. If a patient with bacteriuria is symptomatic, treatment should be initiated according to culture results and sensitivity testing. Although bacteriuria can sometimes be cleared without removal of the catheter, the risk of a new episode continues while the catheter is in place.[105] Ideally, the catheter should be removed as soon as possible. In one study, only 36% of untreated women with asymptomatic bacteriuria had sterile urine within 2 weeks after catheter removal, and 17% progressed to symptomatic bacteriuria; however, 81% of patients treated with a single dose of trimethoprim-sulfamethoxazole had sterile urine within 2 weeks after catheter removal.[106] Thus, it is prudent to obtain a culture at the time of catheter removal and to treat any bacteriuria detected.

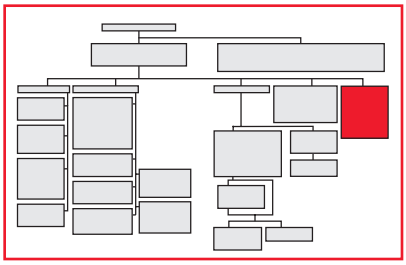
A condom catheter is often used in male patients in place of a urethral catheter when neurologic injury or incontinence mandates long-term drainage. The available data are not sufficient to establish the ideal care of these devices and the true infection rate associated with their use. UTI rates as low as 0% in 79 patients managed with condom catheter drainage[107] and as high as 53%[105] to 63%[108] have been reported. Severe noninfectious local complications (e.g., ulceration and maceration of the penis) also can occur.[107,108]

Because indwelling urinary catheters are a major source of nosocomial infection, they should be employed only when necessary and removed as soon as practicable. The most effective method of reducing infections among patients with urinary catheters is to use completely closed urinary drainage systems and to limit breaks in the closed system.[109] The incidence of new infections doubles on any day in which a closed urinary drainage system is opened. [110] Urine samples for culture should be aspirated with a needle and syringe from the catheter lumen after antiseptic cleansing of the catheter sampling port. The catheter junction should not be disconnected to obtain a specimen. The use of a preconnected and sealed catheter and drainage bag system has been shown to result in a 2.7-fold reduction in the rate of catheter-associated UTIs and an adjusted risk ratio for death of 0.29.[111]

Antibiotic irrigation systems do not reduce infections, but they do increase the incidence of resistant organisms.[110] Systemic antibiotics reduce infections to a modest degree in the first 4 days of catheterization but at the expense of an increase in resistant organisms. The infection rate is higher in females than in males, in older patients than in younger ones, and in patients with critical illness than in those without critical illness.[109] Patients with nosocomial diarrhea and an indwelling bladder catheter have a ninefold higher risk of subsequent UTI than patients with an indwelling bladder catheter who do not have diarrhea.[112]

Although most UTIs acquired by hospitalized patients are assumed to be simple bladder infections, there is no strong correlation between location of infection and clinical symptoms.[113,114] Many patients with upper UTIs do not have flank pain, fever, or other signs of systemic infection, and patients with a bladder infection may not have dysuria or suprapubic tenderness. Many patients with upper UTIs are treated without the diagnosis ever being made. Systemic infection and associated bacteremia or complications such as intrarenal or perinephric abscesses occur more commonly in immunocompromised patients (e.g., those with urinary tract obstruction or diabetes).[115] In patients with a neurogenic bladder or indwelling bladder catheters, urinary sepsis may develop without symptoms referable to the urinary tract. However, symptoms of localized flank or low back pain, along with systemic signs, such as fever, rigors, sweats, and nausea, are relatively specific indicators of renal infection.[116]

If a patient has fever and bacteriuria during the postoperative period, the surgeon should perform a careful evaluation to determine whether he or she has pyelonephritis or a postoperative intra-abdominal infectious complication. Pyelonephritis can be treated solely with antimicrobial therapy in most cases, whereas all postoperative intra-abdominal infectious complications call for surgical intervention as well as antimicrobial therapy. No simple methods are available to distinguish between these diagnoses. The operating surgeon should carefully evaluate all of the patient's clinical signs and symptoms. A hospitalized patient with pyelonephritis should usually receive antimicrobial therapy for at least 14 days. An agent demonstrated to be effective against the causative organism by in vitro sensitivity testing should be used. In any patient who has severe signs of systemic infection or does not respond promptly to treatment, ultrasonography, renal scanning, or I.V. pyelography should be done to rule out obstruction. If obstruction is found, it must be corrected. If the patient has an indwelling bladder catheter, the catheter should be removed, appropriate therapy started, and a new, clean catheter inserted.[116]



Enteric Infection

Any organism that can cause food-borne enteric infection in the community can do so in the hospital,[117] but cultures for routine enteric pathogens are not useful for patients who have been hospitalized for more than 3 days.[118] The most important nosocomial enteric disease to confront most surgeons is antibiotic-associated diarrhea, which can range from trivial, self-limited episodes of diarrhea to fulminant disease with systemic signs of sepsis, collapse, and death.

