

# Surgical Site Infections in Orthopaedics: The Role of Antibiotics

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## Abstract

In spite of advancements of surgical techniques and operating room technologies, surgical site infections still remain a major problem. Bacteria have also evolved specially in nosocomial settings and both prophylactic and therapeutic use of antibiotics has to be rationally decided based on individual cases

**Keywords:** Surgical site infections, orthopaedics, antibiotics, prophylaxis

## Introduction

Up until the middle of the 19th century, surgery was feared largely because of the significant likelihood of developing life-threatening wound infections, also known as ‘hospital gangrene.’ Before the advent of sterilization techniques and antibiotics, a majority of surgical incision sites became infected and mortality rates of 70–80% were not uncommon in patients with deep or extensive infections [1].

Even today, SSIs are the commonest and costliest nosocomial infections in surgical patients, accounting for up to 16% of nosocomial infections in all hospitalized patients and 38% of all infections in surgical patients [2]. SSIs in orthopaedics are further complicated by the presence of foreign material in the form of implants used for osteosynthesis in trauma patients, and prosthesis used in joint replacement surgeries. Bacterial

biofilm formation on inert surfaces of orthopaedic devices is a contributing factor for SSI, particularly in the setting of infection due to *S. aureus* and *S. epidermidis*. In addition, biofilm makes antimicrobial penetration difficult and confers antimicrobial resistance. The prevalence of SSIs for all orthopaedic procedures is reported to be between 0.6 and 2.55% [2]. Periprosthetic joint infection (PJI) is one of the leading causes of failure following total knee arthroplasty (TKA) and total hip arthroplasty (THA), and is one of the most common reasons for revision shoulder and elbow arthroplasty.

The number of surgical procedures performed globally continues to rise. Not only are more complex surgical procedures being performed, but they are being performed on more challenging patients with multiple comorbidities and even immunosuppression [2]. Hence, in spite of advances in infection control practices, including improved operating room ventilation, sterilization methods, barriers, surgical technique, and availability of antimicrobial prophylaxis, surgical site infections

(SSIs) remain a substantial cause of morbidity, prolonged hospitalization, and death. Direct and indirect costs of SSIs include increased rate of readmissions, longer hospital stay, emergency department visits, outpatient visits, use of ancillary services, intravenous and other antibiotics, loss of productivity, and temporary or permanent disability.

This article aims to discuss the current recommendations for antibiotic usage in the prevention and management of SSI's following various orthopaedic procedures.

## Antibiotic Prophylaxis

The efficacy of antibiotic prophylaxis in reducing SSIs in orthopaedic surgeries by reducing the burden of microorganisms at the surgical site during the operative procedure [3,4], has been clearly established and systemic antimicrobial prophylaxis has been accepted as a universal protocol in the practice of orthopaedic surgery. This is particularly crucial in situations where there is a high risk of infection, especially if the infection could have disastrous consequences (such as in the setting of immune compromise, and /or implantation of a foreign device).

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**Right Indication**

Antibiotic prophylaxis does not include preoperative decontamination and the treatment of established infections.

The appropriate use of perioperative antibiotic prophylaxis is a key intervention for preventing SSIs in clean-contaminated surgery[5]. A recent systematic review by Al Buhairan et al. on effectiveness of antibiotic prophylaxis in patients undergoing total hip and knee replacement found that antibiotic prophylaxis reduced the absolute risk of wound infection by 81% compared with no prophylaxis[6]. On the other hand, inappropriate antibiotic usage such as overuse, misuse, wrong administration time, and insufficient dose may result in the emergence of antibiotic resistance, adverse drug reactions, therapeutic failure and increased treatment costs. Several protocols and guidelines have been developed to provide a standardized approach for rational, safe and effective use of antibiotic prophylaxis [6].

