Prophylactic Antibiotics in Surgery: A Rationale for the Family Physician

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Antibiotic administration can effectively reduce the risk of postoperative wound infection under specific circumstances. Maximal protection is obtained when an antibacterial concentration of a bacteriologically appropriate antibiotic regimen is circulating within target tissues at the time of bacterial contamination. This protection is obtained during a finite period, usually not exceeding four hours following bacterial seeding of tissues. The preservation of intact host defense mechanisms is of ultimate importance in preventing wound infection. When defenses are compromised or when an inoculum is of a size that can overwhelm host defenses, the perioperative administration of antibiotics can significantly reduce infection risk. However, antibiotic use must not lead to a relaxation of good surgical judgment and technique.

A recent prevalence study of antibiotic administration at Duke University Medical Center revealed that 45 percent of surgical patients received an antibiotic during their hospitalization.[1] Sixty-four percent of antimicrobial administration in these patients was judged either not indicated or inappropriate. Another report has revealed that up to one third of all hospitalized patients on antibiotic therapy receive them without adequate indications or documentation of bacteriologic appropriateness.[2]

Family physicians often participate in or conduct operative procedures on their patients and are at least partially responsible for their perioperative care. It is important that they be familiar with principles of antimicrobial prophylaxis to the extent that antibiotic administration will be indicated, bacteriologically appropriate, and effective in reducing infection risk. Unfamiliarity with these principles will only compound the widespread problem of antimicrobial agent misuse. This paper presents a rationale for antimicrobial prophylaxis and recommendations for perioperative antibiotic administration that can be followed for a wide variety of operative procedures.

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Wound Classification and Infection Risk

In 1964 the report of the National Research Council (NRC) on the effect of ultraviolet (UV) light on the control of postoperative wound infections was published in the *Annals of Surgery*.[3] A significant by-product of that report was a definition of surgical wound categories that is utilized to

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this day. Four categories were defined, expressing the relative risk of intraoperative bacterial contamination of the wound: (1) clean, (2) clean-contaminated, (3) contaminated, and (4) dirty.

Clean wounds were associated with no acute inflammation, no break in surgical technique, and no entry into the gastrointestinal or respiratory tract. If the biliary or urinary tract was entered, there was no bacterial colonization of the contents. An additional inclusion into this category was the operative wound associated with an incidental appendectomy. Clean-contaminated wounds were those in which there was a minor break in technique or entry into the respiratory or gastrointestinal tract in the absence of acute inflammation. Wounds associated with significant colonization of the urinary or biliary tract without acute inflammatory changes fell into this category. Also included was an appendectomy wound for acute, nonperforated appendicitis. Contaminated wounds included those made in the face of acute inflammation or associated with a major break in technique (eg, spillage of the contents of a hollow viscus). Fresh, traumatic wounds were also included, as were appendectomies for perforated appendicitis. Finally, dirty wounds were those made in the presence of pus, for a perforated hollow viscus (eg, perforated diverticulitis), or for old neglected trauma. Also included were open fractures and wounds that entered joint spaces.

The National Research Council study was conducted in five university centers. Wound infection rates were defined for each category, since antibiotic administration was not controlled in the study protocol. The overall infection rate for all five hospitals was 7.4 percent. Clean wound rates averaged 5 percent, and clean-contaminated wounds, approximately 10 percent. Contaminated wound infection rates were 16 percent, and the average rate for dirty wounds was almost 30 percent. A close correlation was seen between these rates and those of Cruse and Foord,[4] who conducted a now classic study in Calgary, Alberta, Canada, at the Foothills Hospital, which examined the determinants of postoperative wound infections. Their average rates for clean, clean-contaminated, contaminated, and dirty wounds were, respectively, 2, 10, 18, and 42 percent, and their overall rate was 5.1 percent.