The first step in diagnosis is to consider antibiotic-associated colitis in any hospitalized patient with diarrhea. Mild cases may not be associated with any systemic signs or pathologic findings in the colon, and in the majority of mild episodes, there are no identifiable pathogens. More severe cases are marked by one or more of the following signs: nonspecific hyperemia, edema, granularity, or ulceration of colonic mucosa. The most severe cases are marked by pseudomembrane formation.

The single most efficient measure for detecting *C. difficile*–associated diarrhea is to send a stool sample for cytotoxin determination, a procedure that has a sensitivity of 70% to 100%. By sending a sample is sent for stool culture as well, one can increase sensitivity slightly (to 96%); however, if *C. difficile* is grown on the culture, the organism must still be tested for cytotoxin production, and this takes another day.[118,119] Rectal swab cultures transported in anaerobic containers are at least as sensitive as conventional stool cultures,[120] but they are not adequate for detection of cytotoxin.[119] Although it is possible that poly-

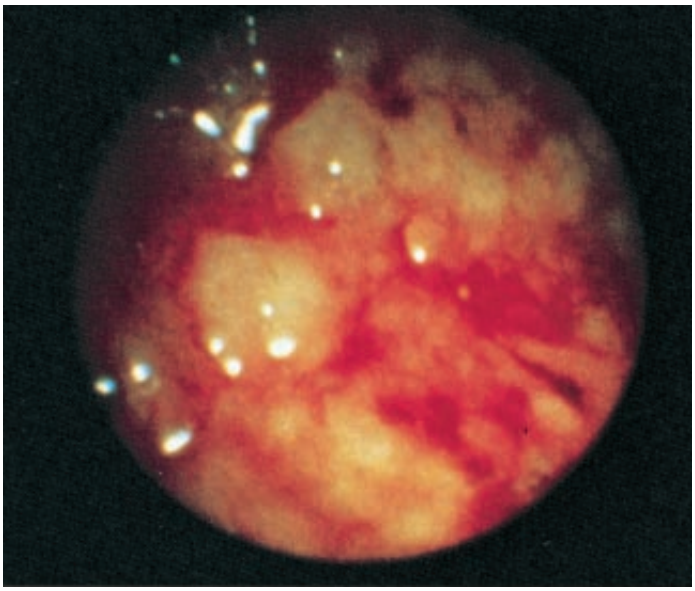


Figure 3 **An endoscopic view of pseudomembrane formation is shown.**

merase chain reaction assays for the cytotoxin gene in stool can eventually be developed, such assays are not available at present. Stool smears for detection of WBCs are not helpful.[118,119] Endoscopy to detect pseudomembranes is indicated if the patient is seriously ill and a prompt diagnosis and initiation of specific treatment are desired. Administration of empirical therapy until a specific pathogen is identified is appropriate in this circumstance.[119]

Severe and persistent cases of antibiotic-associated diarrhea are most commonly associated with the recovery of *C. difficile* by culture and of *C. difficile* toxin by tissue culture assay.[121] In more than 90% of patients who have pseudomembranous colitis, *C. difficile* toxin will be present on tissue culture assay. In antibiotic-associated diarrhea without pseudomembrane formation, positive toxin titers may be found in 70% of patients with signs of colitis and in 11% to 27% of patients without colitis.[122-124]

Pseudomembranes, present in about half of patients with *C. difficile*–associated diarrhea,[119] are elevated, whitish plaques that vary in size from a few millimeters to 1 to 2 cm and may coalesce and slough. Histologically, the plaques show epithelial debris, polymorphonuclear infiltrate, chronic inflammatory cells, and fibrin deposition.[121] The diagnosis of pseudomembrane formation is made by endoscopy [*see Figure 3*]. Most cases involve the rectum and the left colon, but as many as 25% may be missed by rigid sigmoidoscopy; by comparison, the false negative rate with flexible endoscopy is only 10%.[125] Although the great majority of cases involve only the colon, two fatal cases that primarily involved the ileum and the jejunum have been recorded.[126,127] The clinical picture of pseudomembranous colitis includes watery diarrhea in 90% to 95% of cases, with bloody diarrhea in the remaining cases. Abdominal cramps, leukocytosis, and elevated temperature are present in approximately 80% of cases.[121]

All commonly employed antibiotics have been implicated in cases of antibiotic-associated pseudomembranous colitis, including vancomycin[128-130] and antibiotics used for perioperative antibiotic prophylaxis, even in a single dose.[131] Treatment should include cessation of the offending antimicrobial agent, if possible. In mild cases, this step may be all that is necessary: in 23% of such cases, resolution occurs within 2 to 3 days of discontinuance of antibiotic therapy.[119]

