Evidence-Based Use of Perioperative Antibiotics in Otolaryngology

Priyesh N. Patel, MD¹, Asitha D. L. Jayawardena, MD, MPH¹, Rachel L. Walden, MLIS², Edward B. Penn, MD¹, and David O. Francis, MD, MS³

Abstract

Objective. To identify and clarify current evidence supporting and disputing the effectiveness of perioperative antibiotic use for common otolaryngology procedures.

Data Sources. PubMed, Embase (OVID), and CINAHL (EBSCO).

Review Methods. English-language, original research (systematic reviews/meta-analyses, randomized control trials, prospective or retrospective cohort studies, case-control studies, or case series) studies that evaluated the role of perioperative antibiotic use in common otolaryngology surgeries were systematically extracted using standardized search criteria by 2 investigators independently.

Conclusions. Current evidence does not support routine antibiotic prophylaxis for tonsillectomy, simple septorhinoplasty, endoscopic sinus surgery, clean otologic surgery (tympanostomy with tube placement, tympanoplasty, stapedectomy, and mastoidectomy), and clean head and neck surgeries (eg, thyroidectomy, parathyroidectomy, salivary gland excisions). Antibiotic prophylaxis is recommended for complex septorhinoplasty, skull base surgery (anterior and lateral), clean-contaminated otologic surgery (cholesteatoma, purulent otorrhea), and clean-contaminated head and neck surgery (violation of aerodigestive tract, free flaps). In these cases, antibiotic use for 24 to 48 hours postoperatively has shown equal benefit to longer duration of prophylaxis. Despite lack of high-quality evidence, the US Food and Drug Administration suggests antibiotic prophylaxis for cochlear implantation due to the devastating consequence of infection. Data are inconclusive regarding postoperative prophylaxis for nasal packing/splints after sinonasal surgery.

Implications for Practice. Evidence does not support the use of perioperative antibiotics for most otolaryngologic procedures. Antibiotic overuse and variability among providers may be due to lack of formal practice guidelines. This review can help otolaryngologists understand current evidence so they can make informed decisions about perioperative antibiotic usage.

Keywords

perioperative antibiotics, antibiotic prophylaxis, otolaryngology

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Indiscriminate use of antibiotics is associated with increased cost and risks to patients.¹ Antimicrobial misuse has contributed to the development of antibiotic-resistant bacteria.² This is of concern particularly if widening resistance renders available antibiotics ineffective. In addition to commonly cited side effects (eg, gastrointestinal [GI] complaints), recent studies have shown that antibiotic overuse may increase the risk of obesity, type I diabetes, inflammatory bowel disease, and asthma.³⁴ It is therefore incumbent on prescribing clinicians to better understand appropriate, evidence-based indications for antibiotic use.

Otolaryngologists routinely use perioperative antibiotics to prevent infection. This practice seems justified when violating the bacteria-ridden aerodigestive tract due to a perceived risk of surgical site contamination. Surprisingly, data on perioperative antibiotic use in otolaryngology are limited. A relative paucity of well-controlled studies, in addition to the lack of evidence-based guidelines, has resulted in inconsistent practices within and between institutions.⁶⁻⁹ A recent survey by the American Academy of Otolaryngology–Head and Neck Surgery Infectious Diseases Committee reported that members routinely prescribe antibiotics for 12 of 17 common procedures despite acknowledging that there is little evidence to support

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this practice. The present study was conceived to identify and clarify current evidence supporting and disputing the effectiveness of perioperative antibiotic use for common otolaryngology procedures.

**Methods**

In May 2017, a search of PubMed, Embase (OVID), and CINAHL (EBSCOhost) was completed by a medical librarian. PubMed search terms were determined (see Supplemental Table S1 in the online version of the article) and then adapted for other search engines. Additional articles were found by handsearching references of articles populated by our initial search. English-language, original research (ie, systematic reviews/meta-analyses, randomized control trials [RCTs], prospective or retrospective cohort studies, case-control studies, or case series) studies that evaluated the role of “perioperative” oral or intravenous (IV) antibiotic use in common otolaryngology surgeries were extracted. Studies assessing other antibiotic modalities (eg, ear drops, irrigations, powders) or the use of antibiotics for treatment (ie, existing infection, positive cultures) rather than prophylaxis were excluded. Infection of surgical sites was the primary outcome of included studies.

The surgeries addressed in this review included tonsillectomy, septoplasty, rhinoplasty, endoscopic sinus surgery, clean and clean-contaminated otologic procedures, anterior and lateral skull base surgery, and clean and clean-contaminated head and neck surgery. Perioperative was defined a priori as antibiotic dosing occurring preoperatively (60 minutes prior to surgical incision and before induction of anesthesia), intraoperatively (at induction of anesthesia or within 60 minutes of surgical incision), or postoperatively (for some duration of time immediately after surgery).

Two investigators (P.N.P. and A.D.J.) independently reviewed titles and abstracts of all studies identified, and those meeting criteria underwent full-text review. Articles generated from the search and included in this review are summarized in Table 1. The data supporting/refuting perioperative antibiotic use are summarized using Oxford Center for Evidence-Based Medicine—Levels of Evidence (Table 2). Heterogeneity in definition and diagnosis of infection limited study result aggregation for comparison purposes.

**Tonsillectomy**

Tonsillectomy is considered a clean-contaminated procedure. Colonization of the tonsillar fossa by oropharyngeal flora may lead to an inflammatory response and subsequent postoperative sequelae, including fever, pain, and bleeding. A single RCT has shown decreased rates of bleeding, fever, duration of pain, and time for return to normal activities and diet with a 5-day course of preoperative lincomycin.10 An RCT published in 1986 (n = 100) reports reduced tonsillar bacterial counts and decreased postoperative symptoms with the use of antibiotic intraoperatively and up to 24 hours after surgery.11 Similarly, 5 subsequent RCTs12-16 (combined n = 440) and 2 prospective cohort studies17,18 (combined n = 158) found intraoperative IV and postoperative oral antibiotics to reduce fever, odor from the oral cavity, pain, bleeding, and/or days until return of baseline oral intake. When used, a 5-day or 7-day course of antibiotics has no advantage over either a single intraoperative dose or a 3-day course of antibiotics.13,19-21 In addition, preoperative oral antibiotics do not add benefit when compared to intraoperative and postoperative dosing.22 Five RCTs23-28 (combined n = 577), two prospective cohort studies29 (combined n = 95), and 3 retrospective cohort studies30-32 (combined n = 215) were unable to show advantages of intraoperative or postoperative antibiotics in adenoidectomies or tonsillectomies. Two meta-analyses of 4 RCTs33 and 7n RCTs34 found perioperative antibiotic use (intraoperative and/or 7-day postoperative use) to be associated with a 1-day reduction in time to return to a normal diet but no additional benefits related to pain, bleeding, or reduced infection. A systematic review of 5 RCTs found that while...
similar antibiotic regimens reduce rates of fever, there was no effect on pain, bleeding, or time to resume normal diet.\textsuperscript{35} A recent Cochrane systematic review and meta-analysis including 10 RCTs report similar findings.\textsuperscript{36}

