Infection Prophylaxis Update

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ABSTRACT

The use of prophylactic antibiotics in surgery has been debated for numerous years. Although their indications have been elucidated in the general surgery literature, their role in plastic surgery has yet to be clearly defined. Although the incidence of surgical site infections in clean, elective plastic surgery procedures has been reported to be as low as 1.1%, the use of antibiotics has surged over the past 20 years. Much of the increased use has been attributed to common surgical practice and fear of legal ramifications rather than empirically based data. In contrast, there remain numerous physicians who argue against routine antibiotic use in plastic surgery. This article summarizes the recent literature on infection prophylaxis and advises physicians to consider relative risks and benefits when deciding which patients should receive prophylactic antibiotics.

KEYWORDS: Prophylaxis, surgical site infections, antibiotics, plastic surgery

One of the greatest contributions to medicine over the past century has been the discovery of antibiotics.[1–4] Although most of the effectiveness has been attributed to therapeutic treatments, an often-overlooked use has been for prophylactic reasons. Although antibiotic use is more commonly thought to be for treatment of established infection, in fact a significant portion of antibiotics are prescribed for prevention of infection. With the widespread use of antibiotics over the past 20 years, prophylaxis has been reported to account for as high as half of all antibiotics prescribed.[2] This is even evident in the field of plastic surgery, where most cases are clean cases that do not involve potential intra-abdominal contamination. It is unclear whether the risks of antibiotic prophylaxis are higher than the low infection rates for clean surgery.

Surgical cases are generally classified as clean, clean-contaminated, contaminated, or dirty. Clean cases include surgical procedures that are free of infection and do not involve the respiratory, alimentary, or genitourinary tract. The potential for a surgical site infection (SSI) is low and infection rates are usually around 2%. Clean-contaminated cases involve contaminated areas such as the oral and nasal cavity, alimentary tract, axilla, or perineum. These areas are entered under controlled conditions without unusual contamination. Contaminated cases include those that are complicated by a break in sterile technique or exposure to gastrointestinal spillage or are characterized by inflammation without purulence. Traumatic wounds less than 4 hours old are classified as contaminated regardless of their degree of contamination. Chronic open wounds to be grafted or covered are included in this category as well. Dirty cases are those that are grossly contaminated with purulent inflammation and devitalized tissue. Traumatic wounds more than 4 hours old are also defined as dirty. The often-cited infection rates for the traditional classification of operative procedures are as follows: clean ($< 2\%$), clean-contaminated ($\sim 10\%$), contaminated ($\sim 20\%$), and dirty ($\sim 40\%$).[5] Classifications of cases are used by surgeons to predict complications, to determine antibiotic therapy, and to guide surgical treatment.

The timing of administration, tissue concentration, and rate of SSI have been well studied and published in the literature. Over 150 clinical trials have repeatedly documented the effectiveness of prophylactic

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antibiotics in preventing SSIs.[6] Classic animal studies by Miles, Miles, and Burke in the 1950s demonstrated that infection could be prevented if prophylactic antibiotics were given before or at the time of surgery.[7] Animal models experienced lower rates of SSIs if systemic antibiotics were administered before inoculation with bacterium. Since then, numerous studies have focused on the timing of administration,[7–9] including the study by Classen et al involving nearly 3000 patients that was published in the *New England Journal of Medicine* in 1992.[10] Patients in clean or clean-contaminated cases were randomly allocated to receive prophylactic antibiotics either early (2–24 hours before incision), preoperatively (2 hours prior to incision), perioperatively (3 hours after incision), or late (3–24 hours after incision). The rates of SSI were 3.8%, 0.6%, 1.4%, and 3.3%, respectively, showing that prophylactic antibiotics should be administered within 2 hours of incision to maximize tissue concentration levels associated with the lowest risk of infections. Further research has demonstrated that the antibiotic serum concentration, when assayed using high-performance liquid chromatography, was highest when the antibiotic was given within 1 hour prior to incision. The authors concluded that prophylactic antibiotics may best be administered at induction of anesthesia and that giving them "on call" to the operating room may result in too early administration.[11]

