Epidemiology of Surgical Site Infection

Historically, the control of wound infection depended on antimicrobial and aseptic techniques directed at coping with the infecting organism. In the 19th century and the early part of the 20th century, wound infections had devastating consequences and a measurable mortality. Even in the 1960s, before the correct use of antibiotics and the advent of modern preoperative and postoperative care, as much as one quarter of a surgical ward might have been occupied by patients with wound complications. As a result, wound management, in itself, became an important component of ward care and of medical education. It is fortunate that many factors have intervened so that the so-called wound rounds have become a practice of the past. The epidemiology of wound infection has changed as surgeons have learned to control bacteria and the inoculum as well as to focus increasingly on the patient (the host) for measures that will continue to provide improved results.

The following three factors are the determinants of any infectious process:

1. The infecting organism (in surgical patients, usually bacteria).
2. The environment in which the infection takes place (the local response).
3. The host defense mechanisms, which deal systemically with the infectious process.¹

Wounds are particularly appropriate for analysis of infection with respect to these three determinants. Because many components of the bacterial contribution to wound infection now are clearly understood and measures to control bacteria have been implemented, the host factors become more apparent. In addition, interactions between the three determinants play a critical role, and with limited exceptions (e.g., massive contamination), few infections will be the result of only one factor [see Figure 1].

Definition of Surgical Site Infection

Wound infections have traditionally been thought of as infections in a surgical wound occurring between the skin and the deep soft tissues—a view that fails to consider the operative site as a whole. As prevention of these wound infections has become more effective, it has become apparent that definitions of operation-related infection must take the entire operative field into account; obvious examples include sternal and mediastinal infections, vascular graft infections, and infections associated with implants (if occurring within 1 year of the procedure and apparently related to it). Accordingly, the Centers for Disease Control and Prevention currently prefers to use the term surgical site infection (SSI). SSIs can be classified into three categories: superficial incisional SSIs (involving only skin and subcutaneous tissue), deep incisional SSIs (involving deep soft tissue), and organ/space SSIs (involving anatomic areas other than the incision itself that are opened or manipulated in the course of the procedure) [see Figure 2].²,³

Standardization in reporting will permit more effective surveillance and improve results, as well as offer a painless way of achieving quality assurance. The natural tendency to deny that a surgical site has become infected contributes to the difficulty of defining SSI in a way that is both accurate and acceptable to surgeons. The surgical view of SSI recalls one judge’s (probably apocryphal) remark about pornography: “It is hard to define, but I know it when I see it.” SSIs are usually easy to identify. Nevertheless, there is a critical need for definitions of SSI that can be applied in different institutions for use as performance indicators.⁴ The criteria on which such definitions must be based are more detailed than the simple apocryphal remark just cited; they are outlined more fully elsewhere [see 1:8 Preparation of the Operating Room].

STRATIFICATION OF RISK FOR SSI

The National Academy of Sciences–National Research Council classification of wounds [see Table 1], published in 1964, was a landmark in the field.⁵ This report provided incontrovertible data to show that wounds could be classified as a function of probability of bacterial contamination (usually endogenous) in a consistent manner. Thus, wound infection rates could be validly compared from month to month, between services, and between hospitals. As surgery became more complex in the following decades, however, antibiotic use became more standardized and other risk variables began to assume greater prominence. In the early 1980s, the Study on the Efficacy of Nosocomial Infection Control (SENIC) study identified three risk factors in addition to wound class: location of operation (abdomen or chest), duration of operation, and

![Figure 1](image-url) In a homeostatic, normal state, the determinants of any infectious process—bacteria, the surgical site, and host defense mechanisms (represented by three circles)—intersect at a point indicating zero probability of sepsis.
Epidemiology of Surgical Site Infection

Surgical site infection is caused by exogenous or endogenous bacteria; infection is influenced not only by the source of the infecting inoculum but also by the bacterial characteristics.

Ensure that prophylactic antibiotics, if indicated, are present in tissue in adequate concentrations at beginning of operation.

**Endogenous factors or sources of bacteria**

**Bacterial characteristics of importance (virulence and antibiotic resistance)**

**Exogenous factors or sources of bacteria**

**Remote sites of infection**
- Postpone elective operation if possible. Treat remote infection appropriately.

**Skin**
- Nature and site of operation
  - Is the operation
    - Clean
    - Clean-contaminated
    - Contaminated
    - Dirty or infected
  - Size of inoculum required to produce infection
    - Varies in different clinical situations.

**Bowel**
- Operating team–related
  - Comportment
  - Use of impermeable drapes and gowns
  - Surgical scrub
- Operating room–related
  - Traffic control
  - Cleaning
  - Air

**Preventive measures to control bacteria**
- Decontamination of patient’s skin [see Sidebar Preoperative Preparation of the Operative Site]
- Additional antibiotics if indicated, depending on likelihood of contamination and on bacterial inoculum and properties [see Sidebar Antibiotic Prophylaxis of Infection]
Factors contributing to dysfunction of host defense mechanisms can be related to surgical disease, to events surrounding the operation, to the patient’s underlying disease, and to anesthetic management.

**Surveillance and quality assurance**

Local factors influence the susceptibility of the wound environment by affecting the size of the inoculum required to produce infection.

**Surgeon-related**
Factors influenced by the surgeon include:
- Preoperative decisions
- Timing of operation
- Surgical technique
- Transfusion
- Blood loss
- Duration and extent of operation
- Glucose control
- Tissue oxygenation (mask)

**Patient-related**
Patient-related factors include:
- Presence of ≥ 3 concomitant diagnoses
- Underlying disease
- Age
- Drug use
- Preoperative nutritional status
- Smoking

**Anesthesiologist-related**
- Normothermia
- Normovolemia
- Pain control
- Tissue oxygenation
- Glucose control
- Sterility of drugs

**Operating team-related**
Factors influenced by the surgeon and operating team include:
- Duration of operation
- Maintenance of hemostasis and perfusion
- Avoidance of seroma, hematoma, necrotic tissue, wound drains
- Tissue handling
- Cautery use

**Patient-related**
- Age
- \( P_{O_2} \)
- Abdominal procedure
- Tissue perfusion
- Presence of foreign body
- Barrier function
- Diabetes
Patient clinical status (three or more diagnoses on discharge). The National Nosocomial Infection Surveillance (NNIS) study reduced these four risk factors to three: wound classification, duration of operation, and American Society of Anesthesiologists (ASA) class III, IV, or V. Both risk assessments integrate the three determinants of infection: bacteria (wound class), local environment (duration), and systemic host defenses (one definition of patient health status), and they have been shown to be applicable outside the United States. However, the SENIC and NNIS assessments do not integrate other known risk variables, such as smoking, tissue oxygen tension, glucose control, shock, and maintenance of normothermia, all of which are relevant for clinicians (though often hard to monitor and to fit into a manageable risk assessment).

**Bacteria**

Clearly, without an infecting agent, no infection will result. Accordingly, most of what is known about bacteria is put to use in major efforts directed at reducing their numbers by means of asepsis and antisepsis. The principal concept is based on the size of the bacterial inoculum.

Wounds are traditionally classified according to whether the wound inoculum of bacteria is likely to be large enough to overwhelm local and systemic host defense mechanisms and produce an infection [see Table 1]. One study showed that the most important factor in the development of a wound infection was the number of bacteria present in the wound at the end of an operative procedure. Another study quantitated this relation and provided insight into how local environmental factors might be integrated into an understanding of the problem [see Figure 3]. In the years before prophylactic antibiotics, as well as during the early phases of their use, there was a very clear relation between the classification of the operation (which is related to the probability of a significant inoculum) and the rate of wound infection. This relation is now less dominant than it once was; therefore, other factors have come to play a significant role.

---

**CONTROL OF SOURCES OF BACTERIA**

Endogenous bacteria are a more important cause of SSI than exogenous bacteria. In clean-contaminated, contaminated, and dirty-infected operations, the source and the amount of bacteria are functions of the patient’s disease and the specific organs being operated on.

Operations classified as infected are those in which infected tissue and pus are removed or drained, providing a guaranteed inoculum to the surgical site. The inoculum may be as high as $10^{10}$ bacteria/ml, some of which may already be producing an infection. In addition, some bacteria could be in the growth phase rather than the dormant or the lag phase and thus could be more pathogenic. The heavily contaminated wound is best managed by delayed primary closure. This type of management ensures that the wound is not closed over a bacterial inoculum that is almost certain to cause a wound infection, with attendant early and late consequences.