In general, antibiotic prophylaxis is recommended for most orthopaedic procedures because of the amount of tissue dissection, muscle injury and blood loss involved. In procedures where the incidence of surgical site infections tends to be high, for example, open injuries or when the consequences of infection are significant, for example, surgery with implanted material such as in arthroplasty, prophylactic systemic antibiotics must always be administered. On the other hand, there is insufficient evidence to support surgical prophylaxis for minor procedures and clean non-prosthetic-associated procedures[5].

**Right antimicrobial**

The selected antimicrobial agent should fulfil the following criteria[5,7]

1. Be effective against the pathogens most likely to contaminate the surgical site
2. Be bactericidal
3. Be relatively cheap

The choice of antibiotic is further

influenced by multiple patient-specific risk factors including pre-existing infection, recent antimicrobial use, known colonisation with a resistant organism, prolonged hospitalisation, prostheses, weight, renal function, allergy status, comorbidities and immunosuppression[8]. There is little evidence to suggest that broad-spectrum antimicrobial agents result in lower rates of postoperative SSI compared with narrower spectrum antimicrobial agents. The microbial context of the wound and the hospital environment may influence the choice of antibiotic, but coverage should primarily target those organisms known to cause postoperative infection.

In general, a first-generation cephalosporin fulfils these criteria and is regarded as sufficient prophylaxis for the majority of procedures. The most commonly administered drug is cefazolin (dose of 2 gm). It is the most widely studied antimicrobial agent with proven efficacy for antimicrobial prophylaxis[3,7,9]. It has a desirable duration of action, spectrum of activity against organisms commonly encountered in surgery, reasonable safety, and low cost. It is active against streptococci, methicillin-susceptible staphylococci, and some gram-negative organisms. Second-generation cephalosporins such as cefuroxime have broader coverage against gram-negative organisms than cefazolin. For procedures of the alimentary tract, genitourinary tract and hepatobiliary system, site-specific flora, such as gram-negative and anaerobic microorganisms should be adequately covered. In such cases, cefotetan or cefoxitin are suitable agents. For patients with documented allergy to cephalosporins, vancomycin is a reasonable alternative for coverage of staphylococcus, and metronidazole or clindamycin and an aminoglycoside may be used for coverage of anaerobic and gram-negative organisms, respectively. Aztreonam can be combined with clindamycin but not with metronidazole

in the same setting.

Errors in selection or dose of prophylactic antimicrobials are common. However, initiatives such as the Surgical Care Improvement Project (SCIP) have improved the rates of compliance and selection since earlier studies were performed[4,10].

**Resistant organisms**

The approach to selecting antimicrobial surgical prophylaxis for patients known to be colonized or recently infected with drug-resistant pathogens must be individualized. Whether prophylaxis should include coverage for such pathogens depends on many factors including the pathogen, its antimicrobial susceptibility profile, the host, the planned procedure, and the proximity of the likely reservoir of the pathogen to the incision and operative sites[7]. Specific prophylaxis for a resistant gram-negative pathogen in a patient with past infection or colonization may not be necessary for a cutaneous procedure.

**Right route of administration**

Parenteral administration (intravenous or intramuscular) is the preferred route for surgical antimicrobial prophylaxis.

**Right Timing of administration**

It is critical to administer the prophylactic antibiotic at the correct time in order to provide maximum serum and tissue concentration that exceed the minimum inhibitory concentration, at the time of potential contamination. The first dose should always be given before the skin incision is taken. The drug should ideally be administered within 30 minutes and certainly within two hours before the incision is made. Studies have shown that patients receiving antibiotic prophylaxis within the 2-hour window have lower SSI rates than those who receive it more than 3 hours before surgery[3]. However, administration of vancomycin or a fluoroquinolone should begin 120 minutes before surgical