A patient with systemic symptoms should also receive one of the agents with proven efficacy against the disease. The agent with which there has been the most recorded experience is vancomycin, but it is more expensive than the alternatives. The usual dosage is 500 mg/day orally in four divided doses. Metronidazole, 500 mg three or four times daily for at least 10 days, is an effective alternative.[132] Bacitracin, 20,000 to 25,000 units four times daily, is also effective but should be considered the third choice.[119,132] The current recommendation is to begin therapy with metronidazole to reduce the risk of inducing vancomycin-resistant enterococci [*see* Pathogens, *below*].[119,133]

Relapses after treatment for *C. difficile* colitis are common, occurring in 5% to 30% of cases, perhaps because of persistence of the organism in spore form; 92% of these cases respond to a second course of treatment without relapse.[119,132] Cases that do recur involve both persistent infection and new reinfection.[132]

A profound ileus is sometimes associated with the severe form of the disease and may prevent the delivery of oral antibiotics to the site of infection. Limited experience suggests that parenteral metronidazole may be effective in these cases. However, there have been several cases of unsuccessful treatment of *C. difficile*–associated colitis with I.V. metronidazole and of the development of *C. difficile* colitis in patients receiving I.V. metronidazole alone or together with other antibiotics.[132,134] In the most severe cases, the clinical evolution resembles that of toxic colitis associated with inflammatory bowel disease, and the patient may require a colectomy if the disease is unresponsive to nonoperative management. If operative treatment proves necessary, subtotal colectomy is preferred to hemicolectomy.[132] In as many as 5% of cases, colitis may present as acute abdominal pain and tenderness and leukocytosis without diarrhea.[135,136] Any patient with acute abdominal symptoms who has received antibiotics within the past 2 months should be considered for the diagnosis of *C. difficile*–associated colitis.[132] If colitis is suspected because of previous antibiotic administration, sigmoidoscopy may facilitate the correct diagnosis and avert unnecessary abdominal exploration. CT may show thickening of the bowel wall, but operative exploration often does not yield significant findings.[136] Extraintestinal infections have also been reported.[137]

Transfusion-Associated Infection

The transfusion of blood would seem to be an excellent method for transmitting blood-borne diseases; however, transmission of disease by blood transfusion is rare.[138,139] Transfusion-associated malaria is occasionally reported in North America but occurs quite infrequently. The primary method for preventing malaria transmission is careful screening of donors by history. A handful of cases of babesiosis, Chagas disease, trypanosomiasis, toxoplasmosis, and infections with various herpesviruses, parvovirus, or West Nile virus have been reported over many years, but these are rare as well.[138-141]

In the early years of blood collection and transfusion, cases of syphilis related to blood transfusion were reported infrequently. The practice of refrigerating blood, which kills circulating spirochetes within 1 to 2 days, is probably responsible for the absence of transfusion-associated syphilis today. Unfortunately, refrigerating blood does not kill all potential pathogens. Bacterial pathogens that can survive blood storage and cause subsequent symptomatic infection include *Yersinia enterocolitica, Pseudomonas fluorescens, P. putida, Campylobacter jejuni, Escherichia coli, Serratia*

species, *Salmonella* species, *Enterobacter* species, *Providencia* species, *S. aureus,* and streptococci. When transfusion-associated bacteremia or endotoxemia is suspected, the residual blood product in the bag should be examined by means of a hematologic stain, and the blood in the bag and samples of the recipient's blood should be cultured.

Bacterial contamination of transfused blood components accounted for 11% of all fatal transfusion reactions reported to the FDA between 1985 and 1999. In 2001, CDC investigators published a prospective survey of bacterial infections resulting from blood component transfusion in the United States between January 1998 and December 2000.[142] This survey covered approximately 60% to 70% of all transfusions recorded in the United States during that period. The investigators identified 34 confirmed cases of bacterial infection from transfused blood components, nine (27%) of which were responsible for deaths. The estimated rates of transfusion-transmitted bacteremia were one per 100,000 single or pooled units of platelets and one per 5 million units of red blood cells. The estimated fatality rates were one per 500,000 units of platelets and one per 8 million units of red blood cells.