Patients should not have elective surgery in the presence of remote infection, which is associated with an increased incidence of wound infection. In patients with urinary tract infections, wounds frequently become infected with the same organism. Remote infections should be treated appropriately, and the operation should proceed only under the best conditions possible. If operation cannot be appropriately delayed, the use of prophylactic and therapeutic antibiotics should be considered [see Sidebar Antibiotic Prophylaxis of Infection and Tables 2 through 4].

Preoperative techniques of reducing patient flora, especially endogenous bacteria, are of great concern. Bowel preparation, antimicrobial showers or baths, and preoperative skin decontami-
larly preoperative skin decontamination have been proposed frequently. These techniques, particu-

The preoperative shave is a technique in need of reassessment. These techniques, particularly preoperative skin decontamination, may have specific roles in selected patients during epidemics or in units with high infection rates. As a routine for all patients, however, these techniques are unnecessary, time-consuming, and costly in institutions or units where infection rates are low.

The preoperative shave is a technique in need of reassessment. It is now clear that shaving the evening before an operation is asso-

If patient is allergic to cephalosporins or if methicillin-resistant organisms are present

If patient is allergic to cephalosporins or if methicillin-resistant organisms are present

The suggestion has been made that selective gut decontamination (SGD) may be useful in major elective procedures involving the upper GI tract and perhaps in other settings. At present, SGD for prevention of infection cannot be recom-

When infection develops after clean operations, particularly those in which foreign bodies were implanted, endogenous infect-

When infection develops after clean operations, particularly those in which foreign bodies were implanted, endogenous infecting organisms are involved but the skin is the primary source of the infecting bacteria. The air in the operating room and other OR sources occasionally become significant in clean cases; the degree of endogenous contamination can be surpassed by that of exoge-

Clean air systems have very strong advocates, but they also have equally vociferous critics. It is possible to obtain excellent results in clean cases with implants without using these systems. However, clean air systems are here to stay. Nevertheless, the presence of a clean air system does not mean that basic principles of asepsis and antisepsis should be abandoned, because endogenous bacteria must still be controlled.

The use of impermeable drapes and gowns has received con-

When wet, drapes of 270-thread-count cotton that have been water-

There were minimal numbers of endogenous bacteria, and UVL controlled one of the exogenous sources.

Table 2  Parenteral Antibiotics Recommended for Prophylaxis of Surgical Site Infection

<table>
<thead>
<tr>
<th>antibiotic</th>
<th>dose</th>
<th>route of administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefazolin</td>
<td>1 g</td>
<td>I.V. or I.M. (I.V. preferred)</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>1 g</td>
<td>I.V.</td>
</tr>
<tr>
<td>Clindamycin or Metronidazole plus Tobramycin (or equivalent aminoglycoside)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clindamycin or Metronidazole plus Tobramycin (or equivalent aminoglycoside)</td>
<td></td>
<td>I.V.</td>
</tr>
<tr>
<td>Tobramycin (or equivalent aminoglycoside)</td>
<td>1.5 mg/kg</td>
<td>I.V. or I.M. (I.V. preferred for first dose)</td>
</tr>
<tr>
<td>Cefoxitin</td>
<td>1–2 g</td>
<td>I.V.</td>
</tr>
<tr>
<td>Cefotetan</td>
<td>1–2 g</td>
<td>I.V.</td>
</tr>
</tbody>
</table>
Antibiotic Prophylaxis of Infection

Selection

Spectrum. The antibiotic chosen should be active against the most likely pathogens. Single-agent therapy is almost always effective except in colorectal operations, small-bowel procedures with stasis, emergency abdominal operations in the presence of polymicrobial flora, and penetrating trauma; in such cases, a combination of antibiotics is usually used because anaerobic coverage is required.

Pharmacokinetics. The half-life of the antibiotic selected must be long enough to maintain adequate tissue levels throughout the operation.

Administration

Dosage, route, and timing. A single preoperative dose that is of the same strength as a full therapeutic dose is adequate in most instances. The single dose should be given I.V. immediately before skin incision. Administration by the anesthetist is most effective and efficient.

Duration. A second dose is warranted if the duration of the operation exceeds either 3 hours or twice the half-life of the antibiotic. No additional benefit has been demonstrated in continuing prophylaxis beyond the day of the operation, and mounting data suggest that the preoperative dose is sufficient. When massive hemorrhage has occurred (i.e., blood loss equal to or greater than blood volume), a second dose is warranted. Even in emergency or trauma cases, prolonged courses of antibiotics are not justified unless they are therapeutic.

Indications

CLEAN CASES

Prophylactic antibiotics are not indicated in clean operations if the patient has no host risk factors or if the operation does not involve placement of prosthetic materials. Clean operations are further considered clean-contaminated. In clean-contaminated cases, antibiotics generally are not routine unless the operation involves a high risk of contamination.

CATHETER-ASSOCIATED INFECTIONS

Catheters for dialysis or nutrition, pacemakers, and shunts of various sorts are prone to infection mostly for technical reasons, and prophylaxis is not usually required. Meta-analysis indicates, however, that antimicrobial prophylaxis reduces the infection rate in CSF shunts by 50%. Beneficial results may also be achievable for other permanently implanted shunts (e.g., peritoneovenous) and devices (e.g., long-term venous access catheters and pacemakers); however, the studies needed to confirm this possibility will never be done, because the infection rates are low and the sample sizes would have to be prohibitively large. The placement of such foreign bodies is a clean operation, and the use of antibiotics should be based on local experience.

CLEAN-CONTAMINATED CASES

Abdominal procedures. In biliary tract procedures (open or laparoscopic), prophylaxis is required only for patients at high risk: those whose common bile duct is likely to be explored (because of jaundice, bile duct obstruction, stones in the common bile duct, or a reoperative biliary procedure); those with acute cholecystitis; and those older than 70 years. A single dose of cefazolin is adequate. In hepatobiliary and pancreatic procedures, antibiotic prophylaxis is always warranted because these operations are clean-contaminated, because they are long, because they are abdominal, or for all of these reasons. Prophylaxis is also warranted for therapeutic endoscopic retrograde cholangiopancreatography. In gastroduodenal procedures, patients whose gastric acidity is normal or high and in whom bleeding, cancer, gastric ulcer, and obstruction are absent are at low risk for infection and require no prophylaxis; all other patients are at high risk and require prophylaxis. Patients undergoing operation for morbid obesity should receive double the usual prophylactic dose; cefazolin is an effective agent.

Operations on the head and neck (including the esophagus). Patients whose operation is of significance (i.e., involve entry into the oral cavity, the pharynx, or the esophagus) require prophylaxis.

Gynecologic procedures. Patients whose operation is either high-risk cesarean section, abortion, or vaginal or abdominal hysterectomy will benefit from cefazolin. Aqueous penicillin G or doxycycline is preferable for those having hysterectomies and metronidazole for those having cesarean sections. Women delivering by cesarean section should be given the antibiotic immediately after cord clamping.

Urologic procedures. In principle, antibiotics are not required in patients with sterile urine. Patients with positive cultures should be treated. If an operative procedure is performed, a single dose of the appropriate antibiotic will suffice.

(continued)
Antibiotic Prophylaxis of Infection (continued)

CONTAMINATED CASES

Abdominal procedures. In colorectal procedures, antibiotics active against both aerobes and anaerobes are recommended. In appendectomy, SSI prophylaxis requires an agent or combination of agents active against both aerobes and anaerobes; a single dose of cefoxitin, 2 g I.V., or, in patients who are allergic to β-lactam antibiotics, metronidazole, 500 mg I.V., is effective. A combination of an aminoglycoside and clindamycin is effective if the appendix is perforated; a therapeutic course of 3 to 5 days is appropriate but does not seem warranted unless the patient is particularly ill. A laparotomy without a precise diagnosis is usually an emergency procedure and demands preoperative prophylaxis. If the preoperative diagnosis is a ruptured viscus (e.g., the colon or the small bowel), both an agent active against aerobes and an agent active against anaerobes are required. Depending on operative findings, prophylaxis may be sufficient or may have to be supplemented with postoperative antibiotic therapy.