**Tonsillectomy Recommendation:** No perioperative antibiotic use (Evidence: Level 1a, Grade A)

**Septoplasty and Rhinoplasty**

Both septoplasty and rhinoplasty are considered clean-contaminated procedures. Septoplasty classically involves removal of septal cartilage, while rhinoplasty may involve both removal of tissue and the use of graft material within the contaminated nasal cavity. In septoplasty, 2 case series from 1992\textsuperscript{37} and 2000\textsuperscript{38} (total n = 1140) reported nasal infection rates in 0.48\% and 11\% of patients undergoing internal nasal septal surgery, respectively; while the former study suggests a low rate of infection and no need for perioperative antibiotics, the latter implies a relatively high risk of infection without antibiotic use. Three subsequent RCTs\textsuperscript{39-41} (total n = 978) and a prospective cohort study\textsuperscript{42} (n = 35) compared the use of single-dose intraoperative and postoperative antibiotic administration to either placebo or no antibiotics and found no difference in rates of fever, purulent secretions, or septal abscess between groups. A recent meta-analysis of 2 RCTs confirmed that antibiotics do not reduce infection following septoplasty.\textsuperscript{43} A study comparing a single intraoperative dose of penicillin to an extended 5-day course found no difference in infection rates.\textsuperscript{21} While overwhelming data suggest that antibiotics provide no benefit in the setting of septoplasty, inclusion criteria for each mentioned study required that nasal packing be present for <48 hours; thus, current data cannot provide guidance on how prolonged packing may modify infection risk and antibiotic benefit.

Regarding rhinoplasty, a large case series (n = 2000) found that the baseline infection rate was 0.6\% without antibiotic administration.\textsuperscript{44} Two RCTs (total n = 504) involving patients undergoing septrhinoplasty with nasal packing confirmed the absence of benefit for intraoperative and postoperative antibiotics.\textsuperscript{45,46} Unfortunately, these studies failed to differentiate between what is classified as a “simple” septrhinoplasty and a “complex” septrhinoplasty (ie, revision or use of grafting material), which may pose increased infection risk. One RCT (n = 100) supports this assertion as it found that a 7-day course of postoperative antibiotics after complex septrhinoplasty did significantly reduce infection compared to placebo (27\% vs 8\%).\textsuperscript{47} It remains uncertain whether observed benefits are related to the use of graft material or prolonged nasal packing (up to 6 days). Two subsequent RCTs (total n = 364) found that 7 days of postoperative antibiotics did not decrease infection compared to a single intraoperative dose or <24 hours of postoperative antibiotics.\textsuperscript{48,49} Thus, limited data suggest a possible benefit from intraoperative and brief postoperative antibiotic use in complex but not simple septrhinoplasty.

**Septoplasty Recommendation:** No perioperative antibiotic use (Evidence: Level 1a, Grade A)

**Simple Rhinoplasty Recommendation:** No perioperative antibiotic use (Evidence: Level 1b, Grade B)

**Complex Rhinoplasty Recommendation:** Intraoperative and postoperative antibiotic use (<24 hours) (Evidence: Level 1b, Grade B)

**Endoscopic sinus surgery.** Endoscopic sinus surgery is a clean-contaminated procedure. While an expert panel had previously recommended antibiotic use for all clean-contaminated cases, this recommendation now excludes sinus surgery.\textsuperscript{50} Data are lacking to guide recommendations regarding preoperative and intraoperative antibiotic use for endoscopic sinus surgery. A RCT of 93 patients undergoing sinus surgery showed no
difference in infection rate between those treated 2 hours preoperatively with levofloxacin and those given intraoperative cephalosporin (both groups continued antibiotics for 2 postoperative days). This study cannot help determine whether an independent benefit exists for preoperative or intraoperative antibiotics in sinus surgery. Several studies have examined the role of postoperative antibiotics in sinus surgery. RCTs comparing placebo to

<table>
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<th>Table 3. Evidence-Based Recommendations for Perioperative Antibiotic Use in Otolaryngologic Procedures.</th>
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<td>Procedure</td>
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<tr>
<td>---------------------------------------------------------------</td>
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<tr>
<td>Tonsillectomy</td>
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<td>Septoplasty alone</td>
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<td>Simple septorhinoplasty or rhinoplasty (primary, without grafting)</td>
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<td>Complex septorhinoplasty or rhinoplasty (revision with or without grafting)</td>
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<tr>
<td>Sinus surgery</td>
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<td>Clean otologic surgery</td>
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<td>Clean head and neck surgery (ie, thyroidectomy, parotidectomy, neck dissection)</td>
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<tr>
<td>Clean-contaminated head and neck surgery</td>
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Abbreviation: FDA, US Food and Drug Administration.
after nasal surgery. In all, 10 RCTs\(^5\) (total n = 1085) and use of antibiotics when nasal packing or splints are used are no studies that compare outcomes with and without the use of antibiotics when nasal packing or splints (eg, Doyle splint) in nasal surgery may allow for increased colonization of pathogenic bacteria and act as a nidus for local or systemic infection. Unfortunately, there are no studies that compare outcomes with and without the use of antibiotics when nasal packing or splints are used after nasal surgery. In all, 10 RCTs\(^5\) (total n = 1085) and 1 retrospective cohort study\(^6\) (n = 150) evaluating variable duration of perioperative antibiotics have failed to show increased local infection rates with the use of nasal packing (≤48 hours) or nasal splinting (≤7 days). Toxic shock syndrome (TSS), which has been cited as a reason to continue prophylactic antibiotics, has a very low incidence after nasal surgery (16.5 per 100,000), and individual studies are inadequately powered to detect this complication.\(^6\)\(^–\)\(^7\) In 2013, a meta-analysis of 6 RCTs found that nasal packing and splinting do increase infection risk, but estimates had wide confidence bounds (odds ratio [OR], 6.76; 95% CI, 1.20-37.98).\(^7\) In addition, a single intraoperative dose of cefazolin has not shown to reduce the nasal carriage of the toxigenic strain of \textit{Staphylococcus aureus} in most patients.\(^7\) Based on available data, the use of antibiotics for duration of pack or splint use should be considered an option due to potential increased infection rate with nasal packing/splinting.