Until recently, the most severe and most common disease transmitted by blood transfusion in North America was viral hepatitis [*see 8:20 Viral Infection*]. With the development of specific and sensitive tests for detecting hepatitis B surface antigen (HBsAg), the incidence of posttransfusion hepatitis B dropped from 25% to 30% of all cases of transfusion-associated hepatitis to 5% to 10%. However, the advent of serologic tests for hepatitis B did not result in an overall decrease in posttransfusion hepatitis (PTH), because 80% to 90% of cases of PTH were caused by hepatitis C virus (HCV). Since the development of sensitive antibody tests for HCV, the incidence of PTH has dropped dramatically, and since the introduction in 1999 of nucleic acid amplification technology (NAT) (e.g., PCR and transcription-mediated amplification), it has fallen even further, to the point where the current estimated risk is one per 1.9 million transfused units.[143]

The spread of AIDS [*see 8:21 Acquired Immunodeficiency Syndrome*] brought a new risk of transfusion-associated viral disease. The risk of acquiring transfusion-associated HIV infection is extremely low compared with posttransfusion hepatitis; transfusion-associated HIV infection is vastly less likely to occur and has accounted for fewer deaths. Nevertheless, transfusion-associated AIDS is much more frightening to most patients and physicians than PTH because of its usually fatal prognosis. Prevention of HIV transmission during transfusion is accomplished by screening potential donors to eliminate those at high risk for infection and by testing all donated units for HIV with both antibody tests and NAT.[143-145] It has been estimated that predonation screening is 98% effective in eliminating donation of positive units and that postdonation antibody testing is more than 95% effective, for a combined effectiveness of approximately 99.9%.[144] Overall, posttransfusion HIV infections were reduced by 76% between 1985 and 1988, a time during which the overall prevalence of the condition was increasing.[144]

The continued concern about possible HIV transmission during transfusion arises from the so-called window of seronegativity between the time at which a potential donor becomes infected and the time at which the donor's antibody test becomes positive. A 1989 analysis of available data from most United States blood banks concluded that the risk of receiving a unit of blood that contained HIV but was negative for anti-HIV antibody in 1987 was approximately one per 153,000 transfusions on the basis of an average window period of 8 weeks.[144] A 2002 report, making use of data obtained since the introduction of NAT, established the current risk at one per 2.1 million transfusions.[143] In comparison, the risk of experiencing a fatal hemolytic transfusion reaction is one per 100,000 transfusions.[145] Thus, a transfusion recipient is much more likely to die of a hemolytic reaction than of infection.

Analysis of transfusion practices in the United States between 1982 and 1988 reveals a decrease in the number of blood, platelet, and plasma transfusions after 1986; before 1986, the number of these transfusions increased each year. In addition, between 1982 and 1987, the number of autologous units donated increased from 30,000 to 397,000 a year. In 1987, autologous units accounted for 3% of all blood transfused.[146] Since 1987, refinements of operative techniques have reduced the need for transfusion in many procedures, and research has demonstrated that in many cases, transfusion can safely be withheld until hemoglobin levels lower than 7 g/dl are reached [*see 1:4 Bleeding and Transfusion*].[147] In addition to the overall decline in transfusions since the late 1980s, the number of autologous units of blood transfused yearly has declined.[148]

Discussion

Postoperative Fever

Many patients experience fever in the postoperative period without infection. In a prospective study of 871 general surgery patients, 213 (24%) had a documented infection or an unexplained fever in the postoperative period.[149] The most common occurrence was unexplained fever in 81 cases (38%), followed by wound infection in 55 (26%), UTI in 44 (21%), respiratory tract infection in 27 (13%), and other infections in 6 (3%). Of all unexplained fevers, 72% occurred in the first 2 days, and of all occurrences in the first 3 days, 67 (71%) of 95 were unexplained, with only 18 (27%) representing true infection. In another study, 73 (45%) of 162 patients experienced unexplained fever after general surgical or orthopedic procedures; 25% of the unexplained fevers were at least 38.3° C (101° F).[150]

At Harborview Medical Center, 316 (98%) of 322 patients who underwent laparotomy for penetrating trauma had a temperature of at least 37.5° C (99.5° F) orally during the first 5 days after operation. Of these patients, however, only 67 (21%) actually acquired any infection during a 30-day follow-up. Even for the 80 patients whose temperatures were as high as 39° C (102.2° F) orally, only 48% actually acquired an infection before discharge. Fever that persisted or began after postoperative day 4 was more likely to represent true infection. Similarly, an elevated WBC count was nonspecific during the first 5 postoperative days: 89% of all patients had a WBC count greater than 10,000/mm^3.[151,152] A high fever should prompt examination of the patient, but in the absence of systemic signs of sepsis, an extensive laboratory or radiologic workup during the first 4 to 5 days is usually unhelpful.[153]

Magnitude and Significance of Nosocomial Infection

An understanding of the prevalence of nosocomial infections and of the factors predisposing to their occurrence will help in prevention, diagnosis, and treatment. Since 1970, the NNIS system has collected and analyzed data on the frequency of nosocomial infections in a voluntary sample of hospitals (currently numbering 280) in the United States.[154] Although it has been suggested that the NNIS system underestimates the true incidence of nosocomial infections by 30% to 40%,[3,155,156] the large number of cases studied during consecutive years provides a useful description of the most frequently encountered infections, their relative incidences, and the responsible pathogens.