Trauma. The proper duration of antibiotic prophylaxis for trauma patients is a confusing issue—24 hours or less of prophylaxis is probably adequate, and more than 48 hours is certainly unwarranted. When laparotomy is performed for nonpenetrating injuries, prophylaxis should be administered. Coverage of both aerobes and anaerobes is mandatory. The duration of prophylaxis should be less than 24 hours. In cases of penetrating abdominal injury, prophylaxis with either cefoxitin or a combination of agents active against anaerobic and aerobic organisms is required. The duration of prophylaxis should be less than 24 hours, and in many cases, perioperative doses will be adequate. For open fractures, management should proceed as if a therapeutic course were required. For grade I or II injuries, a first-generation cephalosporin will suffice, whereas for grade III injuries, combination therapy is warranted; duration may vary. For operative repair of fractures, a single dose of cefazolin may be given preoperatively, with a second dose added if the procedure is long. Patients with major soft tissue injury with a danger of spreading infection will benefit from cefazolin, 1 g I.V. every 8 hours for 1 to 3 days.

DIRTY OR INFECTED CASES

Infected cases require therapeutic courses of antibiotics; prophylaxis is not appropriate in this context. In dirty cases, particularly those resulting from trauma, contamination and tissue destruction are usually so extensive that the wounds must be left open for delayed primary or secondary closure. Appropriate timing of wound closure is judged at the time of debridement. Antibiotics should be administered as part of resuscitation. Administration of antibiotics for 24 hours is probably adequate if infection is absent at the outset. However, a therapeutic course of antibiotics is warranted if infection is present from the outset or if more than 6 hours elapsed before treatment of the wounds was initiated.

Prophylaxis of Endocarditis

Studies of the incidence of endocarditis associated with dental procedures, endoscopy, or operations that may result in transient bacteremia are lacking. Nevertheless, the consensus is that patients with specific cardiac and vascular conditions are at risk for endocarditis or vascular prosthetic infection when undergoing certain procedures; these patients should receive prophylactic antibiotics. A variety of organisms are dangerous, but viridans streptococci are the most common after dental or oral procedures, and enterococci are most common if the portal of entry is the GU or GI tract. Oral amoxicillin now replaces penicillin V or ampicillin because of superior absorption and better serum levels. In penicillin-allergic patients, clindamycin is recommended; alternatives include cephalaxin, cefadroxil, azithromycin, and clarithromycin. When there is a risk of exposure to bowel flora or enterococci, oral amoxicillin may be given. If an I.V. regimen is indicated, ampicillin may be given, with gentamicin added if the patient is at high risk for endocarditis. In patients allergic to penicillin, vancomycin is appropriate, with gentamicin added in high-risk patients. These parenteral regimens should be reserved for high-risk patients undergoing procedures with a significant probability of bacteremia. In patients receiving penicillin-based prophylaxis because of a history of rheumatic fever, erythromycin rather than amoxicillin should be used to protect against endocarditis. There is consensus concerning prophylaxis for orthopedic prostheses and acquired infection after transient bacteremia. In major procedures, where the risk of bacteremia is significant, the above recommendations are pertinent.

BACTERIAL PROPERTIES

Not only is the size of the bacterial inoculum important; the bacterial properties of virulence and pathogenicity are also significant. The most obvious pathogenic bacteria in surgical patients are gram-positive cocci (e.g., Staphylococcus aureus and streptococci). With modern hygienic practice, it would be expected that S. aureus would be found mostly in clean cases, with a wound infection incidence of 1% to 2%; however, it is in fact an increasingly common pathogen in SSIs. Surveillance can be very useful in identifying either wards or surgeons with increased rates. Operative procedures in infected areas have an increased infection rate because of the high inoculum with actively pathogenic bacteria.

The preoperative hospital stay has frequently been found to make an important contribution to wound infection rates. The usual explanation is that during this stay, either more endogenous bacteria are present or commensal flora is replaced by hospital flora. More likely, the patient’s clinical picture is a complex one, often entailing exhaustive workup of more than one organ system, various complications, and a degree of illness that radically changes the host’s ability to deal with an inoculum, however small. Therefore, multiple factors combine to transform the hospitalized preoperative patient into a susceptible host. Same-day admission should eliminate any bacterial impact associated with the preoperative hospital stay.

Bacteria with multiple antibiotic resistance (e.g., methicillin-resistant S. aureus [MRSA], S. epidermidis, and vancomycin-resistant enterococci [VRE]) can be associated with significant SSI problems. In particular, staphylococci, with their natural virulence, present an important hazard if inappropriate prophylaxis is used.

Many surgeons consider it inappropriate or unnecessary to obtain good culture and sensitivity data on SSIs; instead of conducting sensitivity testing, they simply drain infected wounds, believing that the wounds will heal. However, there have been a number of reports of SSIs caused by unusual organisms; these findings underscore the usefulness of culturing pus or fluid when an infection is being drained. SSIs caused by antibiotic-resistant organisms or unusual pathogens call for specific prophylaxis, perhaps other infection control efforts, and, if the problem persists, a search for a possible carrier or a common source.
I BASIC SURGICAL AND PERIOPERATIVE CONSIDERATIONS

The surgeon’s perioperative rituals are designed to reduce or eliminate bacteria from the operative field. Many old habits are obsolete [see 1.8 Preparation of the Operating Room and Discussion, Hand Washing, below]. Nonetheless, it is clear that surgeons can influence SSI rates.13 The refusal to use delayed primary closure or secondary closure is an example. Careful attention to the concepts of asepsis and antisepsis in the preparation and conduct of the operation is important. Although no single step in the ritual of preparing a patient for the operative procedure is indispensable, it is likely that certain critical standards of behavior must be maintained to achieve good results.

The measurement and publication of data about individuals or hospitals with high SSI rates have been associated with a diminution of those rates [see Table 6].12,13,28 It is uncertain by what process the diffusion of these data relates to the observed improvements. Although surveillance has unpleasant connotations, it provides objective data that individual surgeons are often too busy to acquire but that can contribute to improved patient care. For example, such data can be useful in identifying problems (e.g., the presence of MRSA, a high SSI incidence, or clusters), maintaining quality assurance, and allowing comparison with accepted standards.

**Environment: Local Factors**

Local factors influence SSI development because they affect the size of the bacterial inoculum that is required to produce an infection: in a susceptible wound, a smaller inoculum produces infection [see Figure 2].

**THE SURGEON’S INFLUENCE**

Most of the local factors that make a surgical site favorable to bacteria are under the control of the surgeon. Although Halsted usually receives, deservedly so, the credit for having established the importance of technical excellence in the OR in preventing infection, individual surgeons in the distant past achieved remarkable results by careful attention to cleanliness and technique.29 The Halstedian principles dealt with hemostasis, sharp dissection, fine sutures, anatomic dissection, and the gentle handling of tissues. Mass ligatures, large or braided nonabsorbable sutures, necrotic tissue, and the creation of hematomas or seromas must be avoided, and foreign materials must be judiciously used because these techniques and materials change the size of the inoculum required to initiate an infectious process. Logarithmically fewer bacteria are required to produce infection in the presence of a foreign body (e.g., suture, graft, metal, or pacemaker) or necrotic tissue (e.g., that caused by gross hemostasis or injudicious use of electrocautery devices).

The differences in inoculum required to produce wound infections can be seen in a model in which the two variables are the wound hematocrit and the presence of antibiotic [see Figure 3]. In the absence of an antibiotic and in the presence of wound fluid with a hematocrit of more than 8%, 10 bacteria yield a wound infection rate of 20%. In a technically good wound with no antibiotic, however, 1,000 bacteria produce a wound infection rate of 20%.11 In the presence of an antibiotic, 10³ to 10⁶ bacteria are required.

**Drips**

The use of drips varies widely and is very subjective. All surgeons are certain that they understand when to use a drip. However, certain points are worth noting. It is now recognized that a simple Penrose drain may function as a drainage route but is also an access route by which pathogens can reach the patient.30 It is important that the operative site not be drained through the wound. The use of a closed suction drain reduces the potential for contamination and infection.

Many operations on the GI tract can be performed safely without employing prophylactic drainage.11 A review and meta-analysis from 2004 concluded that (1) after hepatic, colonic, or rectal resection with primary anastomosis and after appendectomy for any stage of appendicitis, drains should be omitted (recommendation grade A), and (2) after esophageal resection and total gastrectomy, drains should be used (recommendation grade D). Additional randomized, controlled trials will be required to determine the value of prophylactic drainage for other GI procedures, especially those involving the upper GI tract.