Table 1: Recommendations for antibiotic therapy for open fractures			
Open fracture Type	Clinical infection rate	Antibiotic choice	Antibiotic duration
I	1.40%	IV Cefazolin 1-2gm	Every 8 hrly for 3 doses
I	3.60%	IV Piperacillin/tazobactam 3.375gm OR IV Cefazolin/Tobramycin	Continue for 24 hrs after wound closure
IIIA	22.70%	IV Piperacillin/tazobactam 3.375gm OR IV Cefazolin/Tobramycin	Three days
		+ IV penicillin 2-4million units if needed	
IIIB	10-50%	IV Piperacillin/tazobactam 3.375gm OR IV Cefazolin/Tobramycin	Continue for 3 days after wound closure
		+ IV penicillin i2-4million units if needed	
IIIC	10-50%	IV Piperacillin/tazobactam 3.375gm OR IV Cefazolin/Tobramycin	Continue for 3 days after wound closure
		+ IV penicillin i2-4million units if needed	

incision because of the prolonged infusion times required for these drugs. Antibiotics can also be used during an operation, if necessary, especially in procedures that last several hours.

### Right duration

In general, repeat antimicrobial dosing following wound closure is not necessary and may increase the risk for development of antimicrobial resistance and Clostridium difficile infection (CDI). A single preoperative dose is adequate for the majority of procedures. Post-procedural doses of intravenous antibiotics (up to 24 hours) are only required in defined circumstances, such as some cardiac and vascular surgeries, and lower limb amputation.

### Repeat Dosing

Repeat dosing is considered:

- For longer procedures (duration of surgery >4 hours), where it is readministered at intervals of one or two times the half-life of the drug (using the same dose)[3].
- When there is excessive blood loss (>1500mL)
- In the setting of factors that shorten antimicrobial half-life, such as extensive burns[3].

Redosing may not be required for

patients in whom the antimicrobial half-life is prolonged, such as renal insufficiency and for clean and clean-contaminated procedures, following closure of the surgical incision, even in the presence of a drain.

### Eradication of carrier status

Several studies have demonstrated that preoperative decolonization of Methicillin resistant staphylococcus aureus (MRSA) reduced SSI rates in colonized surgical patients [3,11,12,13], while others have found no benefit for S. aureus decolonization of patients undergoing surgery[3,14].

The feasibility of screening elective surgical patients for MRSA and methicillin-sensitive S. aureus followed by decontamination by topical mupirocin and chlorhexidine showers was tested and shown to result in significantly reduced rates of post-operative infections[15]. Studies have been performed on universal screening vs targeted screening.

The optimal approach to S. aureus screening and decolonization remains uncertain and should be tailored to individual clinical circumstances.

**Vancomycin is not recommended for routine use in surgical prophylaxis but**

**may be considered as a component of a MRSA prevention bundle for SSIs in selective circumstances[3,5,7,9]**

**Use of vancomycin may be acceptable in the following circumstances :**

- Detection of a cluster of SSIs due to MRSA or methicillin-resistant coagulase-negative staphylococci at an institution
- A patient is known to be colonized with MRSA
- A patient is at high risk for MRSA colonization in the absence of surveillance data (eg, patients with recent hospitalization, nursing home residents, patients on hemodialysis, patients on immunosuppressive medications)
- When a surgical procedure involves a prosthetic joint insertion, sternotomy or vascular graft insertion

The recommended dose of vancomycin is a fixed dose of 1000–1500 mg or a weight adjusted dose of 15-20 mg/kg<sup>5</sup>. Vancomycin is less effective than cefazolin for preventing SSIs caused by MSSA[16,17]. Hence, it should be combined with cefazolin for prevention of SSI due to MRSA and coagulase-negative staphylococci in the above scenarios.

There are no standardized decolonization regimens. Many studies have used mupirocin (2% mupirocin nasal ointment to nares twice daily for five days) and chlorhexidine (2% chlorhexidine gluconate wash daily for five days). Other nasal agents include povidone-iodine and alcohol-based nasal solutions. Further study regarding the role of these agents for prevention of SSI is needed.