Prophylactic antibiotic therapy has been shown over and over to be clearly more effective when begun in the preoperative period with the aim of achieving therapeutic blood levels throughout the operation. Antibiotics started as late as 1 to 2 hours after surgical incision are far less effective, and those given after the wound is closed have virtually no benefit at all.[9]

OTHER CONSIDERATIONS

There are numerous factors that might contribute to an increased risk of postoperative infection. Wound infection rates are influenced by other patient-related risk factors that may include but are not limited to extremes of age, malnutrition, obesity, diabetes, remote infection, steroid therapy, chronic inflammation, and prior radiation.[12–15] Patients who present with these risk factors require special consideration for postoperative complications. In such circumstances, correction or control of the underlying disease should take priority.

Most patients undergoing elective day surgery do not run the risk of colonization with hospital bacteria. In contrast, a direct correlation has been shown to exist between the length of hospital stay prior to surgery and postoperative wound infection rates. Patients who are admitted to a hospital can experience double the infection rate with each additional preoperative week of stay.[5] Colonization with resistant hospital-acquired organisms has been observed to begin within 2 weeks of hospitalization.[16]

Early reports regarding preoperative showering with chlorhexidine to decrease the incidence of postoperative infection have been disproved.[5] Large meta-analyses by Cochrane Database of Systematic Reviews involving more than 10,000 participants have shown no benefit for preoperative showering or bathing with chlorhexidine over other wash products.[17]

Most surgeons prefer to operate in a hairless field. Razor hair removal has been shown to be associated with a higher rate of SSIs when performed the night prior to surgery.[2] Tiny cuts in the dermis with skin flora inoculation have been hypothesized as the reason why razors are associated with a higher rate of infection (5.6%) compared with a depilatory agent (0.6%).[15] Clippers have also been shown to be associated with low infection rates of 1.7%.[16] However, a Cochrane review of 11 randomized controlled trials showed no difference in SSIs when patients are shaved or clipped 1 day prior to surgery or on the day of surgery.[17]

The duration of an operation is another risk factor for SSI. Procedures that last more than 1 hour have a higher postoperative infection rate.[18] This has been well documented in the surgical literature.[19] Research by Andenaes et al has shown that the risk for wound infection is nearly three times higher when the duration of surgery is more than 120 minutes.[20] This increased risk has been attributed to the increased exposure of an open wound to bacterial contamination and the pharmacokinetics of dwindling serum concentrations of prophylactic antibiotics.[21] A surgeon should therefore be continuously cognizant of when to redose prophylactic antibiotics appropriately during prolonged operations.

CURRENT PRACTICE IN PLASTIC SURGERY

Numerous surveys throughout the years reveal the widespread utilization of prophylactic antibiotics in plastic surgery. Questionnaires surveying 1718 plastic surgeons in the 1970s and 1980s showed an increase in the administration of prophylactic antibiotics from prior years.[4,22,23] The questions touched upon the frequency, timing of administration, and factors modifying a surgeon's decision in using prophylactic antibiotics. It was concluded that the overall use of antibiotics was increasing and that the use of alloplastic implants and the medicolegal environment were motivating factors. Other reports have concluded that most plastic surgeons justify their use by personal experience, prior teaching, custom, and medicolegal concerns.[2]

Perrotti et al surveyed 1767 plastic surgeons on the type, route, and duration of antibiotic administration for 10 popular cosmetic surgical procedures.[24] It was found that cephalosporins were the most popular prophylaxis given and that many different antibiotic irrigations were used as well. Antibiotics were frequently used and many physicians continued them to up to 7 days. Administration beyond the perioperative period was seen in 54% of liposuction patients, 52% of face lift patients, 55% of rhinoplasty patients, 65% of abdominoplasty patients, and 70% of breast augmentation patients. In addition, 61% used antibiotics when drains were in place despite literature stating that antibiotic prophylaxis extended to cover lines, tubes, or catheters is unwarranted.[25] In this study, many plastic surgeons similarly justified their use of antibiotics on the basis of common practice, regimen, medicolegal ramifications, and the inability to afford a complication in a cosmetic setting.