INCIDENCE

In the 1986 NNIS report, the overall incidence of nosocomial infection was 33.5 per 1,000 discharges; the range extended from 13.3 per 1,000 pediatric discharges to 46.7 per 1,000 surgical discharges. Generally, the rate of infection is highest in large teaching hospitals and lowest in nonteaching hospitals. The higher incidence of infection among surgical patients is largely attributable to SSI. SSIs are the most frequent adverse events reported for hospitalized surgical patients and account for 38% of all nosocomial infections in surgical patients.[157] Two thirds of SSIs are incisional infections, and one third are organ/space infections.[35,158] Some 38% of all SSIs result in readmission to the hospital.[35]

Across all services, UTIs are the most common infections, accounting for 38.5% of all nosocomial infections, followed by lower respiratory tract infections (17.8%), surgical wound infections (16.6%), primary bacteremias (7.5%), and cutaneous infections (5.8%). All other categories combined account for 13.8% of nosocomial infections. The total incidence of nosocomial infection from all sites on surgical services ranges from 30.8 to 59.3 per 1,000 discharges. The risk that a surgical patient will acquire any infection varies according to the type of procedure performed as well as to the patient's underlying risk.[159]

In the 1993 NNIS report, the most common nosocomial infections for surgical patients after an SSI were UTIs (27%), pneumonias (15%), primary bloodstream infections (7%), and all other sites combined (15%).[159] Of the infected surgical patients, 17% had more than one nosocomial infection, and 9% of surgical patients with nosocomial infections subsequently died; nosocomial infections were reported to have caused or contributed to 60% of the deaths. Of infections related to death, 38% were pneumonias, 21% occurred at the surgical site, and 20% were primary bloodstream infections. The likelihood that a specific infection will be related to death varies with the type of infection [*see Table 1*].

Table 1 Contribution of Nosocomial Infection to Death in Infected Surgical Patients Who Died[159]

Type of Nosocomial Infection	Probability That Infection Was Related to Death (%)
Organ/space surgical site infection	89
Primary bloodstream infection	79
Pneumonia	77
Other	48
Incisional surgical site infection	46
Urinary tract infection	22

Urinary Tract Infection

With so many cases of bacteriuria occurring in catheterized patients, it would be easy to become complacent about the problem. Urinary tract catheterization is performed seven to eight million times a year in acute care hospitals in the United States.[160] Approximately 5% to 8% of catheterized, uninfected patients will acquire a urinary tract infection for each day of catheterization, leading to a cumulative infection rate of 40% to 50% after 10 days.[109] However, the great majority of catheterized patients with bacteriuria are asymptomatic.[109,161] It has been estimated that only 0.7% of catheterized patients will acquire a symptomatic infection and that 8% to 10% of patients will have bacteriuria after the catheter has been removed.[109]

In many of these patients, the bacteriuria resolves without specific therapy after the catheter has been removed. However, a careful study of more than 1,458 patients clearly demonstrated that mortality is higher in catheterized patients who acquire bacteriuria than in those who do not.[160] In this study, 9% of all catheterized patients acquired catheter-related UTIs; these infections were associated with a threefold increase in deaths occurring during hospitalization, even after correction for other factors (e.g., age, severity of illness, hospital service, duration of catheterization, and renal function). In surgical patients between 50 and 70 years of age with normal renal function and without a fatal underlying disease, a 3% increase in the death rate per patient per hospitalization was associated with the occurrence of a UTI. Of all deaths occurring in catheterized patients, 14% were associated with a UTI.[160] By extrapolation, this mortality suggests that as many as 56,000 deaths a year in the United States may be related to catheter-acquired UTI.

Although the risk of bacteremia is small for any individual patient with bacteriuria, the large number of hospitalized patients with bacteriuria means that many bacteremic episodes are seen in this population. UTI is the most commonly diagnosed source of gram-negative sepsis, and the rate of bacteremia secondary to urinary catheters is estimated to be between 0.7% and 2%.[109] In a case-matched study from 1978, a postoperative UTI was associated with a 2.4-day prolongation of hospital stay and an excess cost of more than $500.[162] A subsequent study revealed that 2.3% of postoperative patients with UTIs were subsequently diagnosed as having a wound infection caused by the same organism responsible for the UTI.[163] This finding accounted for 3.4% of the wound infections occurring during the study.