An analysis reported by Altemeier[5] in 1967 indicated that the annual cost of postoperative wound infections in the United States was almost $10 billion, with an overall rate of 7.4 percent. Hospital stay was prolonged five to ten days with wound infections, and there was the potential for considerable disability and loss of earning capacity.[5,6] The intense efforts in the last decade to examine the determinants of wound infection and factors that decrease infection rates and the ravages of infection have been justified. Through an understanding of the bacteriology and pathophysiology of wound infection, progress has been made toward their control.

Determinants of Wound Infection

Tissues become infected if there is a sufficient number or virulence of contaminating bacteria, if host defenses are compromised and incapable of arresting bacterial multiplication, or if the wound tissue themselves are excessively damaged by faulty surgical technique. Halsted's principles of tissue handling are as important today as in his time. Tissues must be gently handled, hemostasis must be thorough, and, where possible, sutures should be fine, monofilament, and nonreactive. Devitalized tissue, ischemia, dead space, and presence of foreign bodies must be minimized.[6,7] Delayed treatment, massive tissue injury, and location adjacent to ostomies or body orifices predispose wounds to infection; and thought should be given to utilizing delayed primary closure. Above all, there must be a *septic awareness* in wound management. About 1870, Lister said, "You must be able to see with your mental eye the septic ferments as distinctly as we see flies or other insects with the corporeal eye—if you do not see them, you will be constantly liable to relax in your precautions."

The major factor that determines surgical wound infections is the introduction of microorganisms of endogenous or exogenous origin into the wound during operation.[3] Normal tissues have a high degree of natural resistance to infection, and inocula of up to 10^6 Staphylococcus aureus can fail to induce infection in normal skin.[8] At time of wounding, however, only about 100 staphylococci are needed to infect wounds,[9] and 10 or fewer Clostridium perfringens can induce an infectious lesion in the presence of foreign bodies and devitalized tissue.[10] For several days after tissues are wounded, their resistance to bacterial infection progressively increases. Neovascularization of injured tissues through granulation largely accounts for this increase in resistance, but it does not occur rapidly enough to protect acute, contaminated wounds from infection.[9] In addition, factors enumerated by the National Research Council's ultraviolet light study[3] and the studies of Cruse and Foord[4] increase the susceptibility of tissues to infection by bacterial contaminants. The factors include advanced age, obesity, malnutrition, steroids, remote site infection, the presence of drains through wounds, and operations and hospital stays of long duration.

When tissues become contaminated by bacteria, an inflammatory response normally contains and destroys the inoculum within the first several hours. Vascular permeability and tissue osmolarity increase during the initial three to five hours following contamination, and after two hours an invasion by leukocytes occurs in response to chemotactants released within the tissues. Wound induration begins to increase after five hours as permeability begins to diminish. The extent of induration determines the ultimate size of the bacterial lesion.[11]

Timing and Duration of Antimicrobial Prophylaxis

Animal studies by Burke[12] have defined a period during this inflammatory sequence when certain variables can alter the evolution of the bacterial lesion. For example, the inoculation of a fixed number of live Staphylococcus aureus organisms into the dermis of a guinea pig results in a skin lesion of a reproducible size. The concomitant or prior intravenous administration of an antibiotic will give an antibacterial concentration in the tissues when the bacteria are injected that will prevent their proliferation and the formation of the dermal lesion. If the injection of an antibiotic occurs one to three hours after the inoculation of the staphylococci, the dermal lesion will form but will be smaller in diameter. The longer the interval between the two inoculations, the larger the ultimate skin lesion will be, until after an interval of four or more hours when the dose of antibiotic will exert no influence on the ultimate lesion size. This time of antibiotic efficacy has been called the "decisive period" of antibiotic prophylaxis by Burke and constitutes an important principle behind the rationale of perioperative antibiotic use to reduce postoperative wound infections.