**Nasal Packing/Splint Recommendation:** Option for postoperative antibiotic use for duration of packing/splint (Evidence: Level 4, Grade C)

**Nasal Surgery Recommendation:** No perioperative antibiotic use: postoperative (Evidence: Level 1a, Grade A), preoperative/intraoperative (Evidence: Level 5, Grade D)

**Nasal packing/splints.** The use of nasal packing (eg, Merocel) and/or splints (eg, Doyle splint) in nasal surgery may allow for increased colonization of pathogenic bacteria and act as a nidus for local or systemic infection. Unfortunately, there are no studies that compare outcomes with and without the use of antibiotics when nasal packing or splints are used after nasal surgery. In all, 10 RCTs\(^5\)\(^–\)\(^6\) (total n = 1085) and 1 retrospective cohort study\(^6\) (n = 150) evaluating variable duration of perioperative antibiotics have failed to show increased local infection rates with the use of nasal packing (≤48 hours) or nasal splinting (≤7 days). Toxic shock syndrome (TSS), which has been cited as a reason to continue prophylactic antibiotics, has a very low incidence after nasal surgery (16.5 per 100,000), and individual studies are inadequately powered to detect this complication.\(^6\)\(^–\)\(^7\) In 2013, a meta-analysis of 6 RCTs found that nasal packing and splinting do increase infection risk, but estimates had wide confidence bounds (odds ratio [OR], 6.76; 95% CI, 1.20-37.98).\(^7\) In addition, a single intraoperative dose of cefazolin has not shown to reduce the nasal carriage of the toxigenic strain of \textit{Staphylococcus aureus} in most patients.\(^7\) Based on available data, the use of antibiotics for duration of pack or splint use should be considered an option due to potential increased infection rate with nasal packing/splinting.

**Nasal Packing/Splint Recommendation:** Option for postoperative antibiotic use for duration of packing/splint (Evidence: Level 4, Grade C)

**Otologic surgery.** No contamination classification schemes have been widely adopted for otologic surgery. A Cochrane review has classified common procedures, including tympanostomy tubes, tympanoplasty (including stapedectomy), and mastoidectomy, as clean otologic procedures.\(^7\) Clean-contaminated or contaminated procedures have variably been used to describe procedures in which cholesteatoma or drainage is encountered.

Several studies have evaluated the role of perioperative antibiotics for otologic surgery. An RCT (n = 71) has found that intraoperative dosing followed by a 5-day course of antibiotics (ampicillin/flucloxacillin) did not reduce amount or change the type pathogens cultured from the ear, drainage, or graft failure rates after tympanoplasty.\(^7\) A large RCT (n = 3481) found that intraoperative and 24 hours of postoperative IV antibiotic (cephalosporin and oxacillin) did not reduce infection or graft failure rates in patients with clean or clean-contaminated otologic procedures compared to placebo.\(^7\) These findings comport with similar RCTs using intraoperative cefuroxime (n = 750)\(^7\) or a 14-day total course of gentamycin/clindamycin (n = 72).\(^7\) Additional RCTs (total n = 354) found no difference in infection or graft failure rate among those given 5 days (or greater) of postoperative antibiotics compared to a single intraoperative dose.\(^7\)\(^–\)\(^8\) In fact, 1 study found that a 9-day postoperative antibiotic course was associated with longer hospital stay and increased GI symptoms.\(^8\) A Cochrane review pooling 11 RCTs evaluating clean and clean-contaminated otologic cases found no difference in postoperative infection and graft failure rate when comparing placebo, intraoperative dosing, and prolonged postoperative dosing.\(^7\)

These studies, pooling clean and clean-contaminated otologic cases, do not allow for differentiation of infectious risk between these surgery types. One study has found increased infectious risk with cholesteatoma and draining perforations and reported a 3-fold decrease in infection when intraoperative antibiotics were used in this group.\(^7\) A retrospective cohort study (n = 195) similarly reported decreased infection with a single intraoperative antibiotic dose when used in cases of draining cholesteatoma (11% vs 1%).\(^8\) Thus, a short dosing of antibiotic may be beneficial in this setting.

Antibiotic prophylaxis in cochlear implantation presents an interesting dilemma due to the potentially devastating consequences of postoperative infection, including meningitis. Despite a lack of randomized controlled studies evaluating postoperative infection in cochlear implantation, the US Food and Drug Administration (FDA) recommends intraoperative antibiotic prophylaxis. A retrospective series without the use of antibiotics (n = 733) demonstrated a 4.1% rate of infection (with no cases of meningitis), and another study demonstrated a 1% infection rate with the use of antibiotics (n = 95).\(^8\)\(^–\)\(^9\) A multicenter survey (n = 1030) paradoxically reported that removal of implants for infection occurred in a higher percentage of patients receiving antibiotics compared to those without prophylaxis (4.5% vs 0.9%) and 0% of meningitis cases in both groups.\(^8\) In addition, a systematic review of 2 case series and a retrospective cohort study concluded that there is no benefit to postoperative antibiotics in reducing complications relative to a single
intraoperative dose. Nonetheless, a single prophylactic dose is recommended given the potentially serious infection sequelae. A single retrospective cohort study has found that a 6-week course of clarithromycin in addition to an intraoperative dose of ceftriaxone reduces skin infection rates by a factor of 8 compared to a single dose of ceftriaxone in those with titanium-silicon implants. The impact of this regimen on rates of meningitis is unclear, and further studies are warranted to support the use of prolonged antibiotics in cochlear implantation.