---

**Table 3** Conditions and Procedures That Require Antibiotic Prophylaxis against Endocarditis

<table>
<thead>
<tr>
<th>CONDITIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac</td>
</tr>
<tr>
<td>Prosthetic cardiac valves (including biosynthetic valves)</td>
</tr>
<tr>
<td>Most congenital cardiac malformations</td>
</tr>
<tr>
<td>Surgically constructed systemic-pulmonary shunts</td>
</tr>
<tr>
<td>Rheumatic and other acquired valvular dysfunction</td>
</tr>
<tr>
<td>Idiopathic hypertrophic subaortic stenosis</td>
</tr>
<tr>
<td>History of bacterial endocarditis</td>
</tr>
<tr>
<td>Mitral valve prolapse causing mitral insufficiency</td>
</tr>
<tr>
<td>Surgically repaired intracardiac lesions with residual hemodynamic abnormality or &lt; 6 mo after operation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PROCEDURES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vascular</td>
</tr>
<tr>
<td>Synthetic vascular grafts</td>
</tr>
<tr>
<td>Dental or oropharyngeal</td>
</tr>
<tr>
<td>Procedures that may induce bleeding</td>
</tr>
<tr>
<td>Procedures that involve incision of the mucosa</td>
</tr>
<tr>
<td>Respiratory</td>
</tr>
<tr>
<td>Rigid bronchoscopy</td>
</tr>
<tr>
<td>Incision and drainage or debridement of sites of infection</td>
</tr>
<tr>
<td>Urologic</td>
</tr>
<tr>
<td>Cystoscopy with urethral dilatation</td>
</tr>
<tr>
<td>Urinary tract procedures</td>
</tr>
<tr>
<td>Catheterization in the presence of infected urine</td>
</tr>
<tr>
<td>Gynecologic</td>
</tr>
<tr>
<td>Vaginal hysterectomy</td>
</tr>
<tr>
<td>Vaginal delivery in the presence of infection</td>
</tr>
<tr>
<td>Gastrointestinal</td>
</tr>
<tr>
<td>Procedures that involve incision or resection of mucosa</td>
</tr>
<tr>
<td>Endoscopy that involves manipulation (e.g., biopsy, dilatation, or sclerotherapy) or ERCP</td>
</tr>
</tbody>
</table>
I BASIC SURGICAL AND PERIOPERATIVE CONSIDERATIONS

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Table 4 Antibiotics for Prevention of Endocarditis

<table>
<thead>
<tr>
<th>Manipulative Procedure</th>
<th>Usual</th>
<th>Prophylactic Regimen*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dental procedures likely to cause gingival bleeding; operations or instrumentation of the upper respiratory tract</td>
<td><strong>Oral</strong> Amoxicillin, 2.0 g 1 hr before procedure</td>
<td><strong>Oral</strong> Clindamycin, 600 mg 1 hr before procedure or Cephalxin or cefadroxil, 2.0 g 1 hr before procedure or Azithromycin or clarithromycin, 500 mg 1 hr before procedure</td>
</tr>
<tr>
<td>Gastrointestinal or genitourinary operation; abscess drainage</td>
<td><strong>Oral</strong> Amoxicillin, 2.0 g 1 hr before procedure</td>
<td><strong>Parenteral</strong> Clindamycin, 600 mg I.V. within 30 min before procedure or Cefazolin, 1.0 g I.M. or I.V. within 30 min before procedure</td>
</tr>
<tr>
<td></td>
<td><strong>Parenteral</strong> Ampicillin, 2.0 g I.M. or I.V. within 30 min before procedure</td>
<td><strong>Parenteral</strong> Cefazolin, 1.0 g I.V. within 30 min before procedure</td>
</tr>
</tbody>
</table>

*Pediatric dosages are as follows: oral amoxicillin, 50 mg/kg; oral or parenteral clindamycin, 20 mg/kg; oral cephalaxin or cefadroxil, 50 mg/kg; oral azithromycin or clarithromycin, 15 mg/kg; parenteral ampicillin, 50 mg/kg; parenteral cefazolin, 25 mg/kg; parenteral gentamicin, 2 mg/kg; parenteral vancomycin, 20 mg/kg. Total pediatric dose should not exceed total adult dose.

† Patients with a history of immediate-type sensitivity to penicillin should not receive these agents.

‡ High-risk patients should also receive ampicillin, 1.0 g I.M. or I.V., or amoxicillin, 1.0 g p.o., 6 hr after procedure.

### Duration of Operation

In most studies,6,10,12 contamination certainly increases with time (see above). Wound edges can dry out, become macerated, or in other ways be made more susceptible to infection (i.e., requiring fewer bacteria for development of infection). Speed and poor technique are not suitable approaches; expeditious operation is appropriate.

#### Electrocautery

The use of electrocautery devices has been clearly associated with an increase in the incidence of superficial SSIs. However, when such devices are properly used to provide pinpoint coagulation (for which the bleeding vessels are best held by fine forceps) or to divide tissues under tension, there is minimal tissue destruction, no charring, and no change in the wound infection rate.30

### Patient Factors

#### Local Blood Flow

Local perfusion can greatly influence the development of infection, as is seen most easily in the tendency of the patient with peripheral vascular disease to acquire infection of an extremity. As a local problem, inadequate perfusion reduces the number of bacteria required for infection, in part because inadequate perfusion leads to decreased tissue levels of oxygen. Shock, by reducing local perfusion, also greatly enhances susceptibility to infection. Fewer organisms are required to produce infection during or immediately after shock [see Figure 4].

To counter these effects, the arterial oxygen tension (PaO2) must be translated into an adequate subcutaneous oxygen level (determined by measuring transcutaneous oxygen tension)32; this, together with adequate perfusion, will provide local protection by increasing the number of bacteria required to produce infection. Provision of supplemental oxygen in the perioperative period may lead to a reduced SSI rate, probably as a consequence of increased tissue oxygen tension,33 though the value of this practice has been questioned.34 If the patient is not intubated, a mask, not nasal prongs, is required.35

#### Barrier Function

Inadequate perfusion may also affect the function of other organs, and the resulting dysfunction will, in turn, influence the patient’s susceptibility to infection. For example, ischemia-reperfusion injury to the intestinal tract is a frequent consequence of hypovolemic shock and bloodstream infection. Inadequate perfusion of the GI tract may also occur during states of fluid and electrolyte imbalance or when cardiac output is marginal. In experimental studies, altered blood flow has been found to be associated with the breakdown of bowel barrier function—that is, the inability of the intestinal tract to prevent bacteria, their toxins, or both from moving from the gut lumen into tissue at a rate too fast to permit clearance by the usual protective mechanisms. A variety of experimental approaches aimed at enhancing bowel barrier function have been studied; at present, however, the most clinically applicable method of bowel protection is initiation of enteral feeding (even if the quantity of nutrients provided does not satisfy all the nutrient requirements) and administration of the amino acid glutamine [see 8:22 Nutritional Support]. Glutamine is a specific fuel for enterocytes and colonocytes and has been found to aid recovery of damaged intestinal mucosa and enhance barrier function when administered either enterally or parenterally.

#### Advanced Age

Aging is associated with structural and functional changes that render the skin and subcutaneous tissues more susceptible to infection. These changes are immutable; however, they must be evaluated in advance and addressed by excellent surgical technique and, on occasion, prophylactic antibiotics [see Sidebar Antibiotic Prophylaxis of Infection]. SSI rates increase with aging until the age of 65 years, after which point the incidence appears to decline.36

![Figure 4](image_url)
Preoperative Preparation of the Operative Site

The sole reason for preparing the patient’s skin before an operation is to reduce the risk of wound infection. A preoperative antiseptic bath is not necessary for most surgical patients, but their personal hygiene must be assessed and preoperative cleanliness established. Multiple preoperative baths may prevent postoperative infection in selected patient groups, such as those who carry *Staphylococcus aureus* on their skin or who have infectious lesions. Chlorhexidine gluconate is the recommended agent for such baths.114

Hair should not be removed from the operative site unless it physically interferes with accurate anatomic approximation of the wound edges.115 If hair must be removed, it should be clipped in the OR.14 Shaving hair from the operative site, particularly on the days before operation or immediately before wound incision in the OR, increases the risk of wound infection. Depilatories are not recommended, because they cause serious irritation and rashes in a significant number of patients, especially when used near the eyes and the genitalia.116

In emergency procedures, obvious dirt, grime, and dried blood should be mechanically cleansed from the operative site by using sufficient friction. In one study, cleansing of contaminated wounds by means of ultrasound debridement was compared with high-pressure irrigation and soaking. The experimental wounds were contaminated with a colloidal clay that potentiates infection 1,000-fold. The investigators irrigated wounds at pressures of 8 to 10 psi, a level obtained by using a 30 ml syringe with a 1.5 in. long 19-gauge needle and 300 ml of 0.85% sterile saline solution. High-pressure irrigation removed slightly more particulate matter (59%) than ultrasound debridement (48%), and both of these methods removed more matter than soaking (26%).117 Both ultrasound debridement and high-pressure irrigation were also effective in reducing the wound infection rate in experimental wounds contaminated with a subinfective dose of *S. aureus*.