PROPHYLACTIC ANTIBIOTICS IN PLASTIC SURGERY

Although much has been written in the literature regarding the benefit of antibiotics in general surgery, there remain no clear guidelines in plastic surgery. Some authors have even published their own guidelines to include no prophylactic antibiotics in clean, elective aesthetic procedures such as rhytidectomy, blepharoplasty, lipoplasty, abdominoplasty, skin lesions, or scar revisions.[26]

One of the largest studies, by Baran et al,[27] involved 1400 consecutive patients who were grouped into one of four categories: (1) reconstructive procedure for trauma, neoplasm, or congenital abnormality in the head or neck; (2) cosmetic surgical procedure; (3) flap or graft procedure for reconstruction of trunk or extremity; or (4) any alloplastic implant placement. Patients were assigned randomly to receive either no prophylaxis or 2 g of Unasyn administered during induction. At the end of the 6-year study, the authors concluded that in all four groups, no statistically significant differences existed between prophylactic antibiotic and placebo subgroups. Although this particular study does not support the use of prophylactic antibiotics, there remain other studies that clearly show a benefit.

Augmentation mammaplasty procedures are clean, elective cosmetic procedures that have low infection rates even in the presence of an implant. Certain studies have shown the benefit of prophylactic antibiotics in light of the presence of an implant and bacteria in the ducts of the breast.[24,28,29] However, there are others who question whether prophylaxis is even necessary.[30–33] A retrospective study of 192 breast augmentations by LeRoy and Given showed no difference in infection rate.[30] Rate of infection for prophylaxis versus no prophylaxis was 0.0 and 0.7%, respectively. Other studies evaluating rates of capsular contracture failed to demonstrate any decrease in the frequency or grade of capsular contracture after 1 year.[34] No specific antibiotic recommendations from national organizations have been made for breast augmentation or other plastic surgery cases involving implants. However, recommendations exist for similar clean orthopedic cases involving implants such as total joint arthroplasty. The preferred antimicrobial in these patients as recommended by the advisory statement from the National Surgical Infection Prevention Project is either cefazolin or cefuroxime.[35] The workgroup recommended that prophylaxis be discontinued within 24 hours after the end of the operation even in the presence of drains and catheters.

Reduction mammoplasty is associated with a higher incidence of infections and wound complications.[36] Even though it is considered a clean case, some plastic surgeons prescribe several days of prophylactic antibiotic treatment because of the extensive dissection, prevalence of dead space, and prolonged operative time. Although it is perhaps a common practice, the scientific support for it is weak. Serletti et al studied infection rates only in reduction mammaplasty patients.[37] They found no difference between patients who received preoperative prophylaxis and those who did not. Their respective infection rates were 8.5 and 6.8%. Their results were further supported by Ahmadi et al, whose research similarly showed no benefit of prophylactic antibiotic use.[38] The prospective study used three arms evaluating those who were given no prophylaxis, preoperative prophylaxis, and preoperative and postoperative prophylaxis. Overall infection rate was 24% with no statistically significant difference between the arms. Kompatscher et al reported findings of a retrospective study examining two groups of breast reductions patients: those who were given preoperative prophylaxis and those who were not.[39] They evaluated about 140 patients in each group and found no detectable intergroup differences: 3.9% (prophylaxis) versus 3.6% (no prophylaxis).