Infection Associated with Intravascular Devices

Nosocomial infection associated with intravascular devices, which are placed for either monitoring or therapeutic purposes, assumed increasing importance during the 1970s and 1980s. In the United States, central venous catheters are in place for approximately 15 million patient-catheter-days per year, resulting in approximately 250,000 catheter-associated bloodstream infections.[70] Of all cases of nosocomial bacteremia occurring in NNIS hospitals between September 1984 and July 1986, 82% were associated with intravascular devices[164]: 27% were associated with parenteral nutrition catheters and 55% with other vascular access devices. Reports from as early as 1963 called attention to the risk of serious systemic infections arising from peripheral I.V. catheters.[165] For ICU patients with bloodstream infections associated with central venous catheters, the attributable mortality is 25% to 35%, and the excess cost for survivors is $34,000 to $56,000 per patient, for a total annual cost of $296 million to $2.3 billion.[70]

In terms of infection risk, pulmonary arterial catheters are no different from central venous catheters, except for their potential to cause right-side heart lesions that could predispose to right-side endocarditis.[166] Pulmonary arterial catheters can be responsible for bloodstream infection, and they require as much attention during insertion and subsequent care as central venous catheters do.[68,167]

The arterial catheters used for monitoring purposes in the ICU have been thought to be less frequently associated with infection than central venous catheters are, but it is clear that life-threatening infections can originate with peripheral arterial lines.[168,169] In early studies of radial artery catheters in which nonquantitative culture techniques were employed, catheter contamination rates of 4% to 39% were recorded, but there were no cases of CRBSI or clinical infection in 605 catheterizations.[170] In these studies, the majority of catheters were removed from patients within 3 days.

Prospective studies of arterial catheters demonstrated that 18% to 35% of the lines were locally infected, as reflected in semiquantitative cultures of at least 15 colonies.[171] In one study, five cases of CRBSI occurred, representing an overall incidence of 4% and an incidence of 23% among locally infected catheters.[171] The incidence of CRBSI was increased in catheters that were inserted by cutdown rather than by percutaneous puncture and in catheters with signs of local inflammation. In another, the clinical features of bloodstream infection arising from an arterial catheter were indistinguishable from the clinical features of episodes arising from a central venous line, and 12% of all nosocomial bacteremias in the ICU originated from an arterial catheter.[171] Clearly, arterial lines as well as venous lines must be considered in the examination of a patient for the source of fever or bloodstream infection in the ICU.[68,169,171,172] Twelve cases of radial artery rupture after arterial line infection have been reported. All but one were associated with *S. aureus* infection, and nearly all demonstrated systemic signs of infection for 2 days or longer after catheter removal.[169] Although there is no published experience with the use of guide wires to change and culture arterial lines in relation to possible catheter-related infection, the technique can be applied with the same rationale used for central venous catheters.

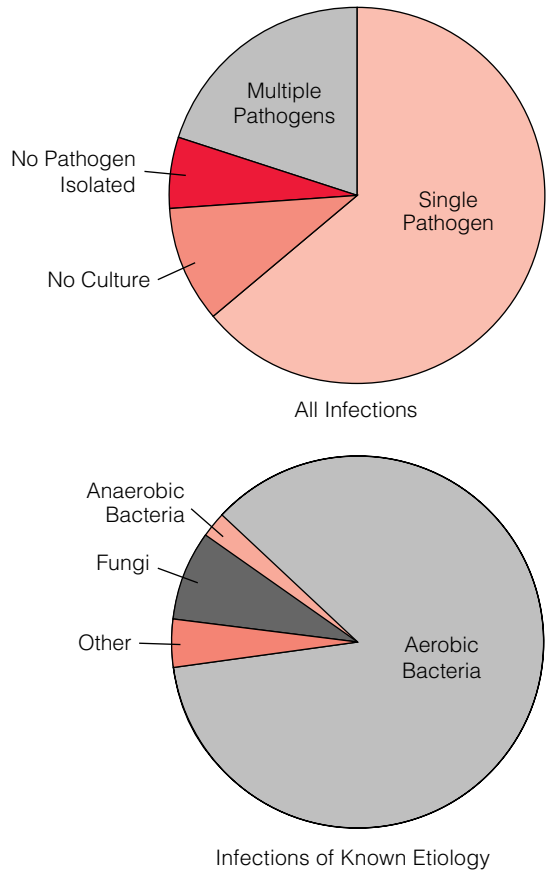


Figure 4 **Illustrated is a breakdown of the etiology of 26,965 nosocomial infections from the National Nosocomial Infections Surveillance System.[173]**

Table 2 Five Most Common Pathogens Isolated from Surgical Patients and Percentage of Total within Each Site[173]

Infection Site	Organism	Isolates at That Site (%)
Urinary tract infection	*Escherichia coli*	29
	Pseudomonas aeruginosa	16
	Enterococci	13
	Proteus species	7
	Klebsiella species	7
Surgical wound infection	*Staphylococcus aureus*	19
	Enterococci	12
	E. coli	12
	P. aeruginosa	10
	Coagulase-negative staphylococci	8
Lower respiratory infection	*P. aeruginosa*	17
	S. aureus	12
	Enterobacter species	11
	Klebsiella species	11
	Serratia species	7
Bacteremia	Coagulase-negative staphylococci	14
	S. aureus	10
	Enterobacter species	9
	Enterococci	9
	Klebsiella species	8
Cutaneous infections	*S. aureus*	19
	P. aeruginosa	13
	Enterococci	11
	Coagulase-negative staphylococci	10
	E. coli	8

