



North American Spine Society

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Revised

Evidence-Based Clinical Guidelines for Multidisciplinary Spine Care

Antibiotic Prophylaxis in Spine Surgery

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Spine Care

Antibiotic Prophylaxis in Spine Surgery



NASS Evidence-Based Clinical Guidelines Committee

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William O. Shaffer, MD	Nothing to disclose.
Paul G. Matz, MD	Nothing to disclose.
Jamie Baisden, MD	Nothing to disclose.
Robert Fernand, MD	Nothing to disclose.

Range Key:

Level A. \$100 to \$1,000
Level B. \$1,001 to \$10,000
Level C. \$10,001 to \$25,000
Level D. \$25,001 to \$50,000
Level E. \$50,001 to \$100,000
Level F. \$100,001 to \$500,000
Level G. \$500,001 to \$1M
Level H. \$1,000,001 to \$2.5M
Level I. Greater than \$2.5M

Comments

Comments regarding the guideline may be submitted to the North American Spine Society and will be considered in development of future revisions of the work.

Special Thanks

The North American Spine Society would like to express its thanks to Dr. Nikolai Bogduk for generating the calculations in Appendix E to explain the prohibitive nature of the sample sizes required to yield Level I data for the efficacy of antibiotic prophylaxis.

North American Spine Society

Clinical Guidelines for Multidisciplinary Spine Care
Antibiotic Prophylaxis in Spine Surgery

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A technical report, including the literature search parameters and evidentiary tables developed by the authors, can be accessed at http://www.spine.org/Documents/Antibiotic_Prophylaxis_TechRept.pdf

I. Introduction

Objective

The objective of the North American Spine Society (NASS) Evidence-Based Clinical Guideline on Antibiotic Prophylaxis in Spine Surgery is to provide evidence-based recommendations to address key clinical questions surrounding the use of prophylactic antibiotics in spine surgery. The guideline is intended to address these questions based on the highest quality clinical literature available on this subject as of June 2011. The goals of the guideline recommendations are to assist in delivering optimum, efficacious treatment with the goal of preventing surgical infection.

Scope, Purpose and Intended User

This document was developed by the North American Spine Society Evidence-based Guideline Development Committee as an educational tool to assist spine surgeons in preventing surgical site infections. This guideline is an update to the 2007 version. The NASS Clinical Guideline on Antibiotic Prophylaxis in Spine Surgery addresses the efficacy and appropriate protocol for antibiotic prophylaxis and discusses redosing, discontinuation, wound drains, as well as special considerations related to the potential impact of comorbidities on antibiotic prophylaxis proto-

col. The recommendations made in this guideline are based on evidence related to open procedures. No evidence was reviewed related to efficacy and protocol for the use of antibiotic prophylaxis in percutaneous procedures.

THIS GUIDELINE DOES NOT REPRESENT A “STANDARD OF CARE,” nor is it intended as a fixed treatment protocol. It is anticipated that there will be patients who will require less or more treatment than the average. It is also acknowledged that in atypical cases, treatment falling outside this guideline will sometimes be necessary. This guideline should not be seen as prescribing the type, frequency or duration of intervention. Treatment should be based on the individual patient’s need and doctor’s professional judgment. This document is designed to function as a guideline and should not be used as the sole reason for denial of treatment and services. This guideline is not intended to expand or restrict a health care provider’s scope of practice or to supersede applicable ethical standards or provisions of law.

Patient Population

The patient population for this guideline encompasses adults (18 years or older) undergoing spine surgery.

II. Guideline Development Methodology

Through objective evaluation of the evidence and transparency in the process of making recommendations, it is NASS' goal to develop evidence-based clinical practice guidelines for the diagnosis and treatment of adult patients with various spinal conditions. These guidelines are developed for educational purposes to assist practitioners in their clinical decision-making processes. It is anticipated that where evidence is very strong in support of recommendations, these recommendations will be operationalized into performance measures.

Multidisciplinary Collaboration

With the goal of ensuring the best possible care for adult patients suffering with spinal disorders, NASS is committed to multidisciplinary involvement in the process of guideline and performance measure development. To this end, NASS has ensured that representatives from medical, interventional and surgical spine specialties have participated in the development and review of all NASS guidelines. To ensure broad-based representation, NASS has invited and welcomes input from other societies and specialties

Evidence Analysis Training of All NASS Guideline Developers

NASS has initiated, in conjunction with the University of Alberta's Centre for Health Evidence, an online training program geared toward educating guideline developers about evidence analysis and guideline development. All participants in guideline development for NASS have completed the training prior to participating in the guideline development program at NASS. This training includes a series of readings and exercises, or interactivities, to prepare guideline developers for systematically evaluating literature and developing evidence-based guidelines. The online course takes approximately 15-30 hours to complete and participants have been awarded CME credit upon completion of the course.

Disclosure of Potential Conflicts of Interest

All participants involved in guideline development have disclosed potential conflicts of interest to their colleagues and their potential conflicts have been documented in this guideline. Participants have been asked to update their disclosures regularly throughout the guideline development process.

Levels of Evidence and Grades of Recommendation

NASS has adopted standardized levels of evidence (*Appendix A*) and grades of recommendation (*Appendix B*) to assist practitioners in easily understanding the strength of the evidence and recommendations within the guidelines. The levels of evidence range from Level I (high quality randomized controlled trial) to Level V (expert consensus). Grades of recommendation indi-

cate the strength of the recommendations made in the guideline based on the quality of the literature.

Grades of Recommendation:

A: Good evidence (Level I studies with consistent findings) for or against recommending intervention.

B: Fair evidence (Level II or III studies with consistent findings) for or against recommending intervention.

C: Poor quality evidence (Level IV or V studies) for or against recommending intervention.

I: Insufficient or conflicting evidence not allowing a recommendation for or against intervention.