Otologic Surgery Recommendations: Clean: No perioperative antibiotic use (Evidence: Level 1a, Grade A); Clean-Contaminated or Contaminated: Intraoperative antibiotic use (Evidence: Level 2b, Grade C); Cochlear Implants: FDA recommends single intraoperative dose despite no comparative efficacy studies (Evidence: Level 4, Grade C)

Skull base/oto-neurosurgery. Skull base surgery is classified as clean (eg, lateral or anterolateral procedures) or clean-contaminated if sinonasal mucosa is involved (eg, transsphenoidal pituitary surgery). In case series retrospective cohorts (combined n = 4104), retrospective cohorts (combined n = 334), and a systematic review of 76 studies evaluating clean-contaminated skull base surgeries, rates of meningitis range widely (1.4%-25%), with higher rates occurring in patients with intraoperative cerebrospinal fluid (CSF) leaks, intradural surgeries, and revision surgery. Given the gravity of intracranial complications, intraoperative antibiotics are routinely given. To date, no placebo or controlled study has evaluated the use of antibiotics for clean-contaminated skull base surgery.

A retrospective cohort study (n = 95) evaluating clean-contaminated skull base surgeries found that 24 hours of postoperative antibiotic was beneficial, but extension beyond 48 hours did not provide additional benefit. A prospective cohort (n = 211) comparing the postoperative combination of ceftazidime, metronidazole, and vancomycin for variable duration (mean, 7.7 days) with nonstandard antibiotic therapy (mean, 10.2 days) found lower meningitis (0% vs 8.4%) and wound infection (11% vs 29%) rates. This suggests a potential benefit of broad-spectrum antibiotic coverage for skull base surgery but does not inform the appropriate treatment duration.

A retrospective cohort of endoscopic transsphenoidal surgery patients (n = 170) receiving IV prophylaxis with intraoperative cefazolin or ampicillin/sulbactam, n = 2032) have shown low rates of meningitis (0.69% and 0%, respectively). These more recent studies have demonstrated that a short duration of limited-spectrum antibiotics (as short as 8 hours postoperatively) may be appropriate to prevent infection after clean-contaminated skull base surgery. A systematic review of 5 studies (retrospective and prospective cohorts) concluded that 24 to 48 hours of postoperative prophylaxis is as efficacious as longer courses.

Clean skull base surgeries, including lateral oto-neurosurgical procedures, may warrant even a shorter duration of antibiotics. Case series reported a 0.14% to 9.9% rate of meningitis in these procedures (n = 4677). A single retrospective cohort study (n = 121) found no difference in infection rates between the use of preoperative cefazolin (12 hours prior to surgery) and intraoperative dosing at the time of acoustic neuroma resection. While a case series (n = 434) has shown a small infection rate (0.5%) with the use of intraoperative and postoperative (<24 hours) vancomycin + netilmicin in patients undergoing acoustic neuroma excision, no studies have compared infection rates with and without antibiotics.

Given this limitation, the neurosurgical literature on craniotomies provides the most applicable evidence for antibiotic prophylaxis in the setting of clean lateral skull base surgery. In a retrospective cohort (n = 6243), antibiotic prophylaxis reduced craniotomy incision infections from 8.8% to 4.6% (P < .001). A meta-analysis of 7 RCTs using variable duration of antibiotics showed antibiotics to be beneficial in reducing infection after craniotomy. Another meta-analysis of 8 RCTs similarly showed a decreased wound infection and meningitis rate with single intraoperative dosing of antibiotic compared to placebo (1.1% vs 2.7%). A subsequent meta-analysis of 6 RCTs showed no added benefit from extending prophylaxis postoperatively. These data support the use of a single intraoperative antibiotic dose in clean skull base surgeries.

Skull Base/Oto-Neurosurgery Recommendations: Clean-Contaminated (anterior skull base): intraoperative and postoperative antibiotic use (<24 hours) (Evidence: Level 2a, Grade B); Clean (lateral skull base): intraoperative antibiotic use (Evidence: Level 1a, Grade A)

Head and neck surgery.

Clean head and neck surgery. Many head and neck procedures, including thyroidectomy, parathyroidectomy, salivary gland excisions, and neck dissections, are considered clean surgeries. Considering the low infection rates without the use of antibiotics in case series, prophylaxis may not be necessary for thyroidectomy (0.001%-2.6%; total n =
Further retrospective cohorts\(^{137,138}\) (total n = 364) and an RCT using sulbactam/ampicillin\(^{131}\) (n = 500) showed no difference in postoperative infection rates with and without single intraoperative antibiotic use in clean head and neck surgery (1.1% vs 0.57%, 0.4% vs 1.4%, and 0.01% vs 0.02%, respectively). Furthermore, 1 retrospective cohort study (n = 464) showed that intraoperative followed by postoperative antibiotics (cefazolin or clindamycin for 24-48 hours) did not significantly decrease surgical site infections compared to no antibiotic use (24% vs 19%).\(^{132}\) One recent large multicenter retrospective cohort study (n = 2926) found a low (1%) infection rate overall but also that the rates of antibiotic prophylaxis were lower in those patients experiencing infections (14.3% vs 38.9%, \(P = .008\)). When eliminating a center with high infection rates, the rate of infection was not statistically lower in those receiving antibiotics (0.4% vs 0.8%, \(P = .118\)).\(^{133}\) These concordant studies suggest no need for antibiotic prophylaxis in clean head and neck surgical cases.