For nonemergency procedures, the necessary reduction in microorganisms can be achieved by using povidone-iodine (10% available povidone-iodine and 1% available iodine) or chlorhexidine gluconate both for mechanical cleansing of the intertriginous folds and the umbilicus and for painting the operative site. Which skin antiseptic is optimal is unclear. The best option appears to be chlorhexidine gluconate or an iodophor.118 The patient should be assessed for evidence of sensitivity to the antiseptic (particularly if the agent contains iodine) to minimize the risk of an allergic reaction. What some patients report as iodine allergies are actually irritations. Iodine in alcohol or in water is associated with an increased risk of skin irritation,50 particularly at the edges of the operative field, where the iodine concentrates as the alcohol evaporates. Iodine should therefore be removed after sufficient contact time with the skin, especially at the edges. Iodophors do not irritate the skin and thus need not be removed.

PATIENT FACTORS

Surgeons have always known that the patient is a significant variable in the outcome of operation. Various clinical states are associated with altered resistance to infection. In all patients, but particularly those at high risk, SSI creates not only wound complications but also significant morbidity (e.g., reoperation, incisional hernia, secondary infection, impaired mobility, increased hospitalization, delayed rehabilitation, or permanent disability) and occasional mortality.22 SENIC has proposed that the risk of wound infection be assessed not only in terms of prob-

**Table 5** Parenteral Antibiotics Commonly Used for Broad-Spectrum Coverage of Colonic Microflora

<table>
<thead>
<tr>
<th>COMBINATION THERAPY OR PROPHYLAXIS</th>
<th>COLONIC MICROFLORA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aerobic Coverage</strong></td>
<td></td>
</tr>
<tr>
<td>Amikacin</td>
<td>Ciprofloxacin</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>Gentamicin</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>Tobramycin</td>
</tr>
<tr>
<td><strong>Anaerobic Coverage</strong></td>
<td></td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>Metronidazole</td>
</tr>
<tr>
<td>Clindamycin</td>
<td></td>
</tr>
<tr>
<td><strong>SINGLE-DRUG THERAPY OR PROPHYLAXIS</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Aerobic-Anaerobic Coverage</strong></td>
<td></td>
</tr>
<tr>
<td>Ampicillin-sulbactam</td>
<td>Imipenem-cilastatin*</td>
</tr>
<tr>
<td>Cefotetan</td>
<td>Piperacillin-tazobactam</td>
</tr>
<tr>
<td>Cefoxitin</td>
<td>Ticarcillin-clavulanate</td>
</tr>
<tr>
<td>Cefazoixime</td>
<td></td>
</tr>
</tbody>
</table>

*This agent should be used only for therapeutic purposes; it should not be used for prophylaxis.*
ability of contamination but also in relation to host factors. According to this study, patients most clearly at risk for wound infection are those with three or more concomitant diagnoses; other patients who are clearly at risk are those undergoing a clean-contaminated or contaminated abdominal procedure and those undergoing any procedure expected to last longer than 2 hours. These last two risk groups are affected by a bacterial component, but all those patients who are undergoing major abdominal procedures or lengthy operations generally have a significant primary pathologic condition and are usually older, with an increased frequency of concomitant conditions. The NNIS system uses most of the same concepts but expresses them differently. In the NNIS study, host factors in the large study are evaluated in terms of the ASA score. Duration of operation is measured differently as well, with a lengthy operation being defined by the NNIS as one that is at or above the 75th percentile for operating time. Bacterial contamination remains a risk factor, but operative site is eliminated.

Shock has an influence on the incidence of wound infection [see Figure 4]. This influence is most obvious in cases of trauma, but there are significant implications for all patients in regard to maintenance of blood volume, hemostasis, and oxygen-carrying capacity. The effect of shock on the risk of infection appears to be not only immediate (i.e., its effect on local perfusion) but also late because systemic responses are blunted as local factors return to normal.

Advanced age, transfusion, and the use of steroids and other immunosuppressive drugs, including chemotherapeutic agents, are associated with an increased risk of SSI. Often, these factors cannot be altered; however, the proper choice of operation, the appropriate use of prophylaxis, and meticulous surgical technique can reduce the risk of such infection by maintaining patient homeostasis, reducing the size of any infecting microbial inoculum, and creating a wound that is likely to heal primarily.

Smoking is associated with a striking increase in SSI incidence. As little as 1 week of abstinence from smoking will make a positive difference.

Pharmacologic therapy can affect host response as well. Nonsteroidal anti-inflammatory drugs that attenuate the production of certain eicosanoids can greatly alter the adverse effects of infection by modifying fever and cardiovascular effects. Operative procedures involving inhalational anesthetics result in an immediate rise in plasma cortisol concentrations. The steroid response and the associated immunomodulation can be modified by using high epidural anesthesia as the method of choice; pituitary adrenal activation will be greatly attenuated. Some drugs that inhibit steroid elaboration (e.g., etomidate) have also been shown to be capable of modifying perioperative immune responses.

### Table 6  Effect of Surveillance and Feedback on Wound Infection Rates in Two Hospitals

<table>
<thead>
<tr>
<th>Hospital</th>
<th>Period 1</th>
<th>Period 2*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of wounds</td>
<td>Wound infection rate</td>
</tr>
<tr>
<td>Hospital A</td>
<td>1,500</td>
<td>8.4%</td>
</tr>
<tr>
<td>Hospital B</td>
<td>1,746</td>
<td>5.7%</td>
</tr>
</tbody>
</table>

*Periods 1 and 2 were separated by an interval during which feedback on wound infection rates was analyzed.

![Figure 4](Image)

**Figure 4** Animals exposed to hemorrhagic shock followed by resuscitation show an early decreased resistance to wound infection. There is also a persistent influence of shock on the development of wound infection at different times of inoculation after shock. The importance of inoculum size (10⁶/ml to 10⁸/ml) and the effect of antibiotic on infection rates are evident at all times of inoculation.
ANESTHESIOLOGIST-RELATED FACTORS

A 2000 commentary in *The Lancet* by Donal Buggy considered the question of whether anesthetic management could influence surgical wound healing. In addition to the surgeon- and patient-related factors already discussed (see above), Buggy cogently identified a number of anesthesiologist-related factors that could contribute to better wound healing and reduced wound infection. Some of these factors (e.g., pain control, epidural anesthesia, and autologous transfusion) are unproven but nonetheless make sense and should certainly be tested. Others (e.g., tissue perfusion, intravascular volume, and—significantly—maintenance of normal perioperative body temperature) have undergone formal evaluation. Very good studies have shown that dramatic reductions in SSI rates can be achieved through careful avoidance of hypothermia. Patient-controlled analgesia pumps are known to be associated with increased SSI rates, through a mechanism that is currently unknown. Infection control practices are required of all practitioners; contamination of anesthetic drugs by bacteria has resulted in numerous small outbreaks of SSI.

As modern surgical practice has evolved and the variable of bacterial contamination has come to be generally well managed, the importance of all members of the surgical team in the prevention of SSI has become increasingly apparent. The crux of Buggy’s commentary may be expressed as follows: details make a difference, and all of the participants in a patient’s surgical journey can contribute to a continuing decrease in SSI. It is a systems issue.