### Role Of Antibiotics In Open Fractures

By definition, all open fractures are contaminated. The rates of clinical infection are reported to be 1.4% for Type I open fractures, 3.6% for Type II fractures and 22.7% for Type III fractures[18,19]. Antimicrobial therapy

administered in the setting of contaminated wounds is not considered prophylactic; in such cases, a therapeutic course of antimicrobial therapy is warranted. Intravenous antibiotics must be started for all open fractures. Early administration of antibiotics, within 3 hours of injury has been shown to reduce infection rates by almost six-fold [18,20]. In Type I & II open fractures, gram positive infections are more common, and hence a first generation cephalosporin with or without additional gram negative cover is recommended [18,19,21-25]. (Table 1) Type III fractures often have contamination from gram negative organisms, and also anaerobic bacteria if there has been soil contamination as in farm injuries. Penicillin (to combat potential Clostridial infection) must be administered along with gram negative antibiotics in these injuries. Appropriate antibiotics must be administered to combat nosocomial infections by Staphylococcus aureus and gram negative bacilli such as pseudomonas when treating open fractures in-hospital [19].

The precise duration of antibiotic therapy for open fractures is still debated. Messner et al have performed a meta-analysis to determine the duration of antibiotic administration for open fractures [26]. They reported that 1- 3 day administration of intravenous antibiotics offered adequate prophylaxis and that longer duration of administration did not offer any protection against septic complications from open fractures. Cross and Swintowski have advised the use of intravenous antibiotics in open fractures until wound closure is achieved [25].

### Management of Established Surgical Site Infections

In spite of the highest compliance with best practice measures, surgical site infections continue to occur. Post-operative acquisition of infection, which was earlier thought to play a minor role,

has gained attention in recent times [27]. Pathogens may gain access to surgical wounds either hematogenously, through drains, or through slowly healing wounds due to systemic anticoagulation or other factors. Evidence also supports frequent acquisition of MRSA during the postoperative period.

If a postoperative patient develops fever, it is important to ascertain that surgical site infection is indeed the cause of fever. This can be done by a thorough assessment of the surgical site (pain or tenderness, localized swelling, redness, heat) and ruling out other infectious (eg. urinary tract infection in a catheterized patient or a catheter related blood stream infection) and non-infectious causes of fever (thrombophlebitis, deep venous thrombosis, blood transfusion reaction, etc). This has important implications on the initiation and the choice of antibiotic. Management of established surgical site infections involves local control of infection coupled with appropriate antibiotic therapy. Debridement of the surgical site with drainage of purulent material, excision of devitalized tissue and bone, removal/replacement of infected implants if necessary and copious irrigation of the surgical site, plays a vital role in reducing the bacterial load and combating infection. Other local measures for combating infection include use of antibiotic loaded cement beads, application of silver nitrate solutions, etc. In patients with severe infections, the wound is not closed primarily. Instead a vacuum assisted closure (VAC) system is used to provide continuous drainage of infective fluid from the wound. This helps control of infection and formation of healthy granulation tissue that enables secondary closure of the wound at a later date.

Antibiotics targeting the most likely organisms are started but only after obtaining material for culture. Subsequently, antibiotics can be altered based on the culture report and drug sensitivity pattern. Simple infections are usually

monomicrobial and present with localized clinical findings. In contrast, complicated infections can be mono- or polymicrobial and may present with systemic inflammatory response syndrome. Management is determined by the severity and location of the infection and by patient comorbidities. It is always desirable to send relevant swabs/cultures to enable culture-based escalation or de-escalation of antibiotics. A gram stain is available very rapidly and may aid in initiating therapy with an antibiotic. Initial antimicrobial choice is empiric, and in simple infections should cover Staphylococcus and Streptococcus species. Amoxicillin/Clavulanic acid (oral or parenteral), Cefazolin or Cephalexin may be started in uncomplicated infections. Clindamycin and Cephalexin are equally effective for MRSA. If the patient has returned to the hospital following discharge, the possibility of Community acquired MRSA (CA-MRSA) should be considered. In organ/space surgical site infections, broad-spectrum antibiotics with proven effectiveness against gram-positive and gram-negative organisms and anaerobes should be used until pathogen-specific sensitivities are available; coverage can then be narrowed. In the setting of nosocomial infections or the presence of associated comorbidities, antibiotic coverage should cover resistant organisms (viz. MRSA, VRE) and or yeast. In this era of Extended spectrum beta lactamases (ESBLs), carbapenem resistant enterobacteriace (CRE) and other pan resistant organisms, one may have to resort to higher antibiotics like Colistin and Tigecycline occasionally, to treat severe infections. If a patient is recovering clinically and the swab /culture grows an organism, the possibility of contamination should be considered and clinical correlation must be done (eg. Burkholderiacepacia is a common contaminant present in disinfectants). Infectious Diseases consultation may be sought in case of a