Many consider neck dissection a distinct entity within clean procedures owing to greater tissue exposure and factors that may increase infection risk (eg, poor nutritional status, history of radiation). In a prospective cohort study (n = 3660), postoperative infection occurred in 1.6% of patients undergoing thyroidectomy overall but in 5% undergoing simultaneous lymph node operations.\(^{119}\) Alternatively, a retrospective cohort study (n = 296) found no increase in infection when neck dissection was performed with thyroidectomy.\(^{134}\) Comparative studies examining antibiotic use in neck dissections have also been discordant. A retrospective cohort analysis (n = 192) found antibiotic use intraoperatively and for 24 hours postoperatively decreased infection rates nonsignificantly (10% vs 3.3%).\(^{135}\) A prospective cohort study (n = 118) found that cefazolin used for the same duration did significantly lower infection rates (1.7% vs 13.3%, \(P = .02\)), although this study has been criticized for its high rate of infection in the control group.\(^{136}\) Paradoxically, a recent retrospective cohort study (n = 244) reported a 3.3% infection rate in patients receiving antibiotics compared to 0% in patients not receiving antibiotics.\(^{137}\) A recent study of 566 patients undergoing neck dissection showed that cefazolin given for an additional 24 hours after the day of surgery is inferior to cefazolin given on the day of surgery\(^{138}\) and clindamycin given for an additional 24 hours after the day of surgery is inferior to clindamycin-gentamicin.\(^{139}\) Clindamycin has recently been found to be inferior to multiple other regimens,\(^{140-145}\) although it has shown effectiveness in some studies.\(^{146-147}\) Langerman et al\(^ {148}\) have even noted that clindamycin given for an additional 24 hours after the day of surgery is inferior to cefazolin given on the day of surgery only. It remains unclear whether a better alternative to clindamycin in penicillin-allergic patients undergoing clean-contaminated head and neck surgery exists.

While 3 studies have shown that the addition of metronidazole to cefazolin or ampicillin-gentamicin for anaerobic coverage yields significantly lower infection rates compared to placebo (14% vs 55.6%).\(^{140}\) Subsequently, with the exception of a single retrospective cohort study,\(^ {141}\) multiple RCTs and a meta-analysis of 12 studies have demonstrated the benefit of antibiotics compared to placebo or no antibiotics (Table 4).\(^ {140,142-145}\) With consistent evidence supporting the use of antibiotics in clean-contaminated head and neck surgery, additional studies have attempted to define the optimal type and duration of antibiotics. Case series using different antibiotics in a variety of clean-contaminated studies have demonstrated variable wound infection rates: intraoperative and 5-day postoperative piperacillin and ornidazole (n = 53, 3.8%)\(^ {152}\); intraoperative amoxicillin/clavulanic acid or cefuroxime (n = 100, 4%)\(^ {153}\); cefotaxime or cefuroxime started 8 hours postoperatively and continued 1 day postoperatively (n = 33, 15%)\(^ {154}\); intraoperative and 7-day postoperative penicillin ± tinidazole (n = 25, 59%-75%)\(^ {155}\); intraoperative and 1-day postoperative teicoplanin, cefuroxime, and metronidazole (n = 26, 58%)\(^ {156}\), and intraoperative and 7-day postoperative cefazolin and metronidazole (n = 249, 28.1%).\(^ {157}\) Additional comparative studies, which mostly focused on laryngectomy and oral cavity/oropharyngeal cancer resections with or without free flap surgery, are summarized in Table 4. Most of these studies have failed to show a difference in infection rates regardless of antibiotic type, with a few notable exceptions, which are summarized here.

For unclear reasons, in a small RCT (n = 60), 48 hours of cefotaxime was superior to ceftriaxone despite both being third-generation cephalosporins (infection rates: 0% vs 3.3%, respectively, \(P < .05\)).\(^ {158}\) While a meta-analysis from 1991 has suggested that a 1-day course of clindamycin may be superior to other antibiotics, more recent trials regarding the effectiveness of clindamycin have had contradictory results.\(^ {159}\) Intraoperative use of low-dose cefazolin (500 mg) (but not higher doses) appears to increase infection rates relative to clindamycin-gentamicin.\(^ {143}\) Cefazolin has recently been found to be inferior to multiple other regimens,\(^ {146,159-165}\) although it has shown effectiveness in some studies.\(^ {156-172}\) Langerman et al\(^ {148}\) have even noted that clindamycin given for an additional 24 hours after the day of surgery is inferior to cefazolin given on the day of surgery only. It remains unclear whether a better alternative to clindamycin in penicillin-allergic patients undergoing clean-contaminated head and neck surgery exists.

Clean Head and Neck Surgery Recommendation:

No perioperative antibiotic use—optional for neck dissection (Evidence: Level 1b, Grade A)

### Clean-contaminated head and neck surgery

Head and neck surgery is considered clean-contaminated if the aerodigestive tract is violated. An RCT from 1963 analyzed infection rates in a group of 91 patients undergoing cancer operations, including head and neck resections, and found that a 10-day treatment of chloramphenicol yielded significantly lower infection rates compared to placebo (14% vs 55.6%).\(^ {140}\)

The need for prophylactic gram-negative coverage has also been debated. Several studies have shown that

### Table 4

<table>
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<th>Infection Rates</th>
<th>Evidence</th>
<th>Recommendation</th>
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<tr>
<td>Cefazolin</td>
<td>14%</td>
<td>Level 1b</td>
<td>Grade A</td>
</tr>
<tr>
<td>Clindamycin-gentamicin</td>
<td>28.1%</td>
<td>Level 1b</td>
<td>Grade A</td>
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Table 4. Comparative Studies Evaluating Different Antibiotic Treatments in Clean-Contaminated Head and Neck Surgery.

