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Antimicrobial Prophylaxis for Surgical Wounds

Guidelines for Clinical Care

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• Prophylactic administration of antibiotics can decrease postoperative morbidity, shorten hospitalization, and reduce the overall costs attributable to infections. Principles of prophylaxis include providing effective levels of antibiotics in the decisive interval, and, in most instances, limiting the course to intraoperative coverage only. Use in The National Research Council clean contaminated operations is appropriate and, in many instances, has been proven beneficial. Antibiotic prophylaxis is also indicated for clean operations, such as those involved with insertion of prosthetic devices, that are associated with low infection risk and high morbidity. Extension of antibiotic prophylaxis to other categories of clean wounds should be limited to patients with two or more risk factors established by criteria in the study of the efficacy of nosocomial infection control (SENIC) because the baseline infection rate in these patients is high enough to justify their use. Cefazolin (or cefoxitin when anaerobic coverage is necessary) remains the mainstay of prophylactic therapy. Selection of an alternate agent should be based on specific contraindications, local infection control surveillance data, and the results of clinical trials. Newer criteria for determining the risk of "site infection" (wound and intracavitary) are in evolution and may lead to modification of these recommendations over the next several years.

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Prophylactic administration of antibiotics represents their most common use in surgery. Designed to reduce the incidence of postoperative infection, antibiotic prophylaxis may reduce overall costs by avoiding the expenses attributable to infections and by shortening hospital stay. Haley et al[1] have indicated that a surgical wound infection prolongs hospitalization for approximately 1 week and adds a 10% to 20% cost to the total hospital bill. Nationwide, the cost of this excessive hospitalization is likely to be more than $1.5 billion per year.[2] Ehrenkranz et al[3] have proposed that antibiotic prophylaxis for patients undergoing cesarean section could result in a net national annual saving of $9 million for this category of operation alone.

On the other hand, inappropriate and indiscriminate use of prophylactic antibiotics may increase costs through unnecessary drug use, requisite laboratory monitoring, and selection of resistant organisms. These undesirable effects necessitate more expensive infection control measures and antibiotics. As with other adjunctive measures in surgery, the use of antibiotic prophylaxis is not a substitute for good infection control practices, appropriate patient preparation, good judgment, an adequate operating environment, and good technique. Their proper use is not a substitute for excellent patient care.

This article was developed by the Antimicrobial Agents Committee and was approved by the Executive Committee of the Surgical Infection Society as a set of guidelines for selection and use of prophylactic antibiotics for surgical wounds. It does not deal with endoscopic operations, image-directed percutaneous procedures, or endocarditis prophylaxis.

DEFINITION OF ANTIMICROBIAL PROPHYLAXIS FOR SURGICAL WOUNDS

Rigorously defined, prophylactic antibiotics are those given to patients before contamination or infection has occurred. A broader, more practical definition includes clinical situations in which infection or contamination is already present, primary treatment of the infection is surgical, and *anticipatory* antibiotic administration mainly serves to minimize postoperative wound infection (eg, patients with acute appendicitis or acute cholecystitis). Initial antibiotic therapy is *anticipatory, presumptive*, or *empiric*. A diagnosis of infection or possible infection has been made but is not definitive, and there are no culture data. If simple acute appendicitis (cholecystitis) is found at operation, additional doses of antibiotics may be avoided or given in a very short course to minimize subsequent wound infection (*prophylactic*). For findings of complicated appendicitis, continuation of antibiotic therapy is aimed at the underlying infection and is *therapeutic*, not *prophylactic*.

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PRINCIPLES OF ANTIBIOTIC PROPHYLAXIS

Prophylactic antibiotics are recommended when the risk of postoperative infection is high or with lower risk when the consequence of infection is extreme morbidity or mortality. The benefit of the antibiotic prophylaxis should outweigh its risks. The antibiotic selected should be based on the site-specific flora responsible for postoperative wound infection; on the antimicrobial spectrum, toxicity, and kinetic properties of the drug; and on the results of prospective clinical trials.

Identifying Patients at High Risk: Wound Classification and Risk Factors

The risk of postoperative infection depends on patient factors, perioperative care, and intraoperative management. Table 1 summarizes some factors that increased the risk of postoperative infection. The National Research Council (NRC) validated many of these variables and introduced a wound categorization based on the extent of intraoperative contamination (Table 2).[4] This wound classification scheme has served as the basis for recommending antibiotic use, for directing wound management, and for focusing wound surveillance. Conventional recommendations for prophylactic antibiotic administration center on clean contaminated and selected contaminated wounds. These wounds characterize 35% to 40% of all operations. The high rate of infection without the use of antibiotics and its reduction with the use of antibiotics in controlled clinical trials justify prophylaxis.

