CHAPTER 3
Prevention of Infection in Orthopaedic Surgery

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INTRODUCTION
Before the introduction of antiseptic technique and antibiotics, life-threatening wound infections were the usual outcome of a major surgical procedure. The following quotation describes conditions in the nineteenth century: "Not a single wound healed without festering, and small wonder. In the operating theatre—to which one’s nose bore witness as being the favorite retiring room of the nurses’ cats—there was no appliance for washing the hands, nor was there any in the robing room opposite." The instruments lay "open for anyone to handle," and suture needles "were stuck ready in a jam pot of rancid lard." A sign over the operating room read "Prepare to meet thy God."1

It is appropriate to a chapter on preventing orthopaedic infections that the person credited with the introduction of aseptic principles was Joseph Lister, an orthopaedic surgeon. After Pasteur demonstrated that germs were responsible for putrefaction, Lister (in 1867) theorized that bacteria in the ambient air could cause wound infections if they gained access to tissues through the broken skin. He used carbolic acid (a phenol) directly on wounds and later started nebulizing it into the air. He "invented a donkey engine which sprayed a mist of carbolic acid through the operating room, and poisoned the microbes, the patient, and the surgeon alike."2 Semmelweis advocated the use of antiseptics (chlorine solution) on the unbroken skin of the physician’s hands to prevent them from transmitting infections. Surgical gloves were introduced in 1889. Koch described the benefits of heat in sterilizing equipment. Thus modern aseptic techniques were born.

These aseptic techniques decreased but did not eliminate bacterial contamination. After the introduction of antibiotics in the mid-twentieth century, their use in preventing infections after elective surgery was studied, with initially conflicting results. However, after Burke demonstrated the importance of timing the administration of antibiotics to maximize their efficacy, prophylactic antibiotics became standard care before certain operative procedures.3 Antibiotics decreased but did not completely eliminate the incidence of postoperative infections; currently, surgical site infections (SSI) are the second most common cause of nosocomial infections,4,5 with adverse consequences. The development of an SSI increases hospital stay, cost, mortality, and morbidity.6–12

Antimicrobial prophylaxis refers to a critically timed brief course of antibiotics started just before an operation begins. The value of antimicrobial prophylaxis has been clearly established for "clean" and "clean-contaminated" surgery. In "dirty" wounds, by definition, antimicrobials would be given for treatment rather than preventive purposes.

In this chapter, the principles of prophylaxis, the importance of timing, choice of antibiotics, and impact of emerging resistance patterns, with special emphasis on orthopaedic surgical procedures, are addressed.

PRINCIPLES OF PROPHYLAXIS
To effectively prevent an infection, one must be able to:

- Identify the patients at risk.
- Identify procedures that pose risk.
- Define the pathogenesis.
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- Define period of risk.
- Define spectrum of organisms involved.
- Have available safe, effective, and relatively inexpensive agents to which these organisms are sensitive.
- Use an antibiotic that carries a low risk of inducing resistance in the bacterial strains targeted.

Patients at Risk

There are patients at increased risk of SSI: patients known to be colonized with certain bacteria (e.g., *Staphylococcus aureus*), diabetics (especially if uncontrolled), smokers, obese people (>20 percent of ideal body weight), very old patients, patients on steroids, or those with poor nutritional status. A risk index of three variables was developed by the National Nosocomial Infections Study (NNIS), as follows: American Society of Anesthesiology (ASA) preoperative assessment score of 3, 4, or 5; an operation lasting longer than T hours (where T depends on the procedure); and an operation classified as dirty/infected. The index has values of 0, 1, 2, or 3. It is a better predictor of the risk of SSI than the traditional wound classification system.

*Staphylococcus aureus* Colonization

Nasal carriage of *S. aureus* is the most significant independent risk factor for SSI due to that organism. In a study of patients undergoing orthopaedic surgery with prosthetic implants, those who were nasal carriers of *S. aureus* had a relative risk of 8.9 of developing prosthetic infection compared with those who were not carriers. Similar findings have been reported for patients undergoing neurosurgical and cardiac operations. The use of mupirocin prophylactically is addressed later in the chapter.