dilemma.

The precise duration for which antibiotics should be administered for SSIs in orthopaedics is still debated. Antibiotics have variable penetration in bone and infection tends to persist within bone for a longer period. The organisms may be suppressed by the antibiotics, only for the infection to flare up later when the antibiotics are discontinued. Hence in general antibiotics are continued for a longer period in musculoskeletal infections, especially those involving implants. Intravenous antibiotics should be continued for 2-6 weeks, until the wound has healed and there is a significant improvement in the patient's constitutional symptoms, pain and mobility. This should be accompanied by a serial improvement in total leucocyte count, C-reactive proteins and ESR. Radiological evaluation, especially MRI scans are helpful in determining response to treatment. Serial MRI scans may reveal reduction in bone marrow oedema, soft tissue hyperintensities and fluid collection. However, MRI scans are not taken as a guide to discontinuation of antibiotic therapy because bone marrow oedema may persist for a long time, even in the absence of clinical evidence of infection. CT scans are helpful in assessing the bone healing/ fusion. After discontinuing intravenous antibiotics, oral chemotherapy is continued for 6-12 weeks or longer, if necessary. An area of persistent infection may show up as a hot spot on bone scans/FDG 18 labelled CT PET scans. Hence these may be helpful in determining the endpoint of antibiotic therapy.

### **Prosthetic Joint Infections (PJIs)**

Different surgical strategies may be used for a patient with a PJI, depending on a number of factors and these would dictate the deployment of antibiotics. An essential component of the therapeutic approach is a strong collaboration between the involved medical and surgical specialists viz. orthopaedic

surgeons, plastic surgeons, infectious disease specialists and general internists.

### **Debridement and retention of prosthesis:**

Two to 6 weeks of a pathogen-specific intravenous antimicrobial therapy (For staphylococcal PJI, in combination with rifampicin 300–450 mg orally twice daily followed by rifampicin plus a companion oral drug such as ciprofloxacin or levofloxacin, co-trimoxazole, minocycline or doxycycline or oral first-generation cephalosporins (eg, cephalexin) or antistaphylococcal penicillins (eg, dicloxacillin) for a total of 3 months for a THA infection and 6 months for a TKA infection) [27,28,29]. Rifampicin should always be used in combination with other antimicrobials because of its activity against biofilm organisms and because of a high rate of emergence of resistance if used as monotherapy. If the organism (staphylococcus) is resistant to both oxacillin and vancomycin, or if the patient is allergic or intolerant to these drugs, alternatives include daptomycin or linezolid [29,30]. Indefinite chronic oral antimicrobial suppression may follow the above regimen with cephalexin, dicloxacillin, cotrimoxazole, or minocycline based on in vitro susceptibility, allergies, or intolerances. Rifampicin alone and linezolid should not be used for indefinite chronic suppression. It is advisable that patients on chronic oral antimicrobial suppression be monitored both for clinical failure and for antimicrobial toxicity.

For patients with nonstaphylococcal PJI treated with debridement and retention, an induction course of intravenous antimicrobial therapy or highly bioavailable oral antimicrobial therapy is recommended. Chronic oral suppression therapy is controversial in nonstaphylococcal PJIs. Hence, monitoring for treatment failure early after treatment discontinuation is important.