Two studies in humans have confirmed the observations made in animals that antibiotics exert maximal protection against wound infection under two circumstances: when an antibacterial concentration of antibiotic is present in tissues at the time of bacterial inoculation, and when the antibiotic exerts antibacterial activity against contaminants. Stone et al[13] prospectively studied the prophylactic efficacy of cefazolin in elective gastric, biliary, and colon surgery by administering the antibiotic 8 to 12 hours and 1 hour preoperatively and either 1 to 4 hours postoperatively or never at all. Statistically significant reductions in wound infection rates were observed in both groups of patients who received preoperative antibiotics. Infections that occurred were usually caused by bacterial strains that were resistant to cefazolin. There was no advantage to beginning the antibiotic prior to one hour before surgery. Patients who received no antibiotic or doses one to four hours postoperatively had comparable wound infection rates. A retrospective study by Fullen et al[14] of 295 patients who had sustained penetrating abdominal trauma also showed efficacy of preoperative antibiotic prophylaxis in reducing wound infections. The initiation of antibiotics intraoperatively or postoperatively was associated with infection rates four to five times higher than the preoperative group.

Tradition has largely dictated that prophylactic antibiotics be administered for several days beyond an operation, but recent studies have challenged this practice. In gastrointestinal surgery, Stone et al[15] have shown comparable degrees of protection against postoperative infection between perioperative and five to seven days of antibiotic administration. Both of his study groups had antibiotics started immediately prior to surgery. In another recent study, Keighley et al[16] showed no significant advantage to continuing antibiotics for longer than the perioperative period.

Antibacterial Spectrum

A more controversial issue concerns the optimal antibacterial spectrum of perioperative antibiotics. When it is anticipated that contaminating bacterial wound flora will be both aerobic and anaerobic, should antibiotics be directed against the aerobes or the anaerobes, or against both bacterial types? Polk and Lopez-Mayor[17] and Stone et al[13] have demonstrated significant decreases in postoperative wound infection rates in colon surgery utilizing cephalosporin antibiotics with no antibacterial activity against the pathogenic anaerobic flora that colonize the colon. In contrast, Wapnick et al[18] showed no difference in wound infection rates between patients who received kanamycin or a placebo orally prior to elective colon resection. Patients who preoperatively received kanamycin or neomycin plus erythromycin orally did have significantly lower wound infection rates than the kanamycin or placebo groups. An aminoglycoside plus erythromycin exerts a broad spectrum of activity against fecal aerobes and anaerobes.[19] Aminoglycosides alone do not affect anaerobes. These data have demonstrated a superior degree of protection against wound infection in colon surgery when a broader spectrum of antibacterial activity was utilized. All patients had received appropriate mechanical bowel cleansing prior to surgery.

In established infections caused by both aerobic and anaerobic bacteria acting in synergism, it may be sufficient to direct antibiotics against only the aerobes, as long as drainage and debridement are adequate and dead space, foreign bodies, and tissue ischemia are minimized.[20-22] Polk and Lopez-Mayor[17] and Stone et al[13] have demonstrated that the prevention of wound infections can also be accomplished by the perioperative administration of antibiotics active against only aerobes when both aerobes and anaerobes have contaminated tissues. Surgical techniques must be sufficient to leave no tissue environments that would favor the proliferation of the anaerobes. However, the convincing data of Wapnick et al[18] render the final resolution of this controversy dependent upon the outcome of additional well-controlled studies.

Criteria for Prophylactic Antibiotics

For their action to be effective, prophylactic antibiotics must meet a number of criteria. Their pharmacokinetics should permit a rapid equilibrium in tissues within the "decisive period" of antibiotic prophylaxis, and they should exert antibacterial activity against the anticipated contaminating bacterial flora. The duration of administration should be short (ie, for the duration of the operation), and the cost should be low. Finally, the incidence of deleterious side effects should not exceed the anticipated incidence of postoperative infection (eg, clean herniorrhaphy would become infected postoperatively 1 to 2 percent of the time, and the overall risk of antibiotic administration per se is 4.5 percent[23]; hence, antibiotic prophylaxis is not indicated for elective herniorrhaphies). Less toxic antibiotics are recommended for prophylactic use to reserve the antibiotics with more adverse side effects for therapeutic use, for which their utilization is justified. If potentially toxic antibiotics like aminoglycosides, lincomycin, or clindamycin are used, administration should not exceed two or three perioperative doses. Unnecessarily prolonged antibiotic administration is associated with increased chances of adverse reactions, superinfection with bacterial and fungal pathogens, acquisition of resistance in resident bacterial flora, and higher cost.[7]