INTEGRATION OF DETERMINANTS

As operative infection rates slowly fall, despite the performance of increasingly complex operations in patients at greater risk, surgeons are approaching the control of infection with a broader view than simply that of asepsis and antisepsis. This new, broader view must take into account many variables, of which some have no relation to bacteria but all play a role in SSI. To estimate risk, one must integrate the various determinants of infection in such a way that they can be applied to patient care. Much of this exercise is vague. In reality, the day-to-day practice of surgery includes a risk assessment that is essentially a form of logistic regression, though not recognized as such. Each surgeon’s assessment of the probability of whether an SSI will occur takes into account the determining variables:

\[
\text{Probability of SSI} = x + a \text{ (bacteria)} + b \text{ (environment: local factors)} + c \text{ (host defense mechanisms: systemic factors)}
\]

**Table 7** Determinants of Infection and Factors That Influence Wound Infection Rates

<table>
<thead>
<tr>
<th>Variable</th>
<th>Determinant of Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Bacteria</td>
</tr>
<tr>
<td>Bacterial numbers in wound</td>
<td>A</td>
</tr>
<tr>
<td>Potential contamination</td>
<td>A</td>
</tr>
<tr>
<td>Preoperative shave</td>
<td>A</td>
</tr>
<tr>
<td>Presence of 3 or more diagnoses</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>Duration of operation</td>
<td>A</td>
</tr>
<tr>
<td>Abdominal operation</td>
<td>A</td>
</tr>
<tr>
<td>ASA class III, IV, or V</td>
<td></td>
</tr>
<tr>
<td>$O_2$ tension</td>
<td></td>
</tr>
<tr>
<td>Glucose control</td>
<td></td>
</tr>
<tr>
<td>Normothermia</td>
<td></td>
</tr>
<tr>
<td>Shock</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
</tr>
</tbody>
</table>

**Discussion**

Antibiotic Prophylaxis of Surgical Site Infection

It is difficult to understand why antibiotics have not always prevented SSI successfully. Certainly, surgeons were quick to appreciate the possibilities of antibiotics; nevertheless, the efficacy of antibiotic prophylaxis was not proved until the late 1960s. Studies before then had major design flaws—principally, the administration of the antibiotic some time after the start of the operation, often in the recovery room. The failure of studies to demonstrate efficacy and the occasional finding that prophylactic antibiotics worsened rather than improved outcome led in the late 1950s to profound skepticism about prophylactic antibiotic use in any operation.

The principal reason for the apparent ineffectiveness was inadequate understanding of the biology of SSIs. Fruitful study of antibiotics and how they should be used began after physiologic groundwork established the importance of local blood flow, maintenance of local immune defenses, adjuvants, and local and systemic perfusion.

The key antibiotic study, which was conducted in guinea pigs, unequivocally proved the following about antibiotics:
1. They are most effective when given before inoculation of bacteria.
2. They are ineffective if given 3 hours after inoculation.
3. They are of intermediate effectiveness when given in between these times [see Figure 5].

Although efficacy with a complicated regimen was demonstrated in 1964, the correct approach was not defined until 1969. Established by these studies are the philosophical and practical bases of the principles of antibiotic prophylaxis of SSI in all surgical arenas: that prophylactic antibiotics must be given preoperatively within 2 hours of the incision, in full dosage, parenterally, and for a very limited period. These principles remain essentially unchanged despite minor modifications from innumerable subsequent studies. Prophylaxis for colorectal operations is discussed elsewhere [see Infection Prevention in Bowel Surgery, below].

**PRINCIPLES OF PATIENT SELECTION**

Patients must be selected for prophylaxis on the basis of either their risk for SSI or the cost to their health if an SSI develops (e.g., after implantation of a cardiac valve or another prosthesis). The most important criterion is the degree of bacterial contamination expected to occur during the operation. The traditional classification of such contamination was defined in 1964 by the historic National Academy of Sciences–National Research Council study. The important features of the classification are its simplicity, ease of understanding, ease of coding, and reliability. Classification is dependent on only one variable—the bacterial inoculum—and the effects of this variable are now controllable by antimicrobial prophylaxis. Advances in operative technique, general care, antibiotic use, anesthesia, and surveillance have reduced SSI rates in all categories that were established by this classification [see Table 8].

In 1960, after years of negative studies, it was said, “Nearly all surgeons now agree that the routine use of prophylaxis in clean operations is unnecessary and undesirable.” Since then, much has changed: there are now many clean operations for which no competent surgeon would omit the use of prophylactic antibiotics, particularly as procedures become increasingly complex and prosthetic materials are used in patients who are older, sicker, or immunocompromised.

A separate risk assessment that integrates host and bacterial variables (i.e., whether the operation is dirty or contaminated, is longer than 2 hours, or is an abdominal procedure and whether the patient has three or more concomitant diagnoses) segregates more effectively those patients who are prone to an increased incidence of SSI [see Integration of Determinants of Infection, below]. This approach enables the surgeon to identify those patients who are likely to require preventive measures, particularly in clean cases, in which antibiotics would normally not be used.

The prototypical clean operation is an inguinal hernia repair. Technical approaches have changed dramatically over the past 10 years, and most primary and recurrent hernias are now treated with a tension-free mesh-based repair. The use of antibiotics has become controversial. In the era of repairs under tension, there was some evidence to suggest that a perioperative antibiotic (in a single preoperative dose) was beneficial. Current studies, however, do not support antibiotic use in tension-free mesh-based inguinal hernia repairs. On the other hand, if surveillance indicates that there is a local or regional problem with SSI after hernia surgery, antibiotic prophylaxis (again in the form of single preoperative dose) is appropriate. Without significantly more supportive data, prophylaxis for clean cases cannot be recommended unless specific risk factors are present.

Data suggest that prophylactic use of antibiotics may contribute to secondary *Clostridium difficile* disease; accordingly, caution should be exercised when widening the indications for prophylaxis is under consideration. If local results are poor, surgical practice should be reassessed before antibiotics are prescribed.

**ANTIBIOTIC SELECTION AND ADMINISTRATION**

When antibiotics are given more than 2 hours before operation, the risk of infection is increased. I.V. administration in the OR or the preanesthetic room guarantees appropriate levels at the time of incision. The organisms likely to be present dictate the choice of antibiotic for prophylaxis. The cephalosporins are ideally suited to prophylaxis: their features include a broad spectrum of activity, an excellent ratio of therapeutic to toxic dosages, a low rate of allergic responses, ease of administration, and attractive cost advantages. Mild allergic reactions to penicillin are not contraindications for the use of a cephalosporin.

Physicians like new drugs and often tend to prescribe newer, more expensive antibiotics for simple tasks. First-generation cephalosporins (e.g., cefazolin) are ideal agents for prophylaxis. Third-generation cephalosporins are not: they cost more, are not more effective, and promote emergence of resistant strains.

The most important first-generation cephalosporin for surgical patients continues to be cefazolin. Administered I.V. in the OR at the time of skin incision, it provides adequate tissue levels throughout most of the operation. A second dose administered in the OR after 3 hours will be beneficial if the procedure lasts longer than that. Data on all operative site infections are imprecise, but SSIs

![Figure 5](https://example.com/figure5.png)  
**Figure 5** In a pioneer study of antibiotic prophylaxis, the diameter of lesions induced by staphylococcal inoculation 24 hours earlier was observed to be critically affected by the timing of penicillin administration with respect to bacterial inoculation.
can clearly be reduced by this regimen. No data suggest that further doses are required for prophylaxis.

Fortunately, cefazolin is effective against both gram-positive and gram-negative bacteria of importance, unless significant anaerobic organisms are encountered. The significance of anaerobic flora has been disputed, but for elective colorectal surgery, abdominal trauma, appendicitis, or other circumstances in which penicillin-resistant anaerobic bacteria are likely to be encountered, coverage against both aerobic and anaerobic gram-negative organisms is strongly recommended and supported by the data.

Despite several decades of studies, prophylaxis is not always properly implemented. Unfortunately, didactic education is not always the best way to change behavior. Preprinted order forms and a reminder sticker from the pharmacy have proved to be effective methods of ensuring correct utilization.

The commonly heard decision “This case was tough, let’s give an antibiotic for 3 to 5 days” has no data to support it and should be abandoned. Differentiation between prophylaxis and therapy is important. A therapeutic course for perforated diverticulitis is important. A therapeutic course for perforated diverticulitis has no data to support it and should be abandoned. Differentiation between prophylaxis and therapy is appropriate. Data on casual contamination associated with trauma or with operative procedures suggest that 24 hours of prophylaxis or less is quite adequate. Mounting evidence suggests that a single preoperative dose is good care and that additional doses are not required.