While the NRC classification has influenced wound management and the use of prophylactic antibiotics, it is not as predictive as other strategies and does not stratify risk within groups. In 1978, Ehrenkranz[5] prospectively tested a predictive model of stratification of NRC clean wounds in 12 community hospitals. From a population of 9108 hospital patients, he confirmed that remote infection, diabetes, and a lengthy operation imposed high risk of infection. Similarly, Haley et al,[6] in the 1985 study of the efficacy of nosocomial infection control (SENIC), identified four independent and additive risk factors for postoperative wound infection. These factors are operations on the abdomen, operations lasting for more than 2 hours, contaminated or dirty NRC wound classification, and the presence of at least three medical diagnoses.[6]

Table 3 compares the infection rates of the various SENIC and NRC classifications from a population of more than 59 000 patients. Inspection indicates a wider separation of risk of infection by the SENIC classification than by the NRC classification. Two or more SENIC risk factors abrogate the value of the NRC classification. Patients with NRC clean wounds and two or more risk factors have an infection rate that ranges from 8% to 15% and, thus, qualify for antibiotic prophylaxis. These patients accounted for approximately 10% of all clean wounds and about 6% of the population at large. Thus, consideration of the combination of NRC classification and the SENIC risk categories seems appropriate as a guide for administering prophylactic antibiotics, for directing wound management, and for conducting in-hospital epidemiologic research.

This combination is a particularly important consideration because of recent enthusiasm for extending prophylactic antibiotic use to a variety of NRC clean operations that constitute 50% to 60% of all operations performed. Recently, Platt et al[7] proposed benefit from the prophylactic use of cefonicid in patients undergoing a variety of breast operations and in those undergoing inguinal herniorrhaphy. Although the numerical trend and the authors' interpretation favor this position, they have been criticized

Table 1.—Factors Associated With Increased Risk of Postoperative Infection

Patient Factors	Perioperative Factors	Intraoperative Factors
es of age	Long preoperative hospitalization	Intraoperative contamination
dernutrition	No preoperative shower	Lengthy operation
Y	Early shaving of site	Excessive electrocautery
ociated problems	Hair removal	Foreign material
iabetes	Prior antibiotic therapy	Wound drainage
lypoxemia		High hematocrit wound fluid
ote infection		Epinephrine woun injection
icosteroid therapy		Intraoperative hypotension
Recent operation		Massive transfu
Chronic inflammation		Alcohol/hexachlorophene skin preparation
ior site irradiation		

Table 2. National Research Council Wound Classification Criteria*

Classification	Criteria
	Elective (not urgent or emergency), primarily closed; no acute inflammation or transection of gastrointestinal, oropharyngeal, genitourinary, biliary, or tracheobronchial tracts; no technique break (eg, elective inguinal herniorrhaphy)
ted 10%†	Urgent or emergency case that is otherwise "clean"; elective, controlled opening of gastrointestinal, oropharyngeal, biliary, or tracheobronchial tracts; minimal spillage and/o minor technique break; reoperation via "clean" incision within 7 days; blunt trauma, intact skin, negative exploration (eg, vagotomy and pyloroplasty)
(20‹	Acute, nonpurulent inflammation (note absence of purulence); major technique break or major spill from hollow organ; penetrating trauma <4 h old; chronic open wounds to be grafted or covered (eg, acute, nonperforated, nongangrenous appendicitis)
Dirty (40‹	Purulence or abscess; preoperative perforation of gastrointestinal, oropharyngeal, biliary, or tracheobronchial tracts; penetrating trauma >4 h old (eg, perforated appendicitis with abscess)

*Modified from *Ann Surg.*[4]
†Wound infection rate after Cruse et al (*Arch Surg.* 973;10 !06)

Table 3.—Distribution of Patients and Infections by SENIC Risk Factors and National Research Council (NRC) Wound Classification*

	Infection by NRC Wound Classification						
SENIC Risk Factors	Clean	Clean Contaminated	Contaminated	Dirty	SENIC, % of All Patients	SENIC, % of Patients With Infection	SENIC, % of Group With Infection
0			N/A	N/A	46	10¶	
1	3.9			6.7	32	29	
	8.4			10.9	16	35	8.9
				18.8	5		[illegible]
ents							
% of ents Wit ction							
on							4

fied from Haley et al.[6] SENIC indicates study of the efficacy of nosocomia nfection control; and N/A, mutually exclusive criteria. The re example statements indicating how to read this table: The NRC Clean ounds accounted for 55% (†) of all patients and 39% (‡) c ll patients. The infection rate for patients with NRC clean wounds was 2.9 §). Patients with 0 SENIC risk factors accounted for 46% (its and 10% (¶) of all infected patients. The infection rate for patients wit) SENIC risk factors was 1% (#). SENIC risk factors include operations, operations longer than 2 hours, three or more associated diag th Contaminated or Dirty wounds cannot have 0 SENIC risk factors. Patie

for combining groups with nonhomogeneous risk, for providing a liberal definition of infection, and for citing a rate of infection for breast operations that is higher than reported by others.[8] Most of the issues have to do with the inability to stratify risk within the broad group of NRC clean operations. Until more definitive studies are available, the use of prophylactic antibiotics in patients with NRC clean wounds should be limited to those with two or more risk factors or those with potentially serious morbidity or mortality from an infection at the operative site.