PATHOGENS

In 1984, the NNIS reported on 26,965 infections. Of these cases, 64% were caused by single pathogens, 20% were caused by multiple pathogens, 6% had no pathogen identified on culture, and 10% were not cultured [*see Figure 4*].[173] Of the 84% in which a pathogen was identified, 86% were caused by aerobic bacteria, 2% by anaerobes, and 8% by fungi [*see Figure 4 and Table 2*]. Overall on the surgical services, the most common pathogen isolated was *E. coli,* followed by *P. aeruginosa,* enterococci, *S. aureus, Enterobacter* species, *Klebsiella* species, coagulase-negative staphylococci, *Proteus* species, *Candida* species, and *Serratia* species. These 10 types of pathogens accounted for 84% of all isolates. Gram-negative rods were most common in UTIs

and lower respiratory tract infections, though *S. aureus* was the second most common pathogen isolated in lower respiratory tract infections. *S. aureus* was the most common isolate from surgical wound infections, whereas coagulase-negative staphylococci, followed closely by *S. aureus,* were the pathogens most often responsible for primary bacteremias.

As a consequence of changing hospital practices, hospitalized patients today tend to be more severely ill than was once the case. Large amounts of antibiotics are being used in hospitals, and antibiotic-resistant pathogens have become increasingly problematic. Current NNIS data indicate that the frequency with which antibiotics are administered to hospitalized patients who are not in an ICU is approximately 468 defined daily doses (DDD) per 1,000 patient-days.[174] For hospitalized ICU patients, the frequency is between 800 and 1,031 DDD per 1,000 patient-days. MRSA accounts for 51% of total *S. aureus* isolates in ICU patients, 40% in non-ICU patients, and 24% in outpatients with nosocomial infections; the corresponding figures for quinolone-resistant *P. aeruginosa* in relation to total *P. aeruginosa* isolates are 37%, 27%, and 27%.[174] In 2002, the second clinical isolate of vancomycin-resistant *S. aureus* in the United States was reported.[175]

Nosocomial infections with resistant enterococci have become a serious problem. Enterococci were the third most common nosocomial bloodstream isolate reported by NNIS hospitals between 1990 and 1992.[176] The incidence of vancomycin-resistant enterococci (VRE) increased 26-fold between 1989 and 1993, from 0.3% to 7.9%, with a 34-fold rise in ICUs,[177] and the rate has continued to increase. The 2001 NNIS report stated that 13% of enterococci were resistant to vancomycin in ICU patients, 12% in non-ICU patients, and 5% in outpatients.[174] These strains arise from the patient's endogenous flora, but nosocomial spread within the hospital environment is also an important source.[177,178] The environment around infected patients is heavily contaminated with VRE, and gown and glove isolation techniques are required to stop transmission.[178] Strict application of hand hygiene is also important for reducing the spread of VRE and other nosocomial pathogens. According to the available data and current CDC recommendations, the use of alcohol-based handrub solutions is superior to washing with soap and water: it can be performed more rapidly and is less damaging to the skin.[179]

VRE are also highly resistant to other available antibiotics. Acquisition of VRE is significantly associated with prior hospitalization and with use of third-generation cephalosporins, vancomycin, or multiple antibiotics.[180,181] In one study, 16% of stool specimens submitted for testing for *C. difficile* toxin were colonized with VRE, and all surgical patients in that study had the same strain.[182]

High mortality can be associated with VRE infections. In a study comparing the outcome of patients having VRE bacteremia with the outcome of patients having bacteremia caused by vancomycin-sensitive enterococci (VSE), mortality was 2.3 times higher in those with VRE bacteremia, and 89% of patients with VRE bacteremia were colonized or infected with VRE at another site.[183] Prior treatment with third-generation cephalosporins is another risk factor for increased mortality.[176] Liver transplant patients with VRE bacteremia had a 92% higher mortality than comparable patients with VSE bacteremia, and those with VRE bacteremia also had a higher recurrence rate and greater need for invasive procedures.[184]

Current recommendations include decreased—and possibly restricted—use of vancomycin, as well as aggressive infection control measures whenever VRE are isolated in a hospitalized patient.[177] In particular, vancomycin should not be used as primary treatment for *C. difficile*–associated diarrhea and should be avoided for surgical prophylaxis unless the hospital has a specific problem with MRSA or the patient cannot receive other appropriate antibiotics.