Levels of evidence have very specific criteria and are assigned to studies prior to developing recommendations. Recommendations are then graded based upon the level of evidence. To better understand how levels of evidence inform the grades of recommendation and the standard nomenclature used within the recommendations see *Appendix C*.

Guideline recommendations are written utilizing a standard language that indicates the strength of the recommendation. "A" recommendations indicate a test or intervention is "recommended"; "B" recommendations "suggest" a test or intervention and "C" recommendations indicate a test or intervention "may be considered" or "is an option." "I" or "Insufficient Evidence" statements clearly indicate that "there is insufficient evidence to make a recommendation for or against" a test or intervention. Work group consensus statements clearly state that "in the absence of reliable evidence, it is the work group's opinion that" a test or intervention may be appropriate.

The levels of evidence and grades of recommendation implemented in this guideline have also been adopted by the Journal of Bone and Joint Surgery, the American Academy of Orthopaedic Surgeons, Clinical Orthopaedics and Related Research, the journal Spine and the Pediatric Orthopaedic Society of North America.

In evaluating studies as to levels of evidence for this guideline, the study design was interpreted as establishing only a potential level of evidence. As an example, a therapeutic study designed as a randomized controlled trial would be considered a potential Level I study. The study would then be further analyzed as to how well the study design was implemented and significant shortcomings in the execution of the study would be used to downgrade the levels of evidence for the study's conclusions. In the example cited previously, reasons to downgrade the results of a potential Level I randomized controlled trial to a Level II study would include, among other possibilities: an under-powered study (patient sample too small, variance too high), inadequate randomization or masking of the group assignments and lack of validated outcome measures.

In addition, a number of studies were reviewed several times in answering different questions within this guideline. How a given question was asked might influence how a study was evaluated and interpreted as to its level of evidence in answering that particular question. For example, a randomized control trial reviewed to evaluate the differences between the outcomes of surgically treated versus untreated patients with lumbar spinal stenosis might be a well designed and implemented Level I therapeutic study. This same study, however, might be classified as giving Level II prognostic evidence if the data for the untreated controls were extracted and evaluated prognostically.

Guideline Development Process

Step 1: Identification of Clinical Questions

Trained guideline participants were asked to submit a list of clinical questions that the guideline should address. The lists were compiled into a master list, which was then circulated to each member with a request that they independently rank the questions in order of importance for consideration in the guideline. The most highly ranked questions, as determined by the participants, served to focus the guideline.

Step 2: Identification of Work Groups

Multidisciplinary teams were assigned to work groups and assigned specific clinical questions to address. Because NASS is comprised of surgical, medical and interventional specialists, it is imperative to the guideline development process that a cross-section of NASS membership is represented on each group. This also helps to ensure that the potential for inadvertent biases in evaluating the literature and formulating recommendations is minimized.

Step 3: Identification of Search Terms and Parameters

One of the most crucial elements of evidence analysis to support development of recommendations for appropriate clinical care is the comprehensive literature search. Thorough assessment of the literature is the basis for the review of existing evidence and the formulation of evidence-based recommendations. In order to ensure a thorough literature search, NASS has instituted a Literature Search Protocol (*Appendix D*) which has been followed to identify literature for evaluation in guideline development. In keeping with the Literature Search Protocol, work group members have identified appropriate search terms and parameters to direct the literature search.

Specific search strategies, including search terms, parameters and databases searched, are documented in the technical report that accompanies this guideline.

Step 4: Completion of the Literature Search

Once each work group identified search terms/parameters, the literature search was implemented by a medical/research librarian, consistent with the Literature Search Protocol.

Following these protocols ensures that NASS recommendations (1) are based on a thorough review of relevant literature; (2) are truly based on a uniform, comprehensive search strategy;

and (3) represent the current best research evidence available. NASS maintains a search history in Endnote, for future use or reference.

Step 5: Review of Search Results/Identification of Literature to Review

Work group members reviewed all abstracts yielded from the literature search and identified the literature they will review in order to address the clinical questions, in accordance with the Literature Search Protocol. Members have identified the best research evidence available to answer the targeted clinical questions. That is, if Level I, II and or III literature is available to answer specific questions, the work group was not required to review Level IV or V studies.

Step 6: Evidence Analysis

Members have independently developed evidentiary tables summarizing study conclusions, identifying strengths and weaknesses and assigning levels of evidence. In order to systematically control for potential biases, at least two work group members have reviewed each article selected and independently assigned levels of evidence to the literature using the NASS levels of evidence. Any discrepancies in scoring have been addressed by two or more reviewers. The consensus level (the level upon which two-thirds of reviewers were in agreement) was then assigned to the article.

As a final step in the evidence analysis process, members have identified and documented gaps in the evidence to educate guideline readers about where evidence is lacking and help guide further needed research by NASS and other societies.

Step 7: Formulation of Evidence-Based Recommendations and Incorporation of Expert Consensus

Work groups held face-to-face meetings to discuss the evidence-based answers to the clinical questions, the grades of recommendations and the incorporation of expert consensus. Expert consensus has been incorporated only where Level I-IV evidence is insufficient and the work group has deemed that a recommendation is warranted. Transparency in the incorporation of consensus is crucial, and all consensus-based recommendations made in this guideline very clearly indicate that Level I-IV evidence is insufficient to support a recommendation and that the recommendation is based only on expert consensus.

Consensus Development Process

Voting on guideline recommendations was conducted using a modification of the nominal group technique in which each work group member independently and anonymously ranked a recommendation on a scale ranging from 1 (“extremely inappropriate”) to 9 (“extremely appropriate”). Consensus was obtained when at least 80% of work group members ranked the recommendation as 7, 8 or 9. When the 80% threshold was not attained, up to three rounds of discussion and voting were held to resolve disagreements. If disagreements were not resolved after these rounds, no recommendation was adopted.

After the recommendations were established, work group members developed the guideline content, addressing the literature which supports the recommendations.