Clean Wounds for Which the Use of Prophylactic Antibiotics Is Validated

In some operations, the use of prophylactic antibiotics is ustified in spite of a theoretically small risk of infection. Most of these operations necessitate insertion of prosthetic materials. Infection in these instances results in either great morbidity or mortality (eg, insertion of cardiac valves, prosthetic joints, and prosthetic intravascular grafts). Similarly, antibiotic prophylaxis is usually used in clean operations involving the central nervous system and or those involving cardiopulmonary bypass, whether or not a prosthetic device is inserted. Neither the risk factors described by Ehrenkranz nor those established by the SENIC classification have been systematically evaluated in these patients with high morbidity and low risk of infection. It is likely, however, that many manifest two or more SENIC risk factors. In general, these groups are characterized by advanced age (a usual marker of associated medical problems) and prolonged operations.

Choice of Antibiotics

The choice of an antibiotic for prophylaxis is multifactoal. It depends on the operation to be performed, the ornisms that must be included, the kinetics and toxicities the drug, and its performance in properly designed nical trials.

Spectrum

The microbiologic characteristics of both the operative site and the hospital environment should influence the choice of antibiotics. The usual flora encountered during surgery and the organisms responsible for postoperative infection have been carefully documented in a number of general and site-specific studies. While both *influence* prophylactic antibiotic selection, coverage is directed primarily at those organisms that *cause* postoperative infection. These flora are usually some, but not all, of the endogenous organisms encountered. Antimicrobial prophylaxis in operations that do not violate a hollow viscus or mucosa need to cover only gram-positive skin flora, primarily *Staphylococcus epidermidis* and *Staphylococcus aureus*. Operations involving the gastrointestinal tract, the genitourinary tract, and the hepatobiliary system, as well as some pulmonary operations, must cover both skin flora and additional site-specific organisms. Operations that feature postoperative infections with both aerobic and anaerobic flora should use an inclusive antibiotic regimen. Choosing the most limited effective spectrum is difficult, but important. Precision in this effort avoids unnecessarily broad coverage and minimizes risk for the patient and the environment (overgrowth with opportunistic bacteria and fungi and development of resistant strains).

Risk of Antibiotic Toxicity

The potential toxicity of antibiotics represents an important risk of prophylaxis. The least toxic, effective antibiotic regimen should be chosen. Table 4 represents some important toxicities of commonly used prophylactic antibiotics. In general, the cephalosporin group manifests acceptable toxicities, the majority of which are reversible after withdrawal of the drug. The most significant and frightening toxicity, an anaphylactic reaction to a β-lactam antibiotic (penicillin, cephalosporin, carbapenem, or

Table 4.—Toxicities of Antibiotics Commonly Used for Prophylaxis

Antibiotic Class	Toxicity: Common	Toxicity: Occasional	Toxicity: Rare
Penicillins	Allergic reactions Rash Anaphylaxis (rare) Diarrhea	Hemolytic anemia Drug fever	Seizures Interstitial nephritis Electrolyte imbalance Marrow suppression Pseudomembranous colitis
Cephalosporins	Thrombophlebitis Gastrointestinal symptoms	Allergic reactions Rash Serum sickness Anaphylaxis Drug fever Coagulopathy Eosinophilia	Hemolytic anemia Pancytopenia Abnormal liver enzymes Interstitial nephritis Interstitial pneumonia Pseudomembranous colitis
Aminoglycoside	Nephrotoxicity Ototoxicity	Rash Nausea, vomiting	Myoneural blockade Apnea
Erythromycin	. . .	Gastrointestinal irritation Stomatitis	Allergic reactions Fever Rash Colitis Coagulopathy
Clindamycin	Diarrhea Rash	Colitis Nausea, vomiting	Neutropenia
Vancomycin	Red man syndrome	Thrombophlebitis Chills and fever Ototoxicity	Nephrotoxicity Rashes Neutropenia

monobactam), can often be avoided by obtaining a careful history. If the patient reports a history of an immediate hypersensitivity reaction, an alternate antibiotic should be selected. Aztreonam, a monobactam antibiotic, does not cross-react with penicillin antibodies. It may provide alternative gram-negative prophylaxis for patients allergic to penicillin.[9] If gram-positive organisms are the prophylactic target, vancomycin or clindamycin may be considered. The "red man syndrome" is, however, very common after the first dose of vancomycin, even when the drug is administered appropriately.[10] This syndrome may include flushing, pruritus, chest pain, muscle spasm, or hypotension. These symptoms should not be misinterpreted as an allergic reaction that precludes further use of vancomycin.