Efficacy of Antimicrobial Prophylaxis

Numerous studies to date have demonstrated efficacy of antibiotic prophylaxis in reducing postoperative wound infection rates. Conflicting results of earlier studies caused considerable confusion until well-controlled, prospective, randomized, and often double-blind studies critically tested and confirmed the question of efficacy. Earlier studies that challenged their usefulness were usually poorly controlled and nonrandomized, or they utilized antibiotics for study that were inappropriate for the wound bacteriology. Study groups were often not comparable, and antibiotics were frequently begun too late, beyond the "decisive period" of efficacy.[24]

That antibiotic prophylaxis has succeeded in reducing postoperative wound infection rates is evident from the experience at Cincinnati General Hospital, one of the centers that collaborated in the National Research Council study.[3] The overall incidence of wound infection in Cincinnati where appropriate antibiotic prophylaxis was utilized between 1959 and 1962 was 3.0 percent. Clean wound infection rates were 1.9 percent, and the

Table 1. Recommendations for Antimicrobial Prophylaxis in Surgery

Abdominal Surgery

Colorectal Surgery

1. Neomycin 1 gm + erythromycin 1 gm orally at 1 PM, 2 PM, and 11 PM the day before surgery, combined with mechanical bowel preparation, no additional parenteral agent recommended
2. Unproved alternative: For patients unable to take oral antibiotics, emergency operation, or bowel obstruction
   Doxycycline 200 mg intravenously at induction of anesthesia *or*
   Cefoxitin 1 gm intravenously at induction of anesthesia

Gastroduodenal Surgery

1. Indications:
   Gastric ulcer
   Gastric malignancy
   Bleeding or obstructing duodenal ulcer
2. Regimen: Cefazolin 1 gm intramuscularly on call to operating room or intravenously with induction of anesthesia; repeat dose every 6 hours intravenously for duration of operation

Biliary Tract Surgery

1. Indications:
   Aged over 70 years
   Previous biliary tract surgery
   Presence of jaundice
   Common duct stones
   Acute cholecystitis
2. Regimen: Cefazolin 1 gm intramuscularly on call to operating room or intravenously with induction of anesthesia; repeat dose every 6 hours intravenously for duration of operation

Appendectomy

1. Regimen: Clindamycin 600 mg intramuscularly on call to operating room or intravenously at induction of anesthesia; optional: add gentamicin 2 mg/kg intramuscularly on call to operating room or intravenously at induction of anesthesia
2. Unproved alternatives: Doxycycline 200 mg intravenously at induction of anesthesia *or* cefoxitin 1 gm intravenously at induction of anesthesia
3. Continue antibiotics postoperatively if abscess or perforation is found

Penetrating Abdominal Trauma

1. Regimen: Gentamicin 2 mg/kg + clindamycin 600 mg, both intravenously as soon as possible in emergency room
2. Alternative: Penicillin 1 million units + doxycycline 200 mg intravenously as soon as possible in emergency room; repeat penicillin every 4 hours during operation.
3. Necessity of postoperative antibiotics depends on findings at operation and age of traumatic injury

Cardiovascular Surgery

Cardiac Surgery

1. Indications:
   Prosthetic valve insertion
   Optional for coronary artery bypass grafts without prosthetic valve insertion
2. Regimen: Cefazolin 1 gm intravenously on call to operating room or at induction of anesthesia; repeat dose intravenously or intramuscularly every 6 hours for maximum of 72 hours postoperatively