Step 8: Submission of the Draft Guidelines for Review/Comment

Guidelines were submitted to the full Evidence-Based Guideline Development Committee and the Research Council Director for review and comment. Revisions to recommendations were considered for incorporation only when substantiated by a preponderance of appropriate level evidence.

Step 9: Submission for Board Approval

Once any evidence-based revisions were incorporated, the drafts were prepared for NASS Board review and approval. Edits and revisions to recommendations and any other content were considered for incorporation only when substantiated by a preponderance of appropriate level evidence.

Step 10: Submission for Publication and National Guideline Clearinghouse (NGC) Inclusion

Following NASS Board approval, the guidelines have been slated for publication and submitted for inclusion in the National Guidelines Clearinghouse (NGC). No revisions were made at this point in the process, but comments have been and will be saved for the next iteration.

Step 11: Review and Revision Process

The guideline recommendations will be reviewed every three years by an EBM-trained multidisciplinary team and revised as appropriate based on a thorough review and assessment of relevant literature published since the development of this version of the guideline.

Nomenclature for Medical/Interventional Treatment

Throughout the guideline, readers will see that what has traditionally been referred to as “nonoperative,” “nonsurgical” or “conservative” care is now referred to as “medical/interventional care.” The term medical/interventional is meant to encompass pharmacological treatment, physical therapy, exercise therapy, manipulative therapy, modalities, various types of external stimulators and injections.

III. Recommendations Regarding Antibiotic Prophylaxis in Spine Surgery

A. Efficacy

For patients undergoing open spine surgery, does antibiotic prophylaxis result in decreased infection rates compared to patients who do not receive prophylaxis?

Preoperative prophylactic antibiotics are suggested to decrease infection rates in patients undergoing spine surgery.

Grade of Recommendation: B

Barker et al¹ described a meta-analysis based on a systematic review of the literature concerning the efficacy of prophylactic antibiotics on the incidence of postoperative spinal infection. By pooling data from six randomized controlled trials, they found a 2.2% (10 of 451) infection rate if antibiotics were given and a 5.9% (23 of 392) infection rate if antibiotics were not administered. Whereas each of the individual studies did not find a statistical difference, the pooled data did ($p < 0.01$). In critique of this analysis, the individual studies included in the meta-analysis did not show a statistically significant difference in infection rate with antibiotic use. However, the pooled results did show a significantly lower rate of infection with prophylactic antibiotic use. These data offer Level II therapeutic evidence that antibiotics can lead to lower rates of infection for general spine surgical procedures.

Pavel et al² reported a prospective, randomized controlled trial comparing the use of antibiotic prophylaxis with cephazolin with a placebo on the rate of postoperative infection in orthopedic surgical procedures. When separately analyzed, the infection rate after spinal procedures was 9.2% in the placebo group, compared to 3% in the group who received cephaloridine. In critique of this study, the numbers were too small in the spine subgroup to detect a statistically significant difference. While this is a Level I study relative to orthopedic procedures, it provides Level II therapeutic evidence that the use of perioperative cephalosporin antibiotic can significantly reduce the rate of perioperative infection in the subgroup of patients undergoing orthopedic spinal procedures.

Rubinstein et al³ performed a prospective, randomized controlled trial to investigate the efficacy of a single dose of 1 g of cephazolin in reducing postoperative infections in patients undergoing 'clean' operations on the lumbar spine. Of the 141 patients included in the study, 70 received 1 g intravenous cephalazolin upon arrival to the operative room (approximately two

hours prior to surgery) and 71 received placebo. Presence of infection was assessed at 30 days, with surgical site infection defined as drainage of purulent material from the operative site and a positive bacteriological culture, or inflammation of an area more than 20 mm in diameter; for urinary tract infection, more than 100,000 colony forming units/mL on culture; and for pneumonia, the clinical diagnosis was made by the treating physician. There were 21 wound or urinary infections in the 71 patients who received placebo and nine in the 70 who received cephazolin ($p < 0.05$). Nine patients (12.7%) who received placebo and three (4.3%) who received cephazolin developed wound infections ($p = 0.07$). All but three of the infections in the placebo group were confirmed by bacterial culture. All the organisms isolated from the patients who received placebo (except the group-D streptococci which are inherently resistant) were sensitive to cephazolin whereas in the cephazolin prophylactic group 43% of the organisms isolated were resistant or had reduced sensitivity to the drug. The authors concluded that the administration of a single dose of cephazolin preoperatively is recommended for patients undergoing lumbar spinal surgery. In critique, the sample size was small and the study's follow-up period was short. In addition, the authors expanded the definition of infection to include wound, urinary tract infection and pneumonia in order to achieve statistical significance. Due to these limitations, this potential Level I study provides Level II therapeutic evidence that for uncomplicated spine surgery, a single preoperative dose of cephazolin decreases infection rate; however, it does not significantly decrease the rate of wound infection. The use of cephazolin appears to be associated with an increase in development of resistant organisms.

This clinical guideline should not be construed as including all proper methods of care or excluding or other acceptable methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific procedure or treatment is to be made by the physician and patient in light of all circumstances presented by the patient and the needs and resources particular to the locality or institution

For a typical, uncomplicated lumbar laminotomy and discectomy, a single preoperative dose of antibiotics is suggested to decrease the risk of infection and/or discitis.