Aminoglycosides represent the other end of the toxicity spectrum. Nephrotoxicity and ototoxicity, both frequent with therapeutic courses, are extremely rare as complications of prophylaxis for 48 hours or less. Nevertheless, the ototoxicity is irreversible, aminoglycosides are extremely valuable *therapeutic* agents, and several errors commonly made in the use of prophylactic antibiotics (see below) may significantly increase toxicity. For these reasons, we do not recommend parenteral aminoglycosides for routine prophylaxis. If no other agent is acceptable, aminoglycosides must be used in strict compliance with the pharmacokinetic and duration considerations enumerated below.

Risk of Changing Ecology

Changes in flora and the development of resistant strains are possible sequelae of prophylactic antibiotic use. Many randomized prospective studies have documented infection with organisms resistant to the antibiotic used, especially with extended prophylaxis. Conte et al[11] suggested the evolution of resistant organisms in a study of patients receiving a multidose regimen as an adjunct to open heart operations. Archer and colleagues[12,13] described development of multiply resistant strains of *S epidermidis* in response to prophylaxis with rifampin, rifampin and nafcillin, or cefazolin sodium. Furthermore, they documented colonization of adjacent patients and hospital staff. Sanders and Sanders[14] cite potential evolution of "stably derepressed" β-lactamase–producing mutants as a reason to limit the use of third-generation cephalosporins for prophylaxis. *Clostridium difficile* colonization may complicate prophylaxis, even with a single-dose strategy.[15]

Pharmacokinetics

Burke's description of the decisive interval (the first 3 hours after wounding and/or contamination) in experimental animals has been clearly confirmed in clinical practice.[16,17] To be maximally effective, the antibiotic should be present in adequate concentrations at the operative site as early as possible in the decisive interval and for as long as the wound is open. If a systemic antibiotic(s) is used, intravenous administration of an appropriate dose in the operating room just before the induction of anesthesia is practical. This timing provides the interval required for distribution from the central compartment (bloodstream) to the tissue compartment (wound). *"On call" dosing is no longer acceptable because it may result in premature administration of the antibiotic regimen and insufficient tissue concentrations of drug during the decisive interval.*[18] Initial dosing depends on the volume of distribution, peak levels, plasma clearance, protein binding, and bioavailability of the antibiotic regimen selected. Repeated dosing intraoperatively may be necessary depending on the agent used and the duration of the operation. For agents that are rapidly cleared, repeat dosing at an interval two times the plasma half-life is appropriate. Drug administration according to these tenets assures appropriate tissue levels of the antibiotic, a requisite for effective prophylaxis.[19]

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Duration

The shortest effective course of prophylactic antibiotics hould be used. In many settings, this consists of coverage nly while the patient is in the operating room. With long ıalf-life agents for most operations or with more rapidly leared drugs for shorter procedures, this may amount to single shot" therapy. This approach has the advantages of ost containment, toxicity limitation, and minimal antibitic pressure on the environment. Coverage limited to the ıtraoperative period is one of the most significant recent hanges in antibiotic prophylaxis and is dramatically dif- rent from the 24- to 48-hour coverage previously recom- ıended.[20] It has proved effective for operations involving ıe gastrointestinal tract, for orthopedic operations, and ɔr cesarean section and gynecologic procedures. It re- ıains debatable for cardiac procedures.[21] Extending the ɔurse of antibiotic prophylaxis to "cover" lines, tubes, and ıtheters is unwarranted.

Other Considerations

Ideally, the prophylactic antibiotic(s) selected should ıve been proved effective in randomized, prospective, ıd clinical trials. Ad hoc choices, however, are manda- ry in instances of conflicting allergies or other contrain- cations to the use of the usual drug. In addition, the reg- ıen chosen should be compatible with the findings from e hospital's infection control wound surveillance report. is particularly important for hospitals with a high inci- nce of infection with methicillin-resistant *S aureus* [RSA) and/or *S epidermidis* (MRSE). These isolates are quent enough in some hospitals to represent the "en- mic flora" *Staphylococcus* and to dictate the basis for the oice of antistaphylococcal prophylaxis. While all strains MRSA and MRSE are resistant to *all* β-lactams, they are more virulent than methicillin-sensitive organisms. eir major risk is 3 to 4 days of ineffective β-lactam ther- y while waiting for microbiologic identification. The esence of MRSA and/or MRSE as endemic hospital ra mandates recognition of the problem and the choice an appropriate (usually more expensive) antibiotic. On ational level, this trend is likely to recapitulate the de- opment of penicillin-resistant staphylococci witnessed he late 1950s.

One additional consideration in the choice of a prophy- ic antibiotic is avoidance of a drug valuable for defin- e therapy. If a number of drugs appear equally accept- e for prophylaxis, one should pick the agent least likely be used for definitive therapy. This strategy should ıimize selecting organisms resistant to valuable *thera- tic* agents.