PROCEDURES THAT POSE RISK

Surgical Wounds have been classified into clean, clean/contaminated, contaminated, and dirty/infected. The surgeon anticipates *preoperatively* the surgical wound class that would be present *postoperatively*. Antimicrobial prophylaxis is then designed accordingly.

Clean wounds are those operative wounds in which no inflammation is encountered. The respiratory, alimentary, genital, or uninfected urinary tract is not entered. Clean wounds are primarily closed but, if necessary, drained with closed drainage. Operative incision wounds after blunt trauma can be included in this category if they meet the criteria.

Clean/contaminated wounds are those operative wounds in which the respiratory, alimentary, genital, or urinary tract is entered under controlled conditions and without unusual contamination.

Contaminated wounds are fresh, open, accidental wounds or operations with a major break in surgical technique, gross spillage from the GI tract, or where acute nonpurulent inflammation is encountered.

Dirty/Infected wounds are those old wounds with retained devitalized tissue and those that involve existing clinical infection or perforated viscer.

As mentioned earlier, contaminated and dirty/infected wounds would not be candidates for antibiotic prophylaxis. Antibiotics would be given for treatment instead. Antibiotic prophylaxis is recommended for all clean contaminated procedures, for the insertion of prosthetic devices, or for clean surgeries where the consequences of an infection would be catastrophic (spine surgeries, coronary artery bypass grafting, and vascular procedures).

PATHOGENESIS OF SURGICAL SITE INFECTIONS

Bacterial infection of any wound starts by contamination. This is inevitable even under the most stringent aseptic conditions. After contamination, the interplay of the dose and virulence of the organism and the resistance of the host determine the risk of infection. This has been described by the following equation:

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\text{Risk of SSI} = \text{dose of contaminating organism} \times \text{virulence/resistance of the host}
\]

Virulence of organism: Many bacteria produce substances that can cause injury to tissue, help invade tissue, or evade host defense. These include the endotoxins of gram-negatives, exotoxins of streptococci or clostridia, glycoprotein of slime of coagulase-negative staphylococci, and numerous proteins and exotoxins of *S. aureus*.

Dose of the organism: The probability of a wound infection increases as the dose of bacterial contamination increases. The dose needed to cause infection, however, decreases dramatically if a foreign body is present. In one study, >100,000 organisms of *S. aureus* per gram of tissue were needed to produce a wound infection. In the presence of silk sutures, the dose decreased to <100 organisms. In another model of SSI involving foreign body, the ID₅₀ value was 100 colony-forming units (CFU) when polytetrafluoroethylene (PTFE) tissue cages were used. 10 CFU with PTFE vascular grafts, and 1 CFU for dextran microbeads.

Source of Bacterial Contamination—Spectrum of Organisms Involved

The most common sources of bacterial contamination of surgical sites are the patient’s endogenous skin, mucous
membranes, and viscera. In orthopaedic surgery, the skin is generally the source. In this situation, *Staphylococcus aureus* (or coagulase-negative) would be the most likely pathogen. Other sources of contamination include the hands of the surgical team (and at times vaginal or rectal shedding of organisms), contaminated equipment, contaminated host tissue, or seeding from a remote site of infection.

**Period of Risk—Timing of Antibiotic Administration**

The critical time of contamination of clean wounds is when the skin is broken. For effective prophylaxis, the antimicrobial agent must achieve adequate concentrations in the serum and tissue to kill the bacteria anticipated at the time of incision. Timing therefore is critical. Most failures of antibiotic prophylaxis occur because of inappropriate timing (too early or too late). A Canadian survey of prophylaxis among patients with hip fractures showed that administration was too early (10 percent), too late (39 percent), or too long (78 percent). A common misconception is that if a patient is already receiving antibiotics for a remote-site infection, surgical prophylaxis is not needed. This is false, since, as already mentioned, the antibiotic concentration must peak at the time of surgical incision. Patients who receive prophylaxis too early or too late have an odds ratio of developing an SSI of 4.3 and 5.8, respectively, compared to patients who receive antibiotic prophylaxis within 2 h preoperatively.