<table>
<thead>
<tr>
<th>Study</th>
<th>Design, n</th>
<th>Comparison Group 1 (Infection Rate)</th>
<th>Duration</th>
<th>Comparison Group 2 (Infection Rate)</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Becker and Parell</td>
<td>RCT, n = 55</td>
<td>Cefazolin (38%)a</td>
<td>1 d</td>
<td>Placebo (87%)</td>
<td>1 d</td>
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<tr>
<td>Ketcham et al</td>
<td>RCT, n = 91</td>
<td>Chloramphenicol (14%)a</td>
<td>10 d</td>
<td>Placebo (55.6%)</td>
<td>10 d</td>
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<tr>
<td></td>
<td>RCT, n = 91</td>
<td>Chloramphenicol (8.9%)</td>
<td>10 d</td>
<td>Placebo-chloramphenicol (17.4%)</td>
<td>10 d (7 d abx)</td>
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<tr>
<td>Dor and Klastersky</td>
<td>RCT, n = 102</td>
<td>Ampicillin-cloxacillin (17.3%)a</td>
<td>5 d</td>
<td>Placebo (36%)</td>
<td>5 d</td>
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<tr>
<td>Seagle et al</td>
<td>RCT, n = 50</td>
<td>Cefazolin (16%)a</td>
<td>1 d</td>
<td>Placebo (48%)</td>
<td>1 d</td>
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<td></td>
<td>RCT, n = 102</td>
<td>Ampicillin-cloxacillin (6%)a</td>
<td>6 d</td>
<td>Placebo (24%)</td>
<td>6 d</td>
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<td>RCT, n = 107</td>
<td>Ticarcillin (11%)</td>
<td>4 d</td>
<td>Carbenicillin (8%)</td>
<td>4 d</td>
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<tr>
<td></td>
<td>RCT, n = 140</td>
<td>Carbenicillin (14%)</td>
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<tr>
<td></td>
<td>RCT, n = 80</td>
<td>Clindamycin (16%)</td>
<td>1 d</td>
<td>Clindamycin-netilmicin (9%)</td>
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<tr>
<td>Raine et al</td>
<td>RCT, n = 32</td>
<td>Augmentin (25%)a</td>
<td>2 d</td>
<td>No antibiotic (75%)</td>
<td>NA</td>
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<tr>
<td>Vamvakidis et al</td>
<td>RC, n = 807</td>
<td>Cefuroxime (0.4%)</td>
<td>Intraoperatively</td>
<td>No antibiotic (1.4%)</td>
<td>NA</td>
</tr>
<tr>
<td>Johnson and Yu</td>
<td>RCT, n = 48</td>
<td>Cefoperazone (9.4%)a</td>
<td>1 d</td>
<td>Placebo (78%)</td>
<td>1 d</td>
</tr>
<tr>
<td></td>
<td>RCT, n = 41</td>
<td>Cefotaxime (10%)a</td>
<td>1 d</td>
<td>Placebo (78%)</td>
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<tr>
<td></td>
<td>RCT, n = 107</td>
<td>Cefazolin; 500 mg (53%)a</td>
<td>1 or 5 d</td>
<td>Clindamycin-gentamicin (11%)</td>
<td>1 or 5 d</td>
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<td>Mandell-Brown et al</td>
<td>RCT, n = 56</td>
<td>Clindamycin-gentamicin (7%)</td>
<td>1 d</td>
<td>Clindamycin-gentamicin (3.8%)</td>
<td>5 d</td>
</tr>
<tr>
<td>Johnson et al</td>
<td>RCT, n = 107</td>
<td>Cefazolin; 500 mg (33%)</td>
<td>1 d</td>
<td>Cefazolin; 500 mg (20%)</td>
<td>5 d</td>
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<tr>
<td></td>
<td>RCT, n = 118</td>
<td>Cefazolin; 2 g (8.5%)</td>
<td>1 d</td>
<td>Moxalactam (3.4%)</td>
<td>1 d</td>
</tr>
<tr>
<td></td>
<td>RCT, n = 104</td>
<td>Clindamycin (3.8%)</td>
<td>1 d</td>
<td>Clindamycin-gentamicin (3.8%)</td>
<td>1 d</td>
</tr>
<tr>
<td></td>
<td>RCT, n = 142</td>
<td>Cefazolin or cefotaxime or clindamycin (18.9%)</td>
<td>1 d</td>
<td>Cefazolin or cefotaxime or clindamycin (25%)</td>
<td>5 d</td>
</tr>
<tr>
<td>Saginur et al</td>
<td>RCT, n = 20</td>
<td>Cefamandole (33%)a</td>
<td>8 h</td>
<td>Placebo (55%)</td>
<td>8 h</td>
</tr>
<tr>
<td>Goode et al</td>
<td>RC, n = 77</td>
<td>Cefazolin or cephalixin (NA)</td>
<td>3-21 d</td>
<td>Cefazolin or cephalixin (NA)</td>
<td>3-21 d</td>
</tr>
<tr>
<td>Fee et al</td>
<td>RCT, n = 30</td>
<td>Moxalactam (3%)</td>
<td>1 d</td>
<td>Moxalactam (0%)</td>
<td>2 d</td>
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<tr>
<td>Bartella et al</td>
<td>PC, n = 50</td>
<td>Ampicillin-sulbactam (36%)a</td>
<td>Intraoperatively</td>
<td>Ampicillin-sulbactam, augmentin (4%)</td>
<td>5 d</td>
</tr>
<tr>
<td>Marucci et al</td>
<td>RCT, n = 120</td>
<td>Ceftazidime (10.1%)</td>
<td>Intraoperatively</td>
<td>Ceftazidime (11.6%)</td>
<td>12 h</td>
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<tr>
<td>Elies</td>
<td>RCT, n = 100</td>
<td>Oxacillin mezlocillin (0%)</td>
<td>Intraoperatively</td>
<td>Oxacillin mezlocillin (0%)</td>
<td>1 d</td>
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<td></td>
<td>RCT, n = 92</td>
<td>Oxacillin mezlocillin (0%)</td>
<td>1 d</td>
<td>Oxacillin mezlocillin (0%)</td>
<td>≥3 d</td>
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<tr>
<td>Sawyer et al</td>
<td>RCT, n = 50</td>
<td>Metronidazole-cefazolin (28%)a</td>
<td>2 d</td>
<td>Metronidazole-cefazolin (20%)</td>
<td>≥7 d</td>
</tr>
<tr>
<td>Gehanno et al</td>
<td>RCT, n = 197</td>
<td>Cefotaxime (23.7%)</td>
<td>2 d</td>
<td>Cefotaxime (17%)</td>
<td>6 d</td>
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(continued)
<table>
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<tr>
<th>Study</th>
<th>Design, n</th>
<th>Comparison Group 1 (Infection Rate)</th>
<th>Duration</th>
<th>Comparison Group 2 (Infection Rate)</th>
<th>Duration</th>
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<tr>
<td>Panosetti et al158</td>
<td>RCT, n = 60</td>
<td>Cefotaxime (0%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2 d</td>
<td>Ceftriaxone (3.3%)</td>
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<tr>
<td>Johnson et al188</td>
<td>RCT, n = 109</td>
<td>Cefoperazone (18.9%)</td>
<td>1 d</td>
<td>Cefoperazone (25%)</td>
<td>5 d</td>
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<tr>
<td>Phan et al167</td>
<td>RCT, n = 99</td>
<td>Ampicillin-sulbactam (33%)</td>
<td>1 d</td>
<td>Clindamycin-amikacin (21%)</td>
<td>1 d</td>
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<tr>
<td>Mustafa et al139</td>
<td>RCT, n = 60</td>
<td>Cefotaxime (13%)</td>
<td>1 d</td>
<td>Cefotaxime (10%)</td>
<td>7 d</td>
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<tr>
<td>Righi et al186</td>
<td>RCT, n = 162</td>
<td>Clindamycin-cefonicid (2.5%)</td>
<td>1 d</td>
<td>Clindamycin-cefonicid (3.7%)</td>
<td>3 d</td>
</tr>
<tr>
<td>Rodrigo et al166</td>
<td>RCT, n = 109</td>
<td>Amoxicillin-clavulanate (22.8%)</td>
<td>1 d</td>
<td>Clindamycin-gentamicin (21.2%)</td>
<td>1 d</td>
</tr>
<tr>
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<td>RCT, n = 107</td>
<td>Amoxicillin-clavulanate (22.8%)</td>
<td>1 d</td>
<td>Cefazolin (26%)</td>
<td>1 d</td>
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<tr>
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<td>RCT, n = 102</td>
<td>Clindamycin-gentamicin (21.2%)</td>
<td>1 d</td>
<td>Cefazolin (26%)</td>
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<tr>
<td>Johnson et al168</td>
<td>RCT, n = 242</td>
<td>Ampicillin-sulbactam (14%)</td>
<td>1 d</td>
<td>Clindamycin (14%)</td>
<td>1 d</td>
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<td>Skitarelic et al178</td>
<td>RCT, n = 189</td>
<td>Amoxicillin-clavulanate (21%)</td>
<td>1 d</td>
<td>Cefazolin (24%)</td>
<td>1 d</td>
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<tr>
<td>Robbins et al173</td>
<td>PC, n = 400</td>
<td>Cefazolin-metronidazole (9.5%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2 d</td>
<td>Cefazolin (18.6%)</td>
<td>2 d</td>
</tr>
<tr>
<td>Sawyer et al175</td>
<td>RC, n = 96</td>
<td>Cefazolin-metronidazole (3%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2 d</td>
<td>Cefazolin (36%)</td>
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<tr>
<td>Gerard et al170</td>
<td>RCT, n = 113</td>
<td>Ticarcillin-clavulanic acid (36%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1 d</td>
<td>Clindamycin-amikacin (10%)</td>
<td>1 d</td>
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<tr>
<td>Swanson et al171</td>
<td>RCT, n = 99</td>
<td>Clindamycin (8%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>32 h</td>
<td>Cefonicid (24%)</td>
<td>Intraoperatively</td>
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<tr>
<td>Venditti et al172</td>
<td>RCT, n = 99</td>
<td>Clindamycin-amikacin (0%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>5 d</td>
<td>Cefotetan (4%)</td>
<td>5 d</td>
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<tr>
<td>Busch et al185</td>
<td>RC, n = 418</td>
<td>Cefazolin, clindamycin, cepuroxime, ampicillin-sulbactam and/or metronidazole (14.6%)</td>
<td>≤7 d</td>
<td>Cefazolin, clindamycin, cepuroxime, ampicillin-sulbactam and/or metronidazole (13.2%)</td>
<td>≥8 d</td>
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<td>Mombelli et al191</td>
<td>RCT, n = 140</td>
<td>Carbenicillin (9.7%)</td>
<td>1 d</td>
<td>Carbenicillin (5.9%)</td>
<td>4 d</td>
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<tr>
<td>Tandon et al174</td>
<td>RCT, n = 60</td>
<td>Ampicillin-gentamicin (30%)</td>
<td>5 d</td>
<td>Ampicillin-gentamicin (26.6%)</td>
<td>10 d</td>
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<td>RCT, n = 60</td>
<td>Ampicillin-gentamicin (26.6%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>10 d</td>
<td>Ampicillin-gentamicin-metronidazole (13.3%)</td>
<td>10 d</td>
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<td>Taghy et al187</td>
<td>RCT, n = 90</td>
<td>Cefazolin (4.4%)</td>
<td>2 d</td>
<td>Cefazolin (6.7%)</td>
<td>5 d</td>
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<tr>
<td>Langerman et al159</td>
<td>RC, n = 1865</td>
<td>Ampicillin-sulbactam or cefazolin or metronidazole or metronidazole-cefuroxime (5.1%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1-4 d</td>
<td>None (13%)</td>
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(continued)
Table 4. (continued)