Cost

ɔst is appropriately the last item considered in the choice rophylactic antibiotics. Among otherwise equal antibi- in the selection criteria mentioned above, the least ex- ive should be chosen. The least expensive is not always lrug with the lowest procurement cost. Total expenses de the costs of laboratory monitoring, drug administra- both supplies and personnel), adverse effects, and fail- f prophylaxis (ie, wound infection).

Common Errors in Antibiotic Prophylaxis

nmon errors in antibiotic prophylaxis include choos- ıe wrong agent, administering the initial dose too omitting critical intraoperative doses in long operations, and extending the course for longer than is necessary. All represent failure to adhere to the tenets indicated above. Perhaps the most egregious errors are inappropriate use of valuable therapeutic agents with expanded spectrum and excessively long-term administration. Indiscriminate antibiotic use is costly, exposes the patients to adverse effects, and promotes resistance to the drugs. Recent data suggest that involvement of clinical pharmacists in the overall program of antibiotic prophylaxis, the use of computerized reminders, satellite pharmacies, and strong positions by the professional staff are effective in combating these errors.[22-24]

Alternate Strategies

While the foregoing considers primarily the strategy of parenteral prophylaxis to reduce wound infection, other options are available. These include topical prophylaxis and technical approaches.

Topical prophylaxis has also proved beneficial using antibiotic irrigation or instillation at the time of wound closure. Conceptually, these techniques provide antibiotics in very high concentrations at the site of maximum risk early enough in the decisive interval to be of benefit. Eleven of 13 prospective clinical trials reported up to 1977 documented benefit using either "nonabsorbable" antibiotics (mainly aminoglycoside/bacitracin combinations) or an antibiotic likely to be absorbed from the wound (mainly ampicillin).[25] This technique has proved most efficient in the absence of established infection.[26] *Luminal decontamination* with antibiotics is designed to lower the risk of wound infection by reducing the number of organisms presented to the surgical wound. It has been most frequently applied to colorectal operations (see below). Effective regimens include anaerobic and aerobic coverage and at least one antibiotic with some systemic overlap. Intuitively, topical, luminal, and systemic therapy should enhance one another, but this advantage is difficult to scientifically validate in the clinical setting.[27,28]

Surgical technique, wound management, and overall patient care are of great importance in minimizing the incidence of wound infection. Rarely is one aspect of management of singular importance. It is the sum of the parts that yields favorable results. Delayed primary wound closure around the fifth postoperative day is a specific technique for substantially reducing wound infection.[29,30] The use of delayed primary wound closure, in lieu of primary wound closure, is appropriately applied to situations that feature excessive intraoperative contamination or established infection. Success is reported in 80% to 90% of delayed primary wound closure efforts and failure does not threaten invasive infection or prolong the course of antibiotics. In some hospitals, selective application of this technique has reduced the incidence of wound infections in contaminated and dirty wounds to an attack rate lower than that observed for clean contaminated wounds.

SITE-SPECIFIC CONSIDERATIONS AND RECOMMENDATIONS

Prophylactic antibiotics for specific sites are discussed below and summarized in Table 5. These recommendations are similar to others recently published and are largely cephalosporin-based.[31-33] Cefazolin, the standard of comparison, fulfills most of the criteria indicated above, is not the drug of first choice for definitive treatment of any known infection, and is relatively inexpensive. Its half-life,

Table 5.—Recommendations for Prophylactic Antibiotic Agents by Site

Operations	Bacteria	Intravenous Administration of Antimicrobial	Dose*
Cardiac: all with sternotomy, cardiopulmonary bypass	*Staphylococcus aureus, Staphylococcus epidermidis,* diphtheroids, gram-negative enterics	Cefazolin (vancomycin)	1-2 g (1 g slowly) preinduction, 1-2 g every 8 h for 48 h
Noncardiac vascular: aortic resection and prosthetic bypass	*S aureus, S epidermidis,* diphtheroids, gram-negative enterics	Cefazolin (vancomycin)	1 g (1 g slowly) preinduction, 2 postoperative doses
Orthopedic: insertion of prosthetic joints, open operations	*S aureus, S epidermidis*	Cefazolin (vancomycin)	1 g (1 g slowly) preinduction
Neurosurgery	*S aureus, S epidermidis*	Cefazolin (vancomycin)	1 g (1 g slowly) preinduction
Head and neck: operations involving the mucous membranes and deep tissue (see text)	Oral aerobes and anaerobes, *S aureus,* streptococci	Cefazolin	2 g preinduction
General thoracic: pulmonary and esophageal	Oral anaerobes, *S aureus,* streptococci, gram-negative enterics	Cefazolin	1-2 g preinduction
Gastroduodenal: bariatric, ulcer patients treated with H_2 blockers, bleeding duodenal ulcer, genitourinary or gastric cancer	Oropharyngeal flora and gram-negative enterics, *S aureus*	Cefazolin	1-2 g preinduction
Biliary: all open and laparoscopic procedures (chronically intubated biliary tract)	Gram-negative enterics, *S aureus, Enterococcus fecalis,* clostridia (above plus *Pseudomonas* species)	Cefazolin (culture-based selection)	1-2 g preinduction (preinduction dose and repeat interval based on drug kinetics)
Colorectal: operations that open the colon and/or rectum	Enteric aerobes and anaerobes	Oral neomycin/erythromycin (cefoxitin or cefotetan or cefmetazole)	Operating room day 1: 1 g at 1, 2 and 11 PM (1 g preinduction)
Appendectomy: simple appendicitis (antibiotics are empiric or definitive for complicated appendicitis)	Enteric aerobes and anaerobes	Cefoxitin or cefotetan or cefmetazole	1 g preinduction
Cesarean section	Enteric aerobes and anaerobes, *E fecalis,* group B streptococci	Cefazolin	1 g after umbilical cord is clamped
Hysterectomy	Enteric aerobes and anaerobes, *E fecalis,* group B streptococci	Cefazolin	1 g preindiction
Abdominal trauma	Enteric aerobes and anaerobes	Cefoxin	2 g preinduction