Recently, the Surgical Infection Prevention (SIP) Guideline Writers Workgroup (SIPGW) hosted by the Medicare National SIP project endorsed the national performance measure, which advocates that infusion of the first antimicrobial dose should begin within 60 min before the incision. However, when a fluoroquinolone or vancomycin is indicated, the infusion should begin 120 min before incision, so as to prevent antibiotic-associated reactions. There is no consensus on whether the infusion must be completed before the incision; but when a proximal tourniquet is required, the entire antimicrobial dose should be infused before the tourniquet is inflated.

In addition to achieving adequate tissue concentration at the time of incision, adequate concentrations must be maintained throughout the surgery. Redosing intraoperatively may be indicated depending on the half-life of the antibiotic, the minimal inhibitory concentration (MIC) for the organism, the anticipated level in the tissues, and the duration of the operation (redose if the operation is still in progress two half-lives after the first dose). For cefazolin, a second dose is indicated if the operation is longer than 3 to 4 hours; for vancomycin or ceftriaxone, it is 6 to 8 hours. The antibiotic should also be given in an adequate dose depending on the patient’s body weight or body mass index. A higher dose would be needed for morbidly obese patients.

**Choice of Agent**

Cephalosporins have been the agents most studied and most frequently used in prophylaxis. Of these, cefazolin is the most frequently used. This is because it provides adequate coverage for many clean-contaminated operations, has a favorable safety profile, and is reasonably inexpensive.

However, there is increasing resistance among bacterial pathogens, especially *Staphylococcus* species. The proportion of *S. aureus* causing nosocomial infection that is methicillin-resistant increased from 14.3 percent in 1987 to 39.7 percent in 1997. In the 1997 SENTRY program, this resistant strain was isolated from 26.9, 49.8, 29, and 48 percent of hospitalized U.S. patients with bloodstream, pneumonia, wound, and urinary tract infections respectively. In a study of postoperative infections in patients undergoing vascular surgery, 57.5 percent of *S. aureus* isolates were methicillin-resistant. Of the coagulase-negative staphylococci, more than 80 percent are resistant to oxacillin, and these organisms can cause devastating infections when prosthetic devices are implanted. For these resistant organisms, cefazolin or any of the other cephalosporins would not provide adequate coverage. Some authors have therefore advocated the routine use of vancomycin before surgeries where prosthetic devices are to be inserted. At present, the Centers for Disease Control and Prevention (CDC) does not recommend the routine use of vancomycin but does recommend its use as perioperative prophylaxis under certain circumstances, such as a cluster of methicillin-resistant *S. aureus* or methicillin-resistant coagulase-negative staphylococcal infections or high local frequency of methicillin-resistant *S. aureus* (MRSA). “The decision [to use vancomycin] should involve consideration of local frequency of MRSA isolates, surgical site infection rates for particular operations, review of infection control practices, and consultation between surgeon and infectious disease experts.” However, the CDC does not define what constitutes a high rate, and a threshold has not been defined where the routine use in an institution is considered scientifically acceptable. In a decision analysis model to calculate the clinical benefits and costs associated with the use of either cefazolin or vancomycin for prophylaxis in coronary artery bypass surgery, cefazolin had the advantage against susceptible organisms unless the prevalence of methicillin-resistance was >3 percent. In a study randomizing 885 patients undergoing cardiac surgery to receive either cefazolin or vancomycin as prophylaxis, there was no difference in SSI between the two groups. However, patients who received cefazolin and vancomycin and later developed...
an SSI were more likely to be infected with MRSA. In Europe, where teicoplanin is frequently used (teicoplanin is a glycopeptide of similar spectrum to vancomycin but is not available in the United States), a study comparing teicoplanin to cefazolin in orthopaedic patients did not show significant differences in outcomes at 3 or 12 months.51