Peripheral Vascular Surgery

1. Indications:
   Abdominal aortic and lower leg bypass

Table 1. Recommendations for Antimicrobial Prophylaxis in Surgery, continued

Not indicated for brachial or carotid artery surgery
2. Regimen: Cefazolin 1 gm intramuscularly on call to operating room or intravenously at induction of anesthesia; repeat dose intravenously every 6 hours for duration of operation

Cardiac Pacemaker Insertion
1. Necessity or efficacy of antimicrobial prophylaxis unproven

Thoracic Surgery

Pulmonary Resection
1. Indications: Any resection, including biopsy, in patient with chronic sputum production
2. Regimen: Ampicillin 1 gm intravenously at induction of anesthesia or cefazolin 1 gm intramuscularly on call to operating room or intravenously at induction of anesthesia; repeat dose intravenously every 6 hours for duration of surgery

Otolaryngologic Surgery

Head and Neck Surgery
1. Indications: Head and neck surgery with opening into oral cavity or pharynx
2. Regimen: Cefazolin 1 gm intramuscularly on call to operating room or intravenously at induction of anesthesia; repeat dose intravenously every 6 hours for duration of operation

Orthopedic Surgery

Total Hip Replacement and Other Artificial Joint Insertion
1. Regimen: Cefazolin 1 gm intramuscularly on call to operating room or intravenously at induction of anesthesia; repeat dose intravenously or intramuscularly every 6 hours for maximum of 24 hours postoperatively

Open Fractures
1. Regimen: Cefazolin 1 gm intramuscularly or intravenously in emergency room; repeat doses every 6 hours intramuscularly or intravenously for 3 days

Genitourinary Surgery

Prostatectomy
1. Prophylaxis optional in patients with sterile urine
2. If urine infected, eradicate bacteriuria, if possible, before surgery

Insertion of Penile Prosthesis
1. Necessity or efficacy of antimicrobial prophylaxis unproven

Urinary Diversion with Ileal Loop
1. Same regimen as for colorectal surgery

Obstetrical-Gynecologic Surgery

Vaginal Hysterectomy
1. Prophylaxis optional
2. Regimen: Cefazolin 1 gm intramuscularly on call to operating room or intravenously at induction of anesthesia

Cesarean Section
1. Prophylaxis optional, but may be used for patients in labor or with ruptured membranes
2. Regimen: Cefazolin 1 gm intramuscularly on call to operating room or intravenously at induction of anesthesia or intravenously after cord clamping

Neurological Surgery

Insertion of Ventricular Shunts
1. Necessity or efficacy of antimicrobial prophylaxis unproven

rates for clean-contaminated, contaminated, and dirty wounds were, respectively, 3.8, 5.2, and 10.4 percent, all lower than the other hospitals that participated in the rates reported by the National Research Council study[3] and by Cruse and Foord.[4] Preliminary rates in 1978 for wound infections on a general surgical service at the University of Washington where perioperative antibiotics are routinely used were 1.89, 3.97, 6.67, and 13.3 percent for clean, clean-contaminated, contaminated, and dirty wounds, respectively.[25] Reduced infection rates accrue considerable cost savings to patients and society and are associated with reduced patient morbidity and mortality. Whether the ideal goal of zero infection rates for all wound categories will ever be realized is doubtful, and it will likely not depend on antibiotic administration. Host factors are of ultimate importance, but in this arena knowledge is still woefully incomplete.

Recommendations for Antimicrobial Prophylaxis

Recommendations in Table 1 for antimicrobial prophylaxis at the University of Washington Affiliated Hospitals have been based on an extensive literature review by the authors. The reports cited are randomized, prospective, often double-blind clinical studies. A few recommendations have been made in the absence of data from convincing trials but have been based on the established principles of antimicrobial prophylaxis which have been discussed above. Operative procedures that have been included are those for which perioperative antibiotic administration has been demonstrated effective in reducing postoperative wound infection risk. A few procedures are included for which the necessity or efficacy of antimicrobial prophylaxis has not been demonstrated but in which antibiotic use is a common practice.

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