*Parenthetic text refers to alternate antibiotic or situation. Current data suggest repeat dosing for operations lasting longer than the serum half-life. Preinduction indicates in operating room before initiating anesthesia.

approximately 2 hours, is compatible with "single shot" therapy for shorter operations, but may require repeated dosing for longer procedures. Except for hospital settings and operations in which MRSA and/or MRSE are a major concern, it is likely to remain the predominant "standard" agent for most antimicrobial wound prophylaxis in the near future. Choice of a later-generation cephalosporin should be based on some discrete, practical benefit over cefazolin, usually a need for anaerobic coverage.

Cardiac Operations

Although the intrinsic risk of infection is considered low and there are no confirmatory placebo-controlled trials proving benefit, the use of prophylactic antibiotics is generally recommended because of the potential consequence of mediastinitis. Organisms of concern include primarily skin flora. Most postoperative sternal wound infections are caused by either *S aureus* or *S epidermidis,* while urinary tract infections and pneumonias are usually caused by gram-negative organisms. Prophylaxis is usually cephalosporin-based. The initial dose is given before the induction of anesthesia. Since cardiopulmonary bypass decreases the elimination of the drug, additional intraoperative doses may not be necessary for lengthy operations. Although recent trends in other settings favor only intraoperative coverage, the data are not yet conclusive for patients undergoing cardiac operations.[21] Antimicrobial administration is commonly continued for 48 hours after operation. The choice of the cephalosporin used may also be in evolution. Some have proposed the use of cefamandole or cefuroxime to achieve better staphylococcal coverage.[34,35] Others have not been able to duplicate this reported advantage.[36] MRSA and MRSE represent a serious problem in some hospitals in spite of a relatively low overall rate of infection. In the experience of Gelfand et al,[3] resistant strains accounted for 40% to 50% of the infections in their cardiac surgery patients. These strains represent 25% of the total isolates of *S aureus* and 50% of the total isolates of *S epidermidis* in their hospital. Antibiotic pressure may be responsible for this observation.[11-14] Appropriate adjustments in prophylactic regimens should be made in hospitals with a high incidence of MRSA and MRSE if the overall rate of infection mandates it. Va mycin is the drug of choice in this setting.

Noncardiac Vascular Operations

Like cardiac procedures, *S aureus* and *S epidermidis* are the organisms of prime concern. The incidence of infection is greatly increased when vascular prostheses are required and about 75% of all infections involve the groin.[38-40] Aortic resectional operations are also at increased risk.[41] Kaiser et al[42] and Pitt et al[43] have documented the efficacy of a three-dose course of cefazolin. In addition, Pitt et al compared topical, systemic, and combined cephradine in a placebo-controlled study limited to patients with groin incisions. Topical therapy was as effective as systemic use in this group of patients without foot ulcers or distal open wounds. There was no demonstrated advantage of combined therapy. Prophylactic antibiotics should not be used for carotid endarterectomy or brachial artery repair. There are insufficient data to provide a firm recommendation for extra-anatomic cerebrovascular reconstructions.