Grade of Recommendation: B

Petignat et al⁴ conducted a prospective, randomized controlled trial assessing the efficacy of one preoperative 1.5 g dose of cefuroxime in preventing surgical site infection after lumbar laminotomy and discectomy for herniated disc. Of the 1237 patients included in the study, 613 received 1.5 g intravenous cefuroxime on induction and 624 received placebo. Presence of infection, as defined by the Centers for Disease Control (CDC) guidelines, was assessed at six weeks, three months and six months. Baseline characteristics were similar in patients allocated to cefuroxime (n = 613) or placebo (n=624). Eight (1.3%) patients in the cefuroxime group and 18 patients (2.8%) in the placebo group developed a surgical site infection (p = 0.073). A diagnosis of spondylodiscitis or epidural abscess was made in nine patients in the placebo group, but none in the cefuroxime group (p < 0.01), which corresponded to a number necessary to treat of 69 patients to prevent one of these infections. There were no significant adverse events attributed to either cefuroxime or placebo. Overall, the surgical site infection rate was 1.3% with antibiotics versus 2.8% with placebo (p=0.073), and the discitis rate was 0/613 versus 9/624 (p<0.01), respectively. The authors concluded that a single, preoperative dose of cefuroxime significantly reduces the risk of organ-space infection, most notably spondylodiscitis, after surgery for herniated disc. Cefuroxime is protective against spondylodiscitis. This study provides Level I therapeutic evidence that for uncomplicated lumbar microdiscectomy, a single dose of cefuroxime versus placebo tends to decrease rate of post operative infection and significantly reduces the rate of spondylodiscitis specifically.

Rubinstein et al³ performed a prospective, randomized controlled trial to investigate the efficacy of a single dose of 1 g of cephazolin in reducing postoperative infections in patients undergoing "clean" operations on the lumbar spine. Of the 141 patients included in the study, 70 received 1 g intravenous cephalazolin upon arrival to the operative room (approximately two hours prior to surgery) and 71 received placebo. Presence of infection was assessed at 30 days, with surgical site infection defined as drainage of purulent material from the operative site and a positive bacteriological culture or inflammation of an area more than 20 mm in diameter; for urinary tract infection, more than 100,000 colony forming units/mL on culture; and for pneumonia, the clinical diagnosis was made by the treating physician. There were 21 wound or urinary infections in the 71 patients who received placebo and nine in the 70 who received cephalazolin (p < 0.05). Nine patients (12.7%) who received placebo and three (4.3%) who received cephalazolin developed wound infections (p = 0.07). All but three of the infections in the placebo group were confirmed by bacterial culture. All of the organisms isolated from the patients who received placebo (except the group-D streptococci which are inherently resistant) were

sensitive to cephalazolin whereas in the cephalazolin prophylactic group 43% of the organisms isolated were resistant or had reduced sensitivity to the drug. The authors concluded that the administration of a single dose of cephalazolin preoperatively is recommended for patients undergoing lumbar spinal surgery. In critique, the sample size was small and the study's follow-up period was short. In addition, the authors expanded the definition of infection to include wound, urinary tract infection and pneumonia in order to achieve statistical significance. Due to these limitations, this potential Level I study provides Level II therapeutic evidence that for uncomplicated spine surgery, a single preoperative dose of cephalazolin decreases infection rate; however, it does not significantly decrease the rate of wound infection. The use of cephalazolin appears to be associated with an increase in the development of resistant organisms.

Rohde et al⁵ described a retrospective comparative study designed to report the incidence of post-operative spondylodiscitis in 1642 consecutive cases in which no antibiotic prophylaxis was used and to define the value of a collagenous sponge containing gentamicin in preventing disc space infections. No topical or systemic antibiotics were administered in the first 508 patients. A 4 cm × 4 cm collagenous sponge containing 8 mg of gentamicin was placed in the cleared disc space in the subsequent 1134 patients. Surgery was performed for 1584 primary lumbar disc herniations (two-level discectomy in 39 cases, three-level discectomy in one case) and 169 operations for recurrent herniations. In all patients, the erythrocyte sedimentation rate (ESR) was obtained before surgery and on the first day after surgery. Beginning in January 1992, C-reactive protein (CRP) also was analyzed before surgery, one day after surgery, and six days after surgery. All patients were clinically reexamined on days 10-14 after surgery (day of discharge). Final follow-up was at 60 days. In 19 of these 508 patients, a postoperative spondylodiscitis developed, accounting for an incidence rate of 3.7%. None of the 1134 patients receiving antibiotic prophylaxis developed a postoperative spondylodiscitis during the follow-up period of 60 days. Therefore, the incidence of postoperative spondylodiscitis was 0%. Using the Fisher exact test, the difference in the incidence rates between the patient groups with and without antibiotic prophylaxis during lumbar discectomy was highly significant (p < 0.00001). The authors observed no complications related to the use of a collagenous sponge containing gentamicin for antibiotic prophylaxis. The authors concluded that a 3.7% incidence of postoperative spondylodiscitis was found in the absence of prophylactic antibiotics. Gentamicin-containing collagenous sponges placed in the cleared disc space were effective in preventing postoperative spondylodiscitis. This study provides Level III therapeutic evidence that for uncomplicated lumbar microdiscectomy, topical administration of a gentamicin soaked collagen sponge is more effective than placebo in preventing clinically significant discitis.

This clinical guideline should not be construed as including all proper methods of care or excluding or other acceptable methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific procedure or treatment is to be made by the physician and patient in light of all circumstances presented by the patient and the needs and resources particular to the locality or institution

Future Directions for Research

For practical purposes, the North American Spine Society is satisfied to base its recommendations for the use of prophylactic antibiotics on the results of existing data and does not call for a definitive study to be conducted.

If further evidence is sought to strengthen the recommendations above, randomized controlled trials should be conducted that stratify results on specific patient populations, specific comorbidities, clinical conditions (eg, paraplegia), dosing and route of administration.

Efficacy (Mixed Groups) References

1. Barker FG 2nd. Efficacy of prophylactic antibiotic therapy in spinal surgery: a meta-analysis. *Neurosurgery*. Aug 2002;51(2):391-400; discussion 400-391.
2. Pavel A, Smith RL, Ballard A, Larson IJ. Prophylactic antibiotics in elective orthopedic surgery: a prospective study of 1591 cases. *South Med J*. 1977;Suppl 1:50-55.
3. Rubinstein E, Findler G, Amit P, Shaked I. Perioperative prophylactic cephazolin in spinal surgery. A double-blind placebo-controlled trial. *J Bone Joint Surg Br*. Jan 1994;76B(1):99-102.
4. Petignat C, Francioli P, Harbarth S, et al. Cefuroxime prophylaxis is effective in noninstrumented spine surgery: a double-blind, placebo-controlled study. *Spine (Phila Pa 1976)*. Aug 15 2008;33(18):1919-1924.
5. Rohde V, Meyer B, Schaller C, Hassler WE. Spondylodiscitis after lumbar discectomy. Incidence and a proposal for prophylaxis. *Spine (Phila Pa 1976)*. Mar 1 1998;23(5):615-620.