In the absence of firm recommendations, the use of vancomycin would be appropriate in the context of an outbreak of surgical infections due to methicillin-resistant staphylococci or for a patient known to be colonized with MRSA,42 especially if this patient is to undergo insertion of a prosthetic device. The Society for Health Care Epidemiology of America recently recommended routine surveillance cultures at the time of admission for patients at high risk for MRSA carriage,52 but identifying these patients in a timely manner before surgery is still problematic. The impact of routine use of vancomycin on the epidemiology of glycopeptide resistance is not entirely clear.

In patients with beta-lactam allergy, prophylaxis against gram-positive organisms can be achieved with either vancomycin or clindamycin.18

**DURATION OF PROPHYLAXIS**

Most guidelines recommend that antimicrobial prophylaxis should end within 24 h after the operation,18,53,54 and recently the SIP work group reiterated this recommendation.42 There is no evidence that continuing antibiotics until all drains and catheters are removed will lower infection rates.18,42 Continuing antibiotics beyond 24 h increases cost as well as the risk of bacteremia and line infections.55

**PROPHYLAXIS FOR ORTHOPAEDIC SURGERY**

Most orthopaedic operations are in the category of “clean” (i.e., uninfected operative wound in which no inflammation is encountered and the respiratory, alimentary, genital, or urinary tracts are not entered, with or without insertion of hardware), or “contaminated” (trauma with open wounds). For those “clean” orthopaedic operations where any foreign material is to be implanted, antimicrobial prophylaxis should be given. In general, antimicrobial prophylaxis is recommended for joint replacement, repair of closed fractures and hip fractures, all spinal surgeries, or insertion of any prosthetic device. It is not recommended for elective surgery that does not involve prosthetic device implantation (e.g., arthroscopy).

It has been shown—by the analysis of pooled results from 22 trials in patients undergoing surgery for internal fixation or replacement arthroplasty for a closed fracture of the femur or any other long bone fracture, utilizing any regimen of systemic antibiotics administered at the time of surgery—that a single perioperative antibiotic dose with or without two or more postoperative doses reduced the incidence of an SSI as well as urinary tract and respiratory tract infections.50 A single dose of short-acting antibiotic was inferior to multiple doses of the same antibiotic. Multiple doses of a short-acting antibiotic were equal to a single dose of a long-acting antibiotic. This reflects the need to maintain an adequate concentration of the antibiotic throughout the surgical procedure. Multiple doses of antibiotics given over 24 h or less were equal to the same antibiotic given for a longer period.57

For patients undergoing total joint replacement, metaanalysis of small, randomized trials, many of which were underpowered, revealed that antibiotics given preoperatively and for 24 h to 2 weeks postoperatively reduced the rate of superficial and deep infections compared to placebo. Pooled data were of insufficient power to determine whether the shorter duration is preferable or inferior.57,58

For orthopaedic surgery, the preferred antibiotic in patients undergoing hip or knee replacement is cefazolin.59,60 Vancomycin or clindamycin can be used in patients with beta-lactam allergy. However, the discussion in the previous section regarding the use of vancomycin would be particularly pertinent to orthopaedic surgery, especially if a prosthesis is to be inserted.