Orthopedic Operations

The majority of postoperative infections are caused by *S aureus* or *S epidermidis*. The major problem is that of prosthetic joint infections. Antibiotics are justified in these primary, clean open operations because the morbidity associated with infection is so high, although the risk of infection is low.[44] The high infection rate for some operations (eg, revisions of total knees, ankle fusions, or total hip revisions) justifies their use.[45] Cefazolin reduces overall infection to less than 3% (vs control of 5% to 15%) and is the agent of choice because of low toxicity, low cost, and adequate bone, serum, and soft-tissue levels.[46] Antibiotic courses extended beyond 48 hours are of no benefit, and the trend is toward intraoperative coverage only.[44,46] The use of antibiotic prophylaxis is also indicated for hip-fracture operations.[47] It appears unnecessary in open reduction of low-energy closed fractures.[48]

Data suggest the benefit of prophylactic antibiotics for patients with lower extremity amputation, but the studies are not large enough for definitive recommendations. Kinetic studies and tissue levels depict adequate concentrations of penicillins and cephalosporins in bone, serum, and soft tissue, correlating somewhat with transcutaneous oxygen pressure measurements.[49,50]

Neurosurgical Operations

Prophylactic antibiotics directed at *S aureus* and/or *S epidermidis* are commonly used in clean neurosurgical procedures in spite of the absence of definitive randomized prospective trials. The review by Haines[51] of the best available data justifies this approach. Effective agents that have been used include combinations of cefazolin and gentamicin, gentamicin and vancomycin, and vancomycin, penicillin, cloxacillin, or piperacillin as single agents. Overall wound infection rates were 4% to 8% without and 0.5% to 2% with antibiotics. Vancomycin was effective in a single dose.[52-55] Data regarding antibiotic prophylaxis for cerebrospinal fluid shunt procedures are equivocal. Antibiotic coverage is commonly used as in other operations in which prosthetic materials are inserted.

Head and Neck Operations

Prophylactic antibiotics are aimed primarily at oral anaerobes and aerobic cocci, especially streptococci.[56] They reduce the incidence of severe wound infections by about 50%.[57] Both penicillin- and cephalosporin-based prophylaxis appear effective.[57] Specific operations with reduced infection rates from prophylaxis include orthognathic procedures, craniofacial revisions, maxillofacial fracture corrections, and major resections and reconstructions that involve the mucous membranes and deep tissue. Prophylaxis is not indicated for dentoalveolar procedures, except for immunosuppressed patients.[58] A review of 192 NRC clean head and neck operations failed to yield any significant benefit of perioperative antibiotics, but the sample size was too small to detect small, but possibly real, differences.[59]

General Thoracic Operations

The available information indicating the value of prophylactic antibiotics for elective general thoracic operations precludes firm recommendations. The use of prophylactic antibiotics is standard practice. A variety of gram-negative and gram-positive organisms must be considered. Most of the data are dominated by pulmonary resection for lung cancer. The study by Ilves et al[60] provides the best data for the efficacy of antibiotic prophylaxis. Comparative trials evaluating four doses of penicillin vs cefuroxime or comparing one vs six doses of cefazolin have shown no difference in outcome.[61,62]

Gastroduodenal Operations

The bacteriologic condition of the stomach is a function of gastric acidity. Conditions that decrease gastric acidity remarkably increase gastric flora (primarily with nasopharyngeal aerobes) and increase the incidence of postoperative wound infection.[63] The overall incidence of gastroduodenal operations has decreased since the introduction of appropriate concepts of antibiotic prophylaxis. Most procedures are now either bariatric, for cancer, or for complicated ulcer disease. Virtually all in the latter two groups have been treated with acid-reducing agents. Reports substantiate the value of cephalosporins and the applicability of single-dose prophylaxis when measured by clinical outcome and by antibiotic concentrations in blood, gastric mucosa, and subcutaneous tissue.[64,65]

Biliary Tract Operations

Most postoperative infections occur in patients with positive bile cultures, and most are caused by gram-negative organisms. The majority of wound infections in patients with negative bile cultures are caused by *S aureus*. Postoperative infections with *Enterococcus* species are not rare in patients who receive cephalosporin prophylaxis. Risk stratification for the likelihood of positive bile cultures by established criteria is sometimes used to select patients for prophylactic antibiotics.[66,67] Series reporting the incidence of positive bile cultures from low-risk patients give values ranging from 10% to 50%.[68,69] Accordingly, prophylactic antibiotics are used without stratification by many surgeons.

Cholecystectomy is among the most common operations performed and has been the subject of a number of antibiotic trials. Placebo-controlled trials have proved the value of cefazolin, and comparative trials have demonstrated the applicability of coverage limited to the time of operation.[70,71] In addition, topical therapy has been tested against systemic antibiotics and combined topical and systemic antibiotics and has shown "no difference" in small studies.[72] There are no data to support the preferential use of expanded spectrum cephalosporins. Appropriate recommendations for laparoscopic cholecystectomy are in evolution. Prophylactic antibodies are commonly used as for open cholecystectomy.

Appendectomy

Because it is a common problem and operation may be associated with a high incidence of postoperative infection, appendectomy has been used as a "proving ground" for new antibiotics and strategies. The risk of postoperative infection is a function of technical features of the operation and the state of the appendix. In placebo-controlled trials, the "no antibiotic" wound infection rates range from 4% to 9% for simple appendicitis.[26,73] Perioperative antibiotics reduce the rate of wound infection to 1% to 5%.