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<tr>
<th>Study</th>
<th>Design, n</th>
<th>Comparison Group 1 (Infection Rate)</th>
<th>Duration</th>
<th>Comparison Group 2 (Infection Rate)</th>
<th>Duration</th>
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<tr>
<td>Langerman et al160.c</td>
<td>RC, n = 8836</td>
<td>metronidazole-cefuroxime (5.1%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1-4 d</td>
<td>Clindamycin + other (11%)</td>
<td>1-4 d</td>
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<td>Ampicillin-sulbactam or cefazolin or metronidazole-cefuroxime (5.1%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>DOS only</td>
<td>Ampicillin-sulbactam or cefazolin or metronidazole-cefuroxime (NA)</td>
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<td>Ampicillin-sulbactam (NA)&lt;sup&gt;a&lt;/sup&gt; (DOS + 24 h &lt; DOS)</td>
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<td>Ampicillin-sulbactam (NA)</td>
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<td>Ampicillin-sulbactam (NA)&lt;sup&gt;a&lt;/sup&gt; (ampicillin/sulbactam &lt; clindamycin)</td>
<td>DOS only</td>
<td>Clindamycin (NA)</td>
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<td>Liu et al&lt;sup&gt;190&lt;/sup&gt;</td>
<td>RCT, n = 53</td>
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<td>1 d</td>
<td>Clindamycin (18.5%)</td>
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<tr>
<td>Weber et al&lt;sup&gt;161&lt;/sup&gt;</td>
<td>RCT, n = 212</td>
<td>Ampicillin-sulbactam (13.3%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2 d</td>
<td>Clindamycin (27.1%)</td>
<td>2 d</td>
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<tr>
<td>Johnson et al&lt;sup&gt;177&lt;/sup&gt;</td>
<td>RCT, n = 104</td>
<td>Clindamycin (3.8%)</td>
<td>32 h</td>
<td>Clindamycin-gentamicin (3.8%)</td>
<td>32 h</td>
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<tr>
<td>Khariwala et al180</td>
<td>RC, n = 147</td>
<td>Cephalosporins or penicillins or Quinolones or clindamycin (23.4%)</td>
<td>&lt;2 d</td>
<td>Cephalosporins or penicillins or Quinolones or clindamycin (21.2%)</td>
<td>&gt;2 d</td>
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<tr>
<td>Johnson et al&lt;sup&gt;169&lt;/sup&gt;</td>
<td>RCT, n = 100</td>
<td>Cefazolin (21.6%)</td>
<td>1 d</td>
<td>Clindamycin (19.6%)</td>
<td>1 d</td>
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<td>Bhathena et al184</td>
<td>RCT, n = 50</td>
<td>Cefotaxime (7.1%)</td>
<td>5 d</td>
<td>Cefoperazone (9.8%)</td>
<td>1 d</td>
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<td>Carroll et al183</td>
<td>RCT, n = 74</td>
<td>Clindamycin (10%)</td>
<td>5 d</td>
<td>Clindamycin (11%)</td>
<td>1 d</td>
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<tr>
<td>Pool et al164</td>
<td>RC, n = 266</td>
<td>Cefazolin-metronidazole (8%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1 d</td>
<td>Clindamycin alone, clindamycin-metronidazole, or clindamycin-gentamicin (27%)</td>
<td>1 d</td>
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<tr>
<td>Mucke et al197</td>
<td>RCT, n = 350</td>
<td>No antibiotics (50%)</td>
<td>10 d</td>
<td>Benzylpenicillin (27%)</td>
<td>10 d</td>
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<td>No antibiotics (50%) or benzylpenicillin (27%)&lt;sup&gt;a&lt;/sup&gt;</td>
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<td>Amoxicillin-sulbactam (19.3%)</td>
<td>10 d</td>
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<td></td>
<td></td>
<td>No antibiotics (50%) or Benzylpenicillin (27%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>10 d</td>
<td>Cefuroxime (20.8%)</td>
<td>10 d</td>
</tr>
<tr>
<td>Cohen et al162</td>
<td>RCT, n = 97</td>
<td>Ampicillin-sulbactam (0%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1-22 d</td>
<td>Clindamycin (60%)</td>
<td>1-22 d</td>
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<td>Ampicillin-sulbactam or clindamycin or cefazolin or piperclillin-tazobactam (35.7%)</td>
<td>&lt;2 d</td>
<td>Ampicillin-sulbactam or clindamycin or cefazolin or piperclillin-tazobactam (18.1%)</td>
<td>&gt;2 d</td>
</tr>
</tbody>
</table>