A similar operation involving extensive dissection, prolonged operative time, and a great deal of dead space is abdominoplasty. One study surveying 958 plastic surgeons reported a postoperative infection rate of 7.3%.[40] Although 43% of plastic surgeons surveyed by Krizek would administer prophylactic antibiotics, some have reported no complications without their use.[41] Commonly, abdominoplasty is combined with other gynecologic procedures, making it a clean-contaminated case. Even though the literature lacks evidence-based medicine in regard to prophylaxis, the involvement of potential genitourinary contamination should warrant antibiotic prophylaxis.[42]

Clean-contaminated cases in plastic surgery often involve the nasal or oral cavity, or both. Because of native bacterial flora in these areas, prophylactic antibiotic use is common to prevent SSIs such as wound dehiscence, bone malunion, stitch abscesses, vestibulitis, and septal abscesses.[24] Numerous studies have demonstrated the utility of prophylactic antibiotics in clean-contaminated cases. A prospective, randomized trial by Chloe and Yee enrolled 101 patients with facial fractures to receive either no antibiotics or 1 g of cefazolin preoperatively and an additional dose 8 hours later.[43] Patients enrolled had a wide spectrum of fractures that included mandible fractures, zygoma fractures, and Le Fort fractures. The study clearly demonstrated a reduction in the incidence of postoperative infections; 42% in the no-antibiotic group became infected, and 8.9% in the antibiotic group became infected. Similar prospective randomized trials studying rhinoplasty cases reported low postoperative infection rates of 0 to 7% with prophylactic antibiotics.[44–46] One study further concluded that there was no benefit in giving an additional postoperative 7-day course of oral antibiotics.[44] The patients who were given postoperative antibiotics were found to have significantly higher antibiotic-associated side effects (e.g., nausea, diarrhea, skin rashes, pruritus). The cost for antibiotics and medication to treat the side effects was also significantly higher. The same results were also seen in other clean-contaminated surgeries such as those involving oncologic head and neck resection. A single dose of preoperative antibiotics was shown clearly to reduce SSIs.[47,48] The patients who were further reconstructed with free flaps did not experience a reduction in infection when antibiotics were extended beyond the perioperative period.[49–51]

RISKS VERSUS BENEFITS

Administration of antibiotics is not without risks. Potential allergic or anaphylactic responses can be elicited with a single dose. Cephalosporins remain the most common prophylactic antibiotics, and cross-reactivity with a penicillin allergy is seen in an estimated 10% of individuals.[52] Although most allergies to penicillin and cephalosporins manifest as a simple rash, potential adverse reactions include anaphylaxis, angioedema, urticaria, bronchospasm, hemolytic anemia, interstitial nephritis, thrombocytopenia, and Stevens-Johnson syndrome.[52]

Clostridium difficile is the leading identified cause of nosocomial diarrhea associated with antibiotic therapy. Antibiotics alter the normal fecal flora, and this disturbance of gastrointestinal microecology leads to a colonization by potentially pathogenic microbes. Cephalosporins, clindamycin, and broad-spectrum penicillins are the most common antibiotics associated with a *C. difficile* infection.[53] This infection results in increased length of stay, increased cost of care, and increased mortality (6–30%).[54,55] Candidal vaginitis results from suppression of natural bacterial flora and overgrowth of yeast. It is reported that as many as 2% of patients receiving prophylactic antibiotics develop a yeast infection requiring additional antifungal treatment.[56]

Side effects are also common with antibiotics. Patients experience a wide range of symptoms that commonly include nausea, vomiting, diarrhea, rashes, and pruritus. These potential complications accrue additional costs for the patient and result in potential hospitalization, loss of work, and further antibiotic administration.

In addition, it is important to be cognizant of the increasing problem of selecting for multidrug-resistant organisms.[57] Antibiotic-resistant organisms are an escalating concern in medicine. Although new antibiotics are being researched, it is a close race to stay one step ahead of the microbes. Multidrug-resistant organisms such as methicillin-resistant *Staphylococcus aureus* (MRSA) have become commonplace in the hospital setting. With widespread antibiotic use and misuse, this would only further perpetuate existing problems with microbial resistance.