ENTERIC INFECTION

C. difficile is often found in patients with severe antibiotic-associated enteric infections. In one report, 691 (2%) of 32,757 consecutive postoperative patients experienced watery diarrhea significant enough to stimulate a request for *C. difficile* toxin assay.[185] Of this number, 75 (11% of patients with diarrhea) had a positive toxin assay. All cases were associated with antibiotic administration. Approximately 94% of the patients had received a cephalosporin either alone or in combination with other antibiotics; 29% of these responded to cessation of antibiotics and supportive measures, and the remainder were treated with vancomycin, metronidazole, or bacitracin. Six (14%) of the patients who required specific therapy relapsed after initial response to treatment and were subsequently cured with one or more additional courses of treatment. Two patients died, and the overall hospital stay for the remaining patients was prolonged by an average of 50%.

Most patients with mild cases of antibiotic-associated diarrhea do not have either positive cultures for *C. difficile* or positive toxin assays, and the etiologic role of *C. difficile* is unclear. Many hospitalized patients without diarrhea also have *C. difficile* in the stool, with or without toxin production,[123,186] and the likelihood of isolating this pathogen increases with patients' increasing length of stay.[118] A nonpathogenic yeast, *Saccharomyces boulardii,* when administered by mouth to hospitalized patients receiving antibiotics, significantly reduced the occurrence of antibiotic-associated diarrhea without affecting the rate of acquisition of *C. difficile*.[123]

Some 3% of asymptomatic adults carry *C. difficile* in their stools, but 30% to 40% of healthy neonates may carry the organism. The rate of carriage declines after the age of 1 to 2 years. *C. difficile* can be spread in the hospital and has been isolated from 10% of inanimate objects in the environment of patients with *C. difficile* colonization, compared with 3% in hospital areas with no known cases.[187] In one report,[187] this organism was recovered from the hands of 13% of medical personnel working in a ward with affected patients; in another,[188] it was recovered from 60% of personnel immediately after they had cared for an affected patient. Soap-and-water washing was ineffective in preventing acquisition, but the combination of glove use and chlorhexidine washing was effective. In another medical center,[189] clusters of new nosocomial *C. difficile* diarrhea were prevented by screening all patients with diarrhea by active surveillance (using culture to identify *C. difficile* infection) and by instituting isolation precautions and daily disinfection of infected patients' rooms.

The prevalence of *C. difficile* in the environment is increased when a patient has diarrhea.[187,188] In one prospectively studied cohort, 21% of patients without *C. difficile* in their stools on admission acquired the organism during hospitalization, and 37% of these patients experienced diarrhea; no cases of colitis occurred.[187] Diarrhea was more common in patients who received antibiotics. The rate of acquisition of *C. difficile* was 73% higher if a patient had a roommate colonized with *C. difficile*.

COST

The cost of nosocomial infections, both in dollars and in morbidity, is high. According to one estimate, 8.7 million extra hospital days and $4.5 billion in hospital charges were attributable to nosocomial infections in United States hospitals in 1976.[190]

Estimates of the number of deaths caused by nosocomial infections run as high as 58,000 a year; 9,700 of these deaths and 36% of all costs attributed to nosocomial infections are due to wound infections.[190] The actual numbers may be even higher. Another study found that 63 of 200 consecutive patients dying in the hospital had nosocomial infections; 18 (29%) of the 63 were judged causal and 26 (41%) contributory.[8] Most of the causal and contributory infections were of the lower respiratory tract, and deaths were significantly associated with invasive devices (e.g., intra-arterial and central venous pressure monitoring devices and nasogastric tubes). Of the 57 deaths occurring on the surgical service, 27 (47%) were associated with nosocomial infections.

RISK

The risk of acquiring a nosocomial infection is clearly related to the reason for hospitalization as well as to the underlying disease.[8,191] Patients admitted to the hospital with a fatal underlying disease have a nosocomial infection rate of 24%, compared with 10% in patients with ultimately fatal disease and 2% in those with nonfatal disease. Among 100 consecutive trauma patients admitted to the ICU at Harborview Medical Center in 1986, 42 acquired 64 nosocomial infections, including 23 lower respiratory tract infections, 17 urinary tract infections, and 6 wound infections.[152] These 100 ICU admissions and 101 consecutive trauma admissions to the general ward were examined together. Of 153 patients admitted with injury severity scores of 25 or less, nosocomial infection occurred in 32 (21%). Of 48 patients with injury severity scores higher than 25, nosocomial infection occurred in 26 (54%).[152] A statewide survey of hospitals in Virginia from 1978 to 1982 found that infections in ICU patients accounted for 25% of all cases of nosocomial infections, although fewer than 10% of the beds were in ICUs.[192]

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Acknowledgments

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Figure 4 Albert Miller.