Trauma Patients

The efficacy of antibiotic administration on arrival in the emergency department as an integral part of resuscitation has been clearly demonstrated. The most common regimens have been (1) a combination of an aminoglycoside and clindamycin and (2) cefoxitin alone. These two regimens or variations thereof have been compared in a number of studies. They appear to be equally effective, and either regimen can be recommended with confidence. For prophylaxis, there appears to be a trend toward using a single drug: cefoxitin or cefotetan. If therapy is required because of either a delay in surgery, terrible injury, or prolonged shock, the combination of an agent that is effective against anaerobes with an aminoglycoside seems to be favored. Because aminoglycosides are nephrotoxic, they must be used with care in the presence of shock.

In many of the trauma studies just cited, antibiotic prophylaxis lasted for 48 hours or longer. Subsequent studies, however, indicated that prophylaxis lasting less than 24 hours is appropriate. Single-dose prophylaxis is appropriate for patients with closed fractures.

COMPLICATIONS

Complications of antibiotic prophylaxis are few. Although data linking prophylaxis to the development of resistant organisms are meager, resistant microbes have developed in every other situation in which antibiotics have been utilized, and it is reasonable to expect that prophylaxis in any ecosystem will have the same result, particularly if selection of patients is poor, if prophylaxis lasts too long, or if too many late-generation agents are used.

A rare but important complication of antibiotic use is pseudomembranous enterocolitis, which is induced most commonly by clindamycin, the cephalosporins, and ampicillin [see 8:16 Nosocomial Infection]. The common denominator among different cases of pseudomembranous enterocolitis is hard to identify. Diarrhea and fever can develop after administration of single doses of prophylactic antibiotics. The condition is rare, but difficulties occur because of failure to make a rapid diagnosis.

CURRENT ISSUES

The most significant questions concerning prophylaxis of SSIs already have been answered. An important remaining issue is the proper duration of prophylaxis in complicated cases, in the setting of trauma, and in the presence of foreign bodies. No change in the criteria for antibiotic prophylaxis is required in laparoscopic procedures; the risk of infection is lower in such cases. Cost factors are important and may justify the endless succession of studies that compare new drugs in competition for appropriate clinical niches.

Further advances in patient selection may take place but will require analysis of data from large numbers of patients and a distinction between approaches to infection of the wound, which is only a part of the operative field, and approaches to infections directly related to the operative site. These developments will define more clearly the prophylaxis requirements of patients whose operations are clean but whose risk of wound or operative site infection is increased.

A current issue of some concern is potential loss of infection surveillance capability. Infection control units have been shown to offer a number of benefits in the institutional setting, such as the following:

1. Identifying epidemics caused by common or uncommon organisms.
2. Establishing correct use of prophylaxis (timing, dose, duration, and choice).
3. Documenting costs, risk factors, and readmission rates.
5. Ensuring patient safety.
6. Managing MRSA and VRE.

S. aureus—in particular, MRSA—is a major cause of SSI. Cross-infection problems are a concern, in a manner reminiscent of the preantibiotic era. Hand washing (see below) is coming back into fashion, consistent with the professional behavior toward

### Table 8: Historical Rates of Wound Infection

<table>
<thead>
<tr>
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<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(15,613 patients)</td>
<td>(62,937 patients)</td>
<td>(59,353 patients)</td>
<td>(20,193 patients)</td>
<td>(20,703 patients)</td>
</tr>
<tr>
<td>Clean</td>
<td>5.1</td>
<td>1.5</td>
<td>2.9</td>
<td>1.8</td>
<td>1.3</td>
</tr>
<tr>
<td>Clean-contaminated</td>
<td>10.8</td>
<td>7.7</td>
<td>3.9</td>
<td>2.9</td>
<td>2.5</td>
</tr>
<tr>
<td>Contaminated</td>
<td>16.3</td>
<td>15.2</td>
<td>8.5</td>
<td>9.9</td>
<td>7.1</td>
</tr>
<tr>
<td>Dirty-infected</td>
<td>28.0</td>
<td>40.0</td>
<td>12.6</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Overall</td>
<td>7.4</td>
<td>4.7</td>
<td>4.1</td>
<td>2.8</td>
<td>2.2</td>
</tr>
</tbody>
</table>
cross-infection characteristic of that era. At present, hard evidence is lacking, but clinical observation suggests that *S. aureus* SSIs are especially troublesome and destructive of local tissue and require a longer time to heal than other SSIs do. When *S. aureus* SSIs occur after cardiac surgery, thoracotomy, or joint replacement, their consequences are significant. Prevention in these settings is important. When nasal carriage of *S. aureus* has been identified, mupirocin may be administered intranasally to reduce the incidence of *S. aureus* SSIs.87

The benefits of infection surveillance notwithstanding, as the business of hospital care has become more expensive and financial control more rigid, the infection control unit is a hospital component that many administrators have come to consider a luxury and therefore expendable. Consequently, surveillance as a quality control and patient safety mechanism has been diminished.

It is apparent that SSIs have huge clinical and financial implications. Patients with infections tend to be sicker and to undergo more complex operations. Therefore, higher infection rates translate into higher morbidity and mortality as well as higher cost to the hospital, the patient, and society as a whole. With increasingly early discharge becoming the norm, delayed diagnosis of postdischarge SSI and the complications thereof is a growing problem.82-84 Effective use of institutional databases may contribute greatly to identification of this problem.83

Clearly, the development of effective mechanisms for identifying and controlling SSIs is in the interests of all associated with the delivery of health care.85 The identification of problems by means of surveillance and feedback can make a substantial contribution to reducing SSI rates [see Table 6].12,85

### Hand Washing

The purpose of cleansing the surgeon’s hands is to reduce the numbers of resident flora and transient contaminants, thereby decreasing the risk of transmitting infection. Although the proper duration of the hand scrub is still subject to debate, evidence suggests that a 120-second scrub is sufficient, provided that a brush is used to remove the bacteria residing in the skin folds around the nails.88 The nail folds, the nails, and the fingertips should receive the most attention because most bacteria are located around the nail folds and most glove punctures occur at the fingertips. Friction is required to remove resident microorganisms which are attached by adhesion or adsorption, whereas transient bacteria are easily removed by simple hand washing.

Solutions containing either chlorhexidine gluconate or one of the iodophors are the most effective surgical scrub preparations and have the fewest problems with stability, contamination, and toxicity.89 Alcohols applied to the skin are among the safest known antiseptics, and they produce the greatest and most rapid reduction in bacterial counts on clean skin.90 All variables considered, chlorhexidine gluconate followed by an iodophor appears to be the best option [see Table 9].

The purpose of washing the hands after surgery is to remove microorganisms that are resident, that flourished in the warm, wet environment created by wearing gloves, or that reached the hands by entering through puncture holes in the gloves. On the ward, even minimal contact with colonized patients has been demonstrated to transfer microorganisms.91 As many as 1,000 organisms were transferred by simply touching the patient’s hand, taking a pulse, or lifting the patient. The organisms survived for 20 to 150 minutes, making their transfer to the next patient clearly possible.

A return to the ancient practice of washing hands between each patient contact is warranted. Nosocomial spread of numerous organisms—including *C. difficile*, MRSA, VRE, and other antibiotic-resistant bacteria; and viruses—is a constant threat.

Hand washing on the ward is complicated by the fact that overwashing may actually increase bacterial counts. Dry, damaged skin harbors many more bacteria than healthy skin and is almost impossible to render even close to bacteria free. Although little is known about the physiologic changes in skin that result from frequent washings, the bacterial flora is certainly modified by alterations in the lipid or water content of the skin. The so-called dry hand syndrome was the impetus behind the development of the alcohol-based gels now available. These preparations make it easy for surgeons to clean their hands after every patient encounter with minimal damage to their skin.

### Infection Prevention in Bowel Surgery

At present, the best method of preventing SSIs after bowel surgery is, once again, a subject of debate. There have been three principal approaches to this issue, involving mechanical bowel preparation in conjunction with one of the following three antibiotic regimens55,92-97:

1. Oral antibiotics (usually neomycin and erythromycin),20,96
2. Intravenous antibiotics covering aerobic and anaerobic bowel flora,16,20,55,94,95 or
3. A combination of regimens 1 and 2 (meta-analysis suggests that the combination of oral and parenteral antibiotics is best).97

The present controversy, triggered by a clinical trial,16 a review,20 and three meta-analyses, relates to the need for mechanical bowel preparation,17-19 which has been a surgical dogma since the early 1970s. The increased SSI and leak rates noted have been attributed to the complications associated with vigorous bowel preparation, leading to dehydration, overhydration, or electrolyte abnormalities.