For patients undergoing open spine surgery without spinal implants, does antibiotic prophylaxis result in decreased infection rates compared to patients who do not receive prophylaxis?

Prophylactic antibiotics are suggested to decrease the rate of spinal infections following uninstrumented lumbar spinal surgery.

Grade of Recommendation: B

Petignat et al¹ conducted a prospective, randomized controlled trial assessing the efficacy of one preoperative 1.5 g dose of cefuroxime in preventing surgical site infection after lumbar laminotomy and discectomy for herniated disc. Of the 1237 patients included in the study, 613 received 1.5 g intravenous cefuroxime on induction and 624 received placebo. Presence of infection, as defined by the Centers for Disease Control (CDC) guidelines, was assessed at six weeks, three months and six months. Baseline characteristics were similar in patients allocated to cefuroxime (n = 613) or placebo (n=624). Eight (1.3%) patients in the cefuroxime group and 18 patients (2.8%) in the placebo group developed a surgical site infection (P =0.073). A diagnosis of spondylodiscitis or epidural abscess was made in nine patients in the placebo group, but none in the cefuroxime group (p < 0.01), which corresponded to a number necessary to treat of 69 patients to prevent one of these infections. There were no significant adverse events attributed to either cefuroxime or placebo. Overall surgical site infection rate was 1.3% with antibiotics versus 2.8% with placebo (p=0.073), and discitis rate was 0/613 versus 9/624 (p<0.01), respectively. The authors concluded that a single, preoperative dose of cefuroxime significantly reduces the risk of organ-space infection, most notably spondylodiscitis, after surgery for herniated disc. Cefuroxime is protective against spondylodiscitis. This study provides Level I therapeutic evidence that for uncomplicated lumbar microdiscectomy, a single preoperative 1.5 g dose of cefuroxime is more effective in preventing infection than placebo.

Luer et al² described a retrospective case control study comparing postoperative infections after laminectomy/discectomy to examine variables that may be associated with infection. The antibiotic protocol included a single intravenous dose of 1 g cefazolin with varied timing (within one hour preoperatively, to within two hours, to greater than two hours, to post incision). Infection was confirmed via bacterial cultures. The clinical evaluation for infection was not described. Of the 22 patients with documented wound infection, 12 had received prophylactic antibiotics with 33% (4/12) having received cefazolin within two hours of incision versus 57% (8/14) of the uninfected matched controls, p=0.001. The surgical incision was closed less than two hours after incision in 43% (6/14) of uninfected patients and 17% (2/12) with infection (p<0.001). The authors reported that wound culture data did not indicate infection by organisms resistant to cefazolin. They concluded that the choice of cefazolin appears adequate but administration needs to occur in the appropriate time frame. This small study provides Level III therapeutic evidence that antibiotic prophylaxis with cephalosporin more than two hours prior to incision appears to yield a higher infection rate, and dosing within two hours of incision may improve infection rate.

Piotrowski et al³ performed a retrospective comparative study of 5041 patients, evaluating the rate of postoperative discitis during two time periods: one in which perioperative antibiotics were given, and one in which they were not. During the former, the rate of discitis was 0.6%; during the latter, it was 2.3% (p<0.001). This was statistically significant. There were no other

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reported differences during these two time periods. In critique of this large study, while it was stated that first or second-generation cephalosporin were given, the dosing protocol was not detailed. This study offers Level III therapeutic evidence that perioperative antibiotics lower the infection rate at the level of the disc after lumbar disc surgery.

Rohde et al⁴ described a retrospective comparative study designed to report the incidence of post-operative spondylodiscitis in 1642 consecutive cases in which no antibiotic prophylaxis was used and to define the value of a collagenous sponge containing gentamicin in preventing disc space infections. No topical or systemic antibiotics were administered in the first 508 patients. A 4 cm × 4 cm collagenous sponge containing 8 mg of gentamicin was placed in the cleared disc space in the subsequent 1134 patients. Surgery was performed for 1584 primary lumbar disc herniations (two-level discectomy in 39 cases, three-level discectomy in one case) and 169 operations for recurrent herniations. In all patients, the erythrocyte sedimentation rate (ESR) was obtained before surgery and on the first day after surgery. Beginning in January 1992, C-reactive protein (CRP) also was analyzed before surgery, one day after surgery, and six days after surgery. All patients were clinically reexamined on days 10-14 after surgery (day of discharge). Final follow-up was at 60 days. In 19 of these 508 patients, a postoperative spondylodiscitis developed, accounting for an incidence rate of 3.7%. None of the 1134 patients receiving antibiotic prophylaxis developed a postoperative spondylodiscitis during the follow-up period of 60 days. Therefore, the incidence of postoperative spondylodiscitis was 0%. Using the Fisher exact test, the difference in the incidence rates between the patient groups with and without antibiotic prophylaxis during lumbar discectomy was highly significant ($p < 0.00001$). The authors observed no complications related to the use of a collagenous sponge containing gentamicin

for antibiotic prophylaxis. The authors concluded that a 3.7% incidence of postoperative spondylodiscitis was found in the absence of prophylactic antibiotics. Gentamicin-containing collagenous sponges placed in the cleared disc space were effective in preventing postoperative spondylodiscitis. This study provides Level III therapeutic evidence that for uncomplicated lumbar microdiscectomy, topical administration of a gentamicin soaked collagen sponge is more effective than placebo in preventing clinically significant discitis.