(continued)
antibacterial regimens with increased gram-negative coverage are associated with fewer infectious complications (ie, ampicillin-sulbactam over clindamycin). However, data are not clear especially since the preponderance of studies has failed to show benefit from improved gram-negative coverage, including the addition of aminoglycosides. Further large-scale RCTs or well-designed meta-analyses of current data are needed to decipher the optimal regimen for infection prophylaxis in clean-contaminated cases.

The use of antibiotics intraoperatively only has been shown to be inferior to the additional use of 24-hour postoperative antibiotics (ampicillin-sulbactam) but not a 12-hour postoperative course (cefuroxime). In an RCT using oxacillin and mezlocillin, a 0% infection rate was seen in both patients receiving intraoperative antibiotics only and those receiving 24 hours of additional postoperative treatment. Further large-scale RCTs or well-designed meta-analyses of current data are needed to decipher the optimal regimen for infection prophylaxis in clean-contaminated cases.

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Microvascular free flaps are a unique entity within clean-contaminated surgery. Several authors have found clindamycin to be inferior to other regimens and suggested the need to consider the addition of a second antibiotic to improve coverage of aerobic gram-negative bacteria. Amoxicillin-sulbactam has been found to be superior to cefuroxime and other penicillins. Studies have not found any benefit from prolonged duration of antibiotics in reducing postsurgical infections. However, these studies have compared either 1-day or 2-day regimens to longer durations, and it remains unclear if a 2-day period of treatment is superior to a 1-day course. As such, some have advocated for a 48-hour postoperative antibiotic prophylaxis for free flap cases.

**Clean-Contaminated Head and Neck Surgery**

**Recommendation:** Intraoperative and postoperative antibiotic use (24-48 hours) (Evidence: Level 1b, Grade A)

**Limitations**

Heterogeneity in the definition and diagnosis of infection limited study result aggregation for comparison purposes. In addition, there are limited antibiotic data available for some surgical procedures, which can prevent robust conclusions in regards to prophylaxis. Nonetheless, this study highlights the best available data to help guide clinical practice while acknowledging the need for higher level studies in several specific surgical interventions. The primary outcome measure in most studies was gross wound infection, but head and neck anatomy lends itself to having many different outcomes that may be secondarily affected by an infection (eg, graft success in tympanoplasty, pain in tonsillectomy). This study attempts to incorporate some of these outcomes, but a comprehensive review of different outcome measures is beyond the scope of this work.

**Implications for Practice**

Evidence does not support routine perioperative antibiotics for a large number of otolaryngologic procedures. Prophylactic
antibiotics should be administered in complex septorhinoplasty, skull base surgery, and clean-contaminated head and neck surgery. Prophylaxis can be considered in otologic surgery in the setting of draining ears or cholesteatoma, cochlear implant (due to FDA recommendations), and clean neck dissections. Antibiotic prophylaxis should not extend beyond 24 hours postoperatively except in cases of clean-contaminated skull base surgery, microvascular free flap surgery, and nasal packing use. These recommendations are based on current available literature, and while they provide general management guidance, they are not meant to supersede clinical judgment.

Author Contributions

Priyesh N. Patel, design of the work, data acquisition, interpretation of data, manuscript drafting and revision; Asitha D. Jayawardeniya, design of the work, data acquisition, interpretation of data, manuscript drafting and revision; Rachel L. Walden, data acquisition, interpretation of data, manuscript drafting and revision; Edward B. Penn, design of the work, interpretation of data, manuscript revision; David O. Francis, design of the work, interpretation of data, manuscript revision.

Disclosures

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Sponsorships: None.

Funding source: None.

Supplemental Material

Additional supporting information is available in the online version of the article.

References


Cayonu M, Acar A, Horasanli E, Altundag A, Salihoglu M. Comparison of totally occlusive nasal pack, internal nasal