RECOMMENDATIONS

Recommendations in regard to antibiotic prophylaxis in plastic surgery have been scarce. The following recommendations are based upon guidelines set by the National Surgical Infection Prevention Project and guidelines published by Martin on antimicrobial prophylaxis in surgery.[35,58]

Patients undergoing surgery should be evaluated individually in the preoperative, perioperative, and postoperative setting for risk factors, including, but not limited to, diabetes, obesity, malnutrition, advanced age, recent surgery, steroid treatments, prior radiation, immunosuppression, prolonged surgery, insertion of foreign body, hypotension, transfusion, and so on.[26] All medical abnormalities such as blood glucose should be tightly controlled to allow optimal wound healing.[59–61] Sterile technique should also be followed meticulously to prevent unnecessary contamination. Antibiotic prophylaxis cannot compensate for poorly controlled medical problems or poor sterile technique.

Consideration of prophylactic antibiotic use is based upon the patient, surgical procedure, and risk factors. The selection of an appropriate antimicrobial drug depends on the identification of the most likely pathogens associated with a given procedure as well as the expected antibiotic susceptibility of those pathogens. For most clean procedure involving the skin, 1 to 2 g of cefazolin, dosed appropriately by weight, provides adequate coverage for skin flora. Clindamycin 600 mg or vancomycin 1 g (in patients with normal renal function) can be substituted for individuals with a penicillin or cephalosporin allergy. Broader spectrum antibiotics are used to cover microbes of the nose, mouth, or gastrointestinal tract. Unasyn 1.5 mg or clindamycin and an aminoglycoside can be used to cover anaerobes and gram-negative organisms of the mouth.

Table 1 Antibiotic Prophylactic Agents, Dose, and Half-Life—Redosing Recommended after Two Half-Lives

Antibiotic	Dose	Half-Life (hours)
Cefazolin (Ancef)	1–2 g IV	1.8
Vancomycin (Vancocin)	1 g IV	4–6
Clindamycin (Cleocin)	600 mg IV	2.4–3
Ampicillin/sulbactam (Unasyn)	1.5 g IV	1
Ceftriaxone (Rocephin)	1 g IV	5.8–8.7
Cefoxitin (Mefoxin)	1 g IV	0.6–1
Aminoglycoside	3 mg/kg IV	2
Metronidazole (Flagyl)	500 mg IV	8
Ciprofloxacin (Cipro)	400 mg IV	3–5

Ideally, a prophylactic antibiotic should achieve a high peak tissue concentration at the site of the wound before the first incision and should be maintained until the time of closure. Infusion of the first dose of antibiotic should begin within 30 minutes before incision. Administration should be repeated intraoperatively if the operation is still continuing two half-lives (4 hours for cefazolin) after the first dose to ensure adequate antimicrobial tissue concentrations (Table 1). This regimen has been shown to be benign, cost effective, and does not lead to the selection of antibiotic-resistant organisms.[61] Aside from dirty cases and selective contaminated cases, there are no indications for a postoperative antibiotic regimen after 24 hours, including individuals to be discharged home with drains.[25,58,62–64] These recommendations pertain to most but not all cases. Physicians are encouraged to use sound clinical judgment to recognize the unique cases in which an alternative approach may need to be used.

For clean, uncomplicated surgical procedures, antibiotics have not been shown to be beneficial in reducing infection.[65–68] These include uncomplicated cases such as lesion excision, scar revision, dermabrasion, and laser resurfacing (Table 2). However, consideration should be given to antiviral prophylaxis in laser resurfacing.