Future Directions for Research

For practical purposes, the North American Spine Society is satisfied to base its recommendations for the use of prophylactic antibiotics on the results of existing data and does not call for a definitive study to be conducted.

If further evidence is sought to strengthen the recommendations above, randomized controlled trials should be conducted that stratify results on specific patient populations, specific comorbidities, clinical conditions (eg, paraplegia), dosing and route of administration.

Efficacy (Noninstrumented) References

1. Petignat C, Francioli P, Harbarth S, et al. Cefuroxime prophylaxis is effective in noninstrumented spine surgery: a double-blind, placebo-controlled study. *Spine (Phila Pa 1976)*. Aug 15 2008;33(18):1919-1924.
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For patients undergoing open spine surgery with spinal implants, does antibiotic prophylaxis result in decreased infection rates as compared to patients who do not receive prophylaxis?

Prophylactic antibiotics may be considered to decrease the rate of infections following instrumented spine fusion.

Grade of Recommendation: C

Rechtine et al¹ described a retrospective case series study of 235 consecutive fracture patients. Of the 235 patients, 117 underwent surgical stabilization. Of the 117 patients, 12 suffered a perioperative infection, two had a staphylococcal infection and 10 had a polymicrobial infection with gram-negative and gram-positive organisms. There was a statistically higher infection rate in completely neurologically injured patients compared to those with no deficit or incomplete injuries. The authors concluded that aggressive and earlier intervention is required in this patient population. In critique, the study was designed to assess the incidence of spinal infection in a spine trauma population and does not state the duration of follow-up. This study provides Level IV therapeutic evidence that the infection rate in instrumented spinal surgery for trauma in patients receiving antibiotic prophylaxis is 10%. With neurologic injury, the infection rate is higher and the infections are polymicrobial. It supports the efficacy of prophylactic antibiotics in instrumented spinal surgery in patients with incomplete cord injury or in spinal fractures without cord injury. However, in the subgroup with spinal cord injury, infections were more likely a result of multiple organisms including gram-negative species. This study raises compelling questions about antibiotic choice for prophylaxis in spinal cord injury patients. This does not answer the question directly but gives epidemiological evidence that instrumented spinal procedures have a higher than expected infection rate and when spinal cord injury occurs the rate is much higher and frequently complicated. This suggests that more varied and comprehensive prophylaxis needs to be undertaken in the specific subsets of spinal trauma and cord injury.

Hellbusch et al² conducted a prospective, randomized controlled trial examining the effects of multiple dosing regimens on the postoperative infection rate in instrumented lumbar spinal fusion. Two hundred sixty-nine patients were randomized into either a preoperative only protocol or preoperative with an extended postoperative antibiotic protocol. Patients in the preoperative only protocol group received a single dose of intravenous cefazolin 1 g or 2 g based on weight 30 minutes before incision. The extended postoperative antibiotic protocol group received the same preoperative dose plus postoperative intravenous cefazolin every eight hours for three days followed by oral cepha-

lexin every six hours for seven days. Because of untoward drug reaction or deviation from the antibiotic protocol, 36 of the 269 patients were eliminated from the study. Therefore, 233 patients completed the entire study; 117 received preoperative antibiotics only, and 116 received pre- and postoperative antibiotics. At 21 days follow-up, there was no significant difference in infection rates between the two antibiotic protocols. The postoperative infection rates were 4.3% for the preoperative only protocol and 1.7% for the preoperative with extended antibiotic protocol. The overall postoperative infection rate was 3%. However, the study did identify five variables that appeared to demonstrate a trend toward increase in infection rate: blood transfusion, electrophysiological monitoring, increased height, increased weight, and increased body mass index. Increased tobacco use trended toward a lower infection rate. Statistical significance was not achieved. The authors concluded that a larger study of 1400 patients would possibly provide more statistically significant information. Although a prospective comparative study by design, for the purpose of this question, this study provides Level IV (case series) evidence that a single dose of cefazolin is as effective as a multiple dosage protocol in lumbar patients undergoing instrumented lumbar procedures when compared to previously reported historical infection rates.

Wimmer et al³ performed a prospective series detailing antibiotic prophylaxis in an instrumented spinal fusion population. There were 110 patients with Cotrel – Doubassait (CD) or Moss Miami instrumentation. Of the 110 patients, 56 were instrumented for painful spondylolisthesis and 54 for scoliosis. Two grams of cefamandole were given preoperatively followed by three postoperative doses of 2 g per day for three days. One infection was reported early in the spondylolisthesis group and one late infection was reported in the scoliosis group. The authors concluded that this prophylactic regimen was effective in decreasing the expected infection rate in this instrumented group. This study offers Level IV therapeutic evidence that perioperative prophylactic antibiotics lowered the infection rates in instrumented spinal surgery when compared to previously reported historical infection rates.

Future Directions for Research

For practical purposes, the North American Spine Society is satisfied to base its recommendations for the use of prophylactic antibiotics on the results of existing data and does not call for a definitive study to be conducted.

If further evidence is sought to strengthen the recommendations above, randomized controlled trials should be conducted that stratify results on specific patient populations, specific comorbidities, clinical conditions (eg, paraplegia), dosing and route of administration.

Efficacy (Instrumented) References

1. Rechtine GR, Bono PL, Cahill D, Bolesta MJ, Chrin AM. Postoperative wound infection after instrumentation of thoracic and lumbar fractures. *J Orthop Trauma*. Nov 2001;15(8):566-569.
2. Hellbusch LC, Helzer-Julien M, Doran SE, et al. Single-dose vs. multiple-dose antibiotic prophylaxis in instrumented lumbar fusion--a prospective study. *Surg Neurol*. Dec 2008;70(6):622-627; discussion 627.
3. Wimmer C, Nogler M, Frischut B. Influence of antibiotics on infection in spinal surgery: A prospective study of 110 patients. *J Spinal Disord*. 1998;11:498-500.