An observational study reported a 26% SSI rate in colorectal

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**Table 9** Characteristics of Three Topical Antimicrobial Agents Effective against Both Gram-Positive and Gram-Negative Bacteria

<table>
<thead>
<tr>
<th>Agent</th>
<th>Mode of Action</th>
<th>Antifungal Activity</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorhexidine</td>
<td>Cell wall disruption</td>
<td>Fair</td>
<td>Poor activity against tuberculosis-causing organisms; can cause ototoxicity and eye irritation</td>
</tr>
<tr>
<td>Iodine/Iodophors</td>
<td>Oxidation and substitution by free iodine</td>
<td>Good</td>
<td>Broad antibacterial spectrum; minimal skin residual activity; possible absorption toxicity and skin irritation</td>
</tr>
<tr>
<td>Alcohols</td>
<td>Denaturation of protein</td>
<td>Good</td>
<td>Rapid action but little residual activity; flammable</td>
</tr>
</tbody>
</table>
Integration of Determinants of Infection

The significant advances in the control of wound infection during the past several decades are linked to a better understanding of the biology of wound infection, and this link has permitted the advance to the concept of SSI. In all tissues at any time, there will be a critical inoculum of bacteria that would cause an infectious process—and of bowel surgery in particular—is required.

The recommended antibiotic regimen for bowel surgery consists of oral plus systemic agents (see above). The approach to mechanical bowel preparation, however, is open. Intuition would suggest that the presence of less liquid and stool in the colon might be beneficial and that a preoperative phosphate enema with 24 hours of fluid might make sense. It is hard to throw out 30 years of apparent evidence on the basis of these three meta-analyses. These studies do, however, present data that cannot be ignored. Protocols for bowel surgery in the modern era of same-day admission, fast track surgery, and rapid discharge will require further study and clinical trials.

<table>
<thead>
<tr>
<th>Traditional Wound Classification System</th>
<th>Simplified Risk Index</th>
<th>All from Traditional Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clean</td>
<td>1.1</td>
<td>2.9</td>
</tr>
<tr>
<td>Clean-contaminated</td>
<td>0.6</td>
<td>3.9</td>
</tr>
<tr>
<td>Contaminated</td>
<td>4.5</td>
<td>23.9</td>
</tr>
<tr>
<td>Dirty-infected</td>
<td>6.7</td>
<td>27.4</td>
</tr>
<tr>
<td>All from SENIC index</td>
<td>1.0</td>
<td>4.1</td>
</tr>
</tbody>
</table>

SENIC—Study of the Efficacy of Nosocomial Infection Control

Table 10 Comparison of Wound Classification Systems

The significant advances in the control of wound infection during the past several decades are linked to a better understanding of the biology of wound infection, and this link has permitted the advance to the concept of SSI. In all tissues at any time, there will be a critical inoculum of bacteria that would cause an infectious process [see Figure 3]. The standard definition of infection in urine and spurtum has been 10⁶ organisms/ml. In a clean dry wound, 10⁴ bacteria produce a wound infection rate of 50% [see Figure 3]. Effective use of antibiotics reduces the infection rate to 10% with the same number of bacteria and thereby permits the wound to tolerate a much larger number of bacteria.

All of the clinical activities described are intended either to reduce the inoculum or to permit the host to manage the number of bacteria that would otherwise be pathologic. One study in guinea pigs showed how manipulation of local blood flow, shock, the local immune response, and foreign material can enhance the development of infection. This study and two others defined an early decisive period of host antimicrobial activity that lasts for 3 to 6 hours after contamination. Bacteria that remain after this period are the infecting inoculum. Processes that interfere with this early response (e.g., shock, altered perfusion, adjuvants, or foreign material) or support it (e.g., antibiotics or total care) have a major influence on outcome.

One investigation demonstrated that silk sutures decrease the number of bacteria required for infection. Other investigators used a suture as the key adjuvant in studies of host manipulation, whereas a separate study demonstrated persistent susceptibility to wound infection days after shock. The common variable is the number of bacteria. This relation may be termed the inoculum effect, and it has great relevance in all aspects of infection control. Applying knowledge of this effect in practical terms involves the following three steps:

1. Keeping the bacterial contamination as low as possible via asepsis and antisepsis, preoperative preparation of patient and surgeon, and antibiotic prophylaxis.
2. Maintaining local factors in such a way that they can prevent the lodgment of bacteria and thereby provide a locally unreceptive environment.
3. Maintaining systemic responses at such a level that they can control the bacteria that become established.

These three steps are related to the determinants of infection and their applicability to daily practice. Year-by-year reductions in wound infection rates, when closely followed, indicate that it is possible for surgeons to continue improving results by attention to quality of clinical care and surgical technique, despite increasingly complex operations. In particular, the measures involved in the first step (control of bacteria) have been progressively refined and are now well established.

The integration of determinants has significant effects [see Figures 3 and 4]. When wound closure was effected with a wound hematocrit of 8% or more, the inoculum required to produce a wound infection rate of 40% was 100 bacteria [see Figure 3]. Ten bacteria produced a wound infection rate of 20%. The shift in the number of organisms required to produce clinical infection is significant. It is obvious that this inoculum effect can be changed dramatically by good surgical technique and further altered by use of prophylactic antibiotics. If the inoculum is always slightly smaller than the number of organisms required to produce infection in any given setting, results are excellent. There is clearly a relation between the number of bacteria and the local environment. The local effect can also be seen secondary to systemic physiologic change, specifically shock. One study showed the low local perfusion in shock to be important in the development of an infection.

One investigation has shown that shock can alter infection rates immediately after its occurrence [see Figure 4]. Furthermore, if
the inoculum is large enough, antibiotics will not control bacteria. In addition, there is a late augmentation of infection lasting up to 3 days after restoration of blood volume. These early and late effects indicate that systemic determinants come into play after local effects are resolved. These observations call for further study, but obviously, it is the combined abnormalities that alter outcome.

Systemic host responses are important for the control of infection. The patient has been clearly implicated as one of the four critical variables in the development of wound infection.\(^6\) In addition, the bacterial inoculum, the location of the procedure and its duration, and the coexistence of three or more diagnoses were found to give a more accurate prediction of the risk of wound infection. The spread of risk is defined better with the SENIC index (1% to 27%) than it is with the traditional classification (2.9% to 12.6%) \[^{6,10,12}\].\[^{6,10,12}\] It is apparent that the problem of SSI cannot be examined only with respect to the management of bacteria. Host factors have become much more significant now that the bacterial inoculum can be maintained at low levels by means of asepsis, antisepsis, technique, and prophylactic antibiotics.\[^{104}\]

Important host variables include the maintenance of normal homeostasis (physiology) and immune response. Maintenance of normal homeostasis in patients at risk is one of the great advances of surgical critical care.\[^{104}\] The clearest improvements in this regard have come in maintenance of blood volume, oxygenation, and oxygen delivery.

One group demonstrated the importance of oxygen delivery, tissue perfusion, and \(P_{\text{O}_2}\) in the development of wound infection.\[^{105}\] Oxygen can have as powerful a negative influence on the development of SSI as antibiotics can.\[^{106}\] The influence is very similar to that seen in other investigations. Whereas a \(P_{\text{O}_2}\) equivalent to a true fractional concentration of oxygen in inspired gas (\(P_{\text{O}_2}\)) of 45% is not feasible, maintenance, when appropriate, of an increased \(P_{\text{O}_2}\) in the postoperative period may prove an elementary and effective tool in managing the inoculum effect.

Modern surgical practice has reduced the rate of wound infection significantly. Consequently, it is more useful to think in terms of SSI, which is not limited to the incision but may occur anywhere in the operative field; this concept provides a global objective for control of infections associated with a surgical procedure. Surveillance is of great importance for quality assurance. Reports of recognized pathogens (e.g., \(S. \text{epidermidis}\) and group A streptococci) as well as unusual organisms (e.g., \(R. \text{bronchiolis}\), \(M. \text{hominis}\), and \(L. \text{dumoffii}\)) in SSIs highlight the importance of infection control and epidemiology for quality assurance in surgical departments.\[^{21-23,26,27}\] (Although these reports use the term wound infection, they are really addressing what we now call SSI.) The importance of surgeon-specific and service-specific SSI reports should be clear \[^{[see Table 6],[12,13,107]}\] and their value in quality assurance evident.

References


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Acknowledgment

Figures 3 and 4 Albert Miller.