For clean cases that are complicated with an implant or have large tissue flaps and dead space, a single dose of prophylaxis is recommended. Although they are considered clean cases, the potential for an SSI is

Table 2 Antibiotic Prophylaxis Recommendations

Class	Subclass	Examples	Recommendations
Clean	**Uncomplicated**	Lesion excision, scar revision, dermabrasion, laser resurfacing	No antibiotic prophylaxis Antiviral prophylaxis for laser resurfacing
	Complicated Large dead space, implant, large tissue flaps	Breast augmentation, breast reduction, tissue expanders, flap reconstruction (clean), malar implants, implant breast reconstruction, abdominoplasty, closed facial and hand fractures, face lift	Single dose of prophylaxis Ancef (Cleocin for PCN allergy)
Clean-contaminated	**Uncomplicated**	Uncomplicated facial or mandible fractures with intraoral incisions, left palate, palate fistula, rhinoplasty	Single dose of prophylaxis Ancef (Cleocin for PCN allergy) Unasyn for mouth organisms
	Complicated Continued contamination, radiation, marginal vascularity, large dead space	Vaginal reconstruction, complicated fractures of the face and mandible, flap reconstruction of radiated tissues, intraoral flap reconstruction, rhinoplasty with implants or grafts, clean lacerations without gross contamination <4 hours old	Multiple dose prophylaxis Ancef (Cleocin for PCN allergy) Unasyn for mouth organisms Rocephin + Flagyl for vaginal cases
Contaminated	Skin grafts, Moh's surgery reconstruction, open comminuted mandible fractures, decubitus ulcer, chronic open wounds and ulcers, clean lacerations without gross contamination open >4 hours		Multiple dose prophylaxis, some may require treatment as therapy Ancef (Cleocin for PCN allergy) Unasyn for mouth organisms Rocephin + Flagyl for vaginal cases
Dirty	Established infections, open hand fractures, replants, animal or human bites, delayed treatment of mandible fractures, grossly contaminated lacerations with devitalized tissue or crush injury		Treatment as therapy, not prophylaxis. Antibiotic and duration based on each individual case Unasyn for bites

PCN, penicillin.

increased in this subclass. These include surgical cases such as breast augmentation, breast reduction, and abdominoplasty, to name a few. Although some studies have shown no benefit in administering prophylactic antibiotics in this subclass, it is believed that a single does of antibiotic will result in minimal risk with regard to this controversial subclass.

Uncomplicated clean-contaminated cases include mandible fractures and simple facial fractures treated with an intraoral approach, hand lacerations less than 4 hours old, cleft palate, and fistula surgeries. A single dose of Ancef for skin cases or Unasyn for intraoral or nasal cases is appropriate coverage. More complicated clean-contaminated cases that involve prior radiation, large dead spaces, compromised vascularity, or poor oral hygiene may deserve multiple doses of prophylaxis to ensure adequate tissue levels of antibiotics. Some examples of complicated clean-contaminated cases are mandibles with poor oral hygiene, head and neck reconstruction, and genitourinary reconstruction of irradiated tissue. Wounds subject to low levels of continuing contamination such as intraoral incisions with marginal tissue closure or perineal wounds with ongoing stool contamination would also be in this category. In these difficult patients, duration of treatment should be individualized.

Antibiotic prophylaxis for contaminated wounds has clearly been shown to reduce infection rates.[5,6,65,69] These most commonly involve open wounds that are colonized with bacteria such as skin graft wounds, decubitus ulcers, and Moh's defects. Some cases may benefit from a full course of antibiotics. Dirty wounds are by definition infected. In this class of surgical wounds, treatment should be further extended beyond prophylaxis to a full course of antibiotic therapy.

CONCLUSION

In summary, administration of prophylactic antibiotics in plastic surgery continues to be a source of rigorous debate. Although benefits of prophylaxis have been demonstrated, the specific indications in plastic surgery continue to be controversial. It is important for a plastic surgeon to be familiar with evolving literature to administer the proper antibiotic for each individual case while balancing risks and benefits.

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