What rate of surgical site infections can be expected with the use of antibiotic prophylaxis, considering both patients with and patients without medical comorbidities?

CONSENSUS STATEMENT: Despite appropriate prophylaxis, the rate of surgical site infections in spine surgery is 0.7% - 10%. The expected rate for patients without comorbidities ranges from 0.7 - 4.3% and for patients with comorbidities ranges from 2.0 - 10%. Current best practice with antibiotic protocols has failed to eliminate (reach an infection rate of 0.0%) surgical site infections.

Chen et al¹ performed a retrospective case control study to determine the role diabetes plays in spinal infection risk. Of the 195 spinal infection patients included in the study, 30 had diabetes and 165 did not. Prophylactic protocols varied and the spinal surgeries were heterogeneous with instrumented and uninstrumented procedures at all levels. Outcomes were reviewed at 30 days for all patients and at one year for patients with fixation. Known risk factors for surgical site infection in spinal surgery were examined: age, gender, tobacco use, body mass index, American Society of Anesthesiologists (ASA) class, intraoperative antibiotic redosing, surgical time, bone allograft use, estimated blood loss (EBL) and drain use. The adjusted relative risk of having diabetes for developing surgical site infection was 4.10 (95% C.I. = 1.37-12.32). Other factors did not appear as risk factors for surgical site infections. The data confirm that diabetes is a risk factor for surgical site infections in spinal arthrodesis surgery. This study provides Level II prognostic evidence that diabetes alone, and not body habitus or other risk factors, increases the risk of infection after spinal surgery.

Hellbusch et al² conducted a prospective, randomized controlled trial examining the effects of multiple dosing regimens on the postoperative infection rate in instrumented lumbar spinal fusion. Two hundred sixty-nine patients were randomized into either a preoperative only protocol or preoperative with an extended postoperative antibiotic protocol. Patients in the pre-

operative only protocol group received a single dose of intravenous cefazolin 1 g or 2 g based on weight 30 minutes before incision. The extended postoperative antibiotic protocol group received the same preoperative dose plus postoperative intravenous cefazolin every eight hours for three days followed by oral cephalexin every six hours for seven days. Because of untoward drug reaction or deviation from the antibiotic protocol, 36 of the 269 patients were eliminated from the study. Therefore, 233 patients completed the entire study; 117 receiving preoperative antibiotics only, and 116 receiving pre- and postoperative antibiotics. At 21 days follow-up, there was no significant difference in infection rates between the two antibiotic protocols. The postoperative infection rates were 4.3% for the preoperative only protocol and 1.7% for the preoperative with extended antibiotic protocol. The overall postoperative infection rate was 3%. However, the study did identify five variables that appeared to demonstrate a trend toward increase in infection rate: blood transfusion, electrophysiological monitoring, increased height, increased weight and increased body mass index. Increased tobacco use trended toward a lower infection rate. Statistical significance was not achieved. The authors concluded that a larger study of 1400 patients would possibly provide more statistically significant information. The overall infection rate even with a prophylaxis was 1.7% - 4.3% with an overall infection rate of 3%. Because the follow-up was not standardized, this potential Level

I study provides Level II prognostic evidence that a 3% infection rate (range: 1.7% - 4.3%) occurs in the face of antibiotic prophylaxis.

Sweet et al³ performed a retrospective comparative study to evaluate the safety and efficacy of adjunctive local application of vancomycin for infection prophylaxis in posterior instrumented thoracic and lumbar spine wounds compared to intravenous cephalexin alone. Since 2000, 1732 consecutive thoracic and lumbar posterior instrumented spinal fusions have been performed with routine 24 hours of perioperative intravenous antibiotic prophylaxis with cephalexin. Since 2006, 911 of these instrumented thoracic and lumbar cases had 2 g of vancomycin powder applied to the wound prior to closure in addition to intravenous antibiotics. A retrospective review for infection rates and complications was performed with an average follow-up of 2.5 years (range: 1-7 years). If wound infection was suspected based on clinical and constitutional symptoms, aspiration was completed. If aspiration demonstrated purulent material or the wound was clinically suspicious for subfascial infection, the wound was explored and aerobic, anaerobic and fungal cultures were obtained. Posterior instrumented thoracic and lumbar fusions were performed in 821 patients using intravenous cephalexin prophylaxis with a total of 21 resulting deep wound infections (2.6%). Coag negative staph was the most commonly isolated organism. Posterior instrumented thoracic and lumbar fusions were performed in 911 patients with intravenous cephalexin plus adjunctive local vancomycin powder with two ensuing deep wound infections (0.2%). The reduction in wound infections was statistically significant ($p < 0.0001$). There were no adverse clinical outcomes or wound complications related to the local application of vancomycin. The authors concluded that adjunctive local application of vancomycin powder decreases the post surgical wound infection rate with statistical significance in posterior instrumented thoracolumbar spine fusions. This study provides Level II prognostic evidence that adjunctive local application of vancomycin powder decreases the post surgical wound infection rate compared with intravenous cephalexin in posterior instrumented thoracolumbar fusion.