Organisms of concern are primarily *Bacteroides* species, *Escherichia coli*, *Klebsiella*, and *Enterobacter*. Many regimens with aerobic and anaerobic coverage provide effective prophylaxis. Cefoxitin has been the subject of several studies and is effective in a short-course regimen.[74-76] Metronidazole, although deficient in its spectrum, has been successfully used as a single agent.[73] Topical agents have also proved effective prophylaxis for simple acute appendicitis.[26]

Colorectal Operations

Mechanical bowel preparation decreases fecal bulk but does not alter the concentration of the organisms in the stool.[77] Extensive study of prophylactic antibiotics in colorectal operations has yielded proponents of oral (luminal) and parenteral regimens. In general, North American surgeons focus on luminal prophylactic antibiotics and emphasize a reduction in the total number of organisms potentially available for intraoperative contamination. Meanwhile, European surgeons may employ only systemic coverage aimed at ameliorating the consequences of any organisms spilled. Both approaches recognize a higher risk of operations involving extraperitoneal rectum than of those limited to the colon and agree on several principles: (1) mechanical preparation is essential, (2) antimicrobial prophylaxis is effective, and (3) gram-positive aerobes as well as gram-negative aerobes and anaerobes should be covered.

Clarke et al[78] documented reduction of postoperative infection from 43% with mechanical bowel preparation alone to 9% with the addition of three preoperative doses of neomycin and erythromycin base in a large Veterans Administration Cooperative study. This is the only study demonstrating a reduction in intra-abdominal infection in the treatment group. Another investigation showed the results of antibiotic preparation of the colon with neomycin and erythromycin to be similar to metronidazole and erythromycin in terms of overall infection.[79] In a multicenter trial involving more than 500 patients, the addition of parenteral cephalothin to the luminal antibiotics showed no difference (5.7% vs 7.8%).[80] A repeat of this latter study design substituting cefoxitin for cephalothin, independently by two separate groups, yielded conflicting results. In one center, parenteral cefoxitin made no difference, while in the other, its addition appeared to be of value.[81,82]

Studies that have focused on mechanical preparation and parenteral antibiotics have shown efficacy of a variety of single agents or combinations providing broad aerobic and anaerobic coverage. Gram-positive coverage is important.[83] Infection rates range from 6% to 20%. A combination of aztreonam-clindamycin or cefotaxime as a single agent yields a similar infection rate of about 6%.[84,85]

Cesarean Section

A review of 58 controlled clinical trials of prophylactic antibiotics in cesarean section showed a 50% to 70% reduction in infection (wound and endometritis), with concomitant cost savings.[86] A variety of different agents, including piperacillin and a number of cephalosporins given after the cord is clamped, have proved effective.[87] Single-dose cefazolin is equivalent to cefotetan.[88] Antibiotic failure is predicted by recovering resistant organisms (usually *Enterococcus* species in cephalosporin-treated patients) from the upper genital tract.[89]

Gynecologic Operations

Patients undergoing vaginal and abdominal hysterectomy benefit from prophylactic antibiotics. Benefit is magnified in patients with risk factors of low socioeconomic status; extremes of age, obesity, or diabetes; or preceding instrumentation. Postoperative site infections may be caused by a variety of aerobic and anaerobic organisms. *Bacteroides* species are usually the dominant anaerobe. Single doses of a variety of cephalosporins are effective. Expanded-spectrum cephalosporins represent no benefit over cefazolin in spite of the bacteriology. Use of cefazolin in lieu of later-generation drugs may also reduce the selection of β-lactamase–producing resistant organisms.[90]

Urologic Operations

The principles of antibiotic prophylaxis for patients undergoing nephrectomy and cystectomy with urinary conduit construction are sufficiently similar to those for abdominal clean contaminated and colorectal operations, respectively, that they do not warrant separate discussion. Luminal preparation for cystectomy and ileal conduit should be enhanced with specific coverage of any organism cultured from the urinary tract. There are, however, no definitive published data.

Abdominal Trauma

Postoperative infections after abdominal trauma vary with the age of the patient, the organ and number of organs injured, and the extent of transfusion required.[91] As with appendicitis, use of antibiotics in penetrating or blunt abdominal trauma is initially presumptive and necessarily directed at a variety of aerobes and anaerobes.[92] Prophylactic therapy is administered only in the face of a laparotomy without injury to a hollow viscus.

A number of antibiotic trials comparing a variety of expanded-spectrum single agents with aminoglycoside-based combinations (usually including gentamicin and clindamycin) show similar efficacy.[91,93-96] Single agents are as effective as aminoglycoside-based combinations. Cefoxitin is usually the standard with which other single agents are compared and, therefore, represents the antibiotic with which the largest experience has been accrued. Short-duration prophylaxis (12 hours) appears as effective as prolonged coverage.[97-99]

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