**Use of Antibiotic Beads for Prophylaxis**

Systemic aminoglycosides are seldom used for prophylaxis because of their poor tissue concentrations and toxicity profile. Beads impregnated with aminoglycosides (gentamicin and tobramycin) are widely used in orthopaedic surgery for the supplemental therapy of established infection. Two trials compared impregnated beads (one with gentamicin and one with cefuroxime) with systemic antibiotics for prophylaxis. Deep prosthetic infections occurred more frequently in the systemic group and superficial infections more frequently in the beads group.61,62 However, beads themselves can act as a biomaterial surface on which bacteria can grow. In a report from the Netherlands, in 18 of 20 of cases of infected prostheses, bacteria were found on the beads. Negative routine cultures were found in 12 of 18 cases.63 The role of beads in prophylaxis is not clear.
Operating Room Environment

The operating room (OR) air contains microbes, and efforts should be made to minimize that. Traffic in the OR increases the number of these microbes, so traffic should be limited. The CDC has published recommendations for maintaining airflow and pressure in the OR.\textsuperscript{18} Since the inoculum of organisms needed to produce an SSI is considerably smaller in the presence of prosthetic material, the use of ultraclean air over the operating field for operations involving prosthesis implants has been advocated. This is done by laminar airflow, which moves particle-free air over the aseptic field at a uniform velocity (0.3 to 0.5 µm/s), sweeping away particles in its path. Laminar airflow can be directed vertically or horizontally. Recirculated air then flows through a high-efficiency particulate air (HEPA) filter.\textsuperscript{64}

The studies with ultraclean air have been done only in orthopaedic surgery.\textsuperscript{65} In a multicenter study of more than 8000 total hip and knee replacements, ultraclean air alone was compared to perioperative antibiotics alone or both. Ultraclean air reduced infection from 3.4 to 1.6 percent, antibiotics alone from 3.4 to 0.8 percent, and both from 3.4 to 0.7 percent. In a case-control study of more than 26,000 patients undergoing total hip or knee replacement, laminar airflow was not a significant factor in reducing infections.\textsuperscript{66} Thus the use of ultraclean air in addition to antimicrobial prophylaxis does not seem to be of added benefit.

Ultraviolet irradiation to sterilize the air in the OR has also been used, with results comparable to those from the use of ultraclean air.\textsuperscript{67}

\section*{USE OF MUPIROCIN}

Many studies have examined the role of mupirocin in preventing SSIs. In a study in orthopaedic patients undergoing prosthesis implantation nasal mupirocin was compared with placebo. The mupirocin group were less likely to develop endogenous \textit{S. aureus} infection, but the overall rate of infection was not different.\textsuperscript{68} In another study,\textsuperscript{69} nasal mupirocin for 5 days and triclosan shower prior to surgery were used in orthopaedics wards. The incidence of SSIs by \textit{S. aureus} decreased from 2.3 to 10 percent. No high-level resistance was detected. Other studies, however, have found marked increases of high-level mupirocin resistance after its widespread use.\textsuperscript{70} In a randomized double-blind placebo-controlled trial involving 3804 patients undergoing a variety of surgical procedures, the use of mupirocin decreased the incidence of \textit{S. aureus} SSIs in patients who were \textit{Staphylococcus} carriers but did not significantly reduce the overall incidence of \textit{S. aureus} SSI.\textsuperscript{71}

As mentioned earlier, the Society for Health Care Epidemiology of America has recently recommended routine surveillance cultures at the time of admission for patients at high risk for MRSA carriage.\textsuperscript{52} Mupirocin may be a useful adjunct in patients who are known to be carriers or at high risk of being carriers (e.g., in cases of diabetes, hemodialysis, recurrent staphylococcal infections, or residence in nursing homes).

\section*{SUMMARY}

Antimicrobial prophylaxis refers to a critically timed brief course of antibiotics started just before an operation begins. The value of antimicrobial prophylaxis has been clearly established for “clean” and “clean-contaminated” surgery. In “dirty” wounds, by definition, antimicrobials would be given for treatment rather than prevention. The choice of agent depends on the anticipated spectrum of organisms. Additional doses of the antibiotic given intraoperatively depend on the half-life of the antibiotic and the duration of surgery. Antibiotics should be stopped within 24 h of the operation. Additional measures (mupirocin, ultraclean air) can be considered for special patient populations and procedures.

\section*{REFERENCES}

PART I  GENERAL PRINCIPLES