### **Resection arthroplasty with or without planned staged reimplantation:**

**1-stage exchange:** Identify the pathogen preoperatively, followed by 4–6 weeks of pathogen-directed intravenous or highly bioavailable oral antimicrobial therapy following the exchange procedure, with or without the use of chronic oral antimicrobial suppression. The latter is controversial and is therefore generally reserved for patients who are unsuitable for, or refuse, further exchange revision, excision arthroplasty, or amputation [29,31].

**2-stage exchange:** No antimicrobial therapy should be used prior to planned resection arthroplasty until tissue cultures or ultrasonicate fluid cultures have been obtained, in order to improve the diagnostic yield. However, prophylaxis for surgical site infections may be used. Four to 6 weeks of pathogen-specific intravenous or highly bioavailable oral antimicrobial therapy is recommended between resection arthroplasty and reimplantation. Delayed reimplantation after 4–6 weeks of intravenous antimicrobial therapy and an antibiotic-free period of 2–8 weeks has been highly successful. Cefazolin or nafcillin is recommended for oxacillin-sensitive staphylococci (MSSA) and vancomycin for MRSA. Rifampin is not routinely recommended as a companion drug in this situation as all foreign material has been removed and there is no need for a biofilm active agent in this setting [29].

### **PJI following amputation:**

Pathogen-specific antimicrobial therapy should be given until 24–48 hours after amputation, assuming all infected bone and soft tissue has been surgically amputated and there is no concomitant sepsis syndrome or bacteremia. If sepsis syndrome or bacteremia are present, treatment duration is to be according to recommendations for these syndromes. Four to 6 weeks of pathogen-specific

intravenous or highly bioavailable oral antimicrobial therapy is recommended if, despite surgery, there is residual infected bone and soft tissue[29]. Indiscriminate and overly lengthy use of antibiotics should be avoided in order to prevent the development of resistant organisms.

### Conclusions

Surgical site infections (SSIs) continue to constitute a major challenge to healthcare institutions as a leading cause of healthcare associated infections (HAIs), despite remarkable developments in the use of surgical techniques, ergonomic advancements in the operating room, and implementation of bundles. *Staphylococcus aureus* and gram negative bacilli such as *E Coli* and *Pseudomonas* are most frequently recovered from SSIs with antibiotic resistant strains such as methicillin-resistant staphylococci, vancomycin resistant enterococci and extended

spectrum beta-lactamase Gram negative bacteria becoming of increasing concern. Preoperative prophylaxis must be employed in orthopaedic surgery using appropriate and targeted antibiotics, administered systemically within 30 minutes to 2 hours of the surgery. Extended / unindicated use of prophylactic antibiotics can result in adverse reactions and antibiotic resistance.

Treatment of established SSIs involves obtaining a specimen for culture, local measures of infection control, coupled with the use of antibiotics as dictated by the culture reports. Systemic antibiotics for 2-6 weeks followed by oral antibiotics for 6-12 weeks, sometimes longer, is recommended. The precise endpoint for antibiotic usage is still debated.

### Key Points

1. Antibiotics should be used to prevent infection, before and during surgery, but not after. The use of too broad spectrum an antibiotic or administering antibiotics

for too long, will drive resistance and lead to adverse reactions

2. Antibiotic prophylaxis does not include preoperative decontamination and treatment of established infections

3. It is vital to obtain a specimen for culture prior to starting antibiotics. Targeted narrow spectrum antibiotics are adequate in most of the situations.

4. The precise duration of antibiotic therapy for SSIs in orthopaedics is still debated. Generally, 2- 6 weeks of IV antibiotics followed by 6- 12 weeks of oral medication is recommended

5. A “bundle” approach, with meticulous attention to multiple risk factors is more rewarding, than solely relying on antibiotics.

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Conflict of Interest: NIL  
Source of Support: NIL

#### How to Cite this Article

Kaneria M V, Zaveri G. Surgical Site Infections in Orthopaedics: The Role of Antibiotics. Journal of Clinical Orthopaedics July-Dec 2019;4(2):26-32