Rubinstein et al⁴ performed a prospective, randomized controlled trial to investigate the efficacy of a single dose of 1 g of cephazolin in reducing postoperative infections in patients undergoing 'clean' operations on the lumbar spine. Of the 141 patients included in the study, 70 received 1 g intravenous cephazolin upon arrival to the operative room (approximately two hours prior to surgery) and 71 received placebo. Presence of infection was assessed at 30 days, with surgical site infection defined as drainage of purulent material from the operative site and a positive bacteriological culture, or inflammation of an area more than 20 mm in diameter; for urinary tract infection, more than 100,000 colony forming units/mL on culture; and for pneumonia, the clinical diagnosis was made by the treating physician. There were 21 wound or urinary infections in the 71 patients who received placebo and nine in the 70 who received cephazolin ($p < 0.05$). Nine patients (12.7%) who received placebo and three (4.3%) who received cephazolin developed wound infections ($p = 0.07$). All but three of the infections in the placebo group were confirmed by bacterial culture. All the organisms isolated from the patients who received placebo (except the group-D strepto-

cocci which are inherently resistant) were sensitive to cephazolin whereas in the cephazolin prophylactic group 43% of the organisms isolated were resistant or had reduced sensitivity to the drug. The authors concluded that the administration of a single dose of cephazolin preoperatively is recommended for patients undergoing lumbar spinal surgery. In critique, the sample size was small and the study's follow-up period was short. In addition, the authors expanded the definition of infection to include wound, urinary tract infection and pneumonia in order to achieve statistical significance. Due to these limitations, this potential Level I study provides Level II prognostic evidence that the rate of infection with appropriate prophylaxis is 4.3%. For uncomplicated lumbar microdiscectomy, a single preoperative dose (1 g) of cephazolin is more effective than placebo in minimizing infection.

Kanayama et al⁵ performed a retrospective comparative study reviewing the rate of surgical site infections in lumbar spine surgeries for two different antibiotic prophylaxis protocols. One group received a preoperative dose and redosing at three hours, and the second group received a prolonged postoperative dosing regimen. A first-generation cephalosporin was administered unless the patient had a history of a significant allergy such as anaphylactic shock, systemic skin eruption, or toxic liver dysfunction. Postoperative-dose group patients received antibiotics for five to seven days after surgery. No postoperative-dose group patients received antibiotics only on the day of surgery; antibiotics were given 30 minutes before skin incision. An additional dose was administered every three hours to maintain therapeutic levels throughout surgery. The rate of surgical site infection was compared between the two prophylaxis groups. At a maximum of six months, a positive wound culture and/or typical infectious signs including a purulent exudate, surrounding erythema, and wound fluctuance detected infections. Laboratory studies were also referenced, such as prolonged elevation in the C-reactive protein value. There were 1133 patients in the postoperative-dose group and 464 patients in the no postoperative-dose group. The rate of instrumentation surgery was not statistically different between the postoperative-dose group (43%) and the no postoperative-dose group (39%). The overall rate of surgical site infection was 0.7%. The infection rate was 0.8% in the postoperative-dose group and 0.4% in the no postoperative-dose group; the difference between the two was not significant. It is important to note that the rate of SSI was determined according to the number of wound infections requiring additional surgical interventions; thus, the rate of surgical site infection necessarily was underestimated in this study. Regarding the organisms of surgical site infection, resistant strains of bacteria were cultured in five (83.3%) of six patients in the postoperative-dose group, whereas none was cultured in the no postoperative-dose group. This study provides Level II prognostic evidence that despite many different regimens of prophylaxis, the best achieved infection rate was 0.7%.

Olsen (2003) et al⁶ performed a retrospective case control study to identify the specific independent risk factors for surgical site infections occurring after laminectomy or spinal fusion. All patient received standard prophylaxis with cephalosporin or vancomycin in penicillin sensitive patients. Infection was defined using the CDC guideline definition, with infections identi-

fied between two and 83 days (median time from surgery to infection was 14 days). Of the 53 of 1918 patients who experienced surgical site infections, 12 were excluded due to missing data. These patients were compared with 179 noninfected matched controls. Infection rate even with prophylaxis was 2.76% with no significant variation in the infection rate during the four-year period. The authors identified postoperative incontinence, obesity, tumor resection and posterior approach as risk factors. This study provides Level III prognostic evidence that incontinence (resulting from neurologic injury), obesity, tumor resection (related to neurologic deficits) and posterior approach increase risk of infection. In the face of antibiotic prophylaxis with all comers and comorbidities represented, a 2.76% infection rate can be expected.

Olsen (2008) et al⁷ described a retrospective case control study designed to determine independent risk factors for surgical site infection following orthopedic spinal operations. All patient received standard prophylaxis with cephalosporin or vancomycin in penicillin sensitive patients. Of 2316 patients, 46 patients with superficial, deep or organ-space surgical site infections were identified and compared with 227 uninfected control patients. The overall rate of spinal surgical site infection during the five years of the study was 2.0% (46/2316). Univariate analyses showed serum glucose levels, preoperatively and within five days after the operation, to be significantly higher in patients in whom surgical site infection developed than in uninfected control patients. Independent risk factors for surgical site infection that were identified by multivariate analysis were diabetes (odds ratio = 3.5, 95% confidence interval = 1.2, 10.0), suboptimal timing of prophylactic antibiotic therapy (odds ratio = 3.4, 95% confidence interval = 1.5, 7.9), a preoperative serum glucose level of >125 mg/dL (>6.9 mmol/L) or a postoperative serum glucose level of >200 mg/dL (>11.1 mmol/L) (odds ratio = 3.3, 95% confidence interval = 1.4, 7.5), obesity (odds ratio = 2.2, 95% confidence interval = 1.1, 4.7), and two or more surgical residents participating in the operative procedure (odds ratio = 2.2, 95% confidence interval = 1.0, 4.7). A decreased risk of surgical site infection was associated with operations involving the cervical spine (odds ratio = 0.3, 95% confidence interval = 0.1, 0.6). The authors concluded that diabetes was associated with the highest independent risk of spinal surgical site infection, and an elevated preoperative or postoperative serum glucose level was also independently associated with an increased risk of surgical site infection. The role of hyperglycemia as a risk factor for surgical site infection in patients not previously diagnosed with diabetes should be investigated further. Administration of prophylactic antibiotics within one hour before the operation and increasing the antibiotic dosage to adjust for obesity are also important strategies to decrease the risk of surgical site infection after spinal operations. This study provides Level III prognostic evidence that infection occurred at a 2% overall rate in all patients in the face of prophylactic antibiotics.

Rechtine et al⁸ described a retrospective case control study of 235 consecutive fracture patients. Of the 235 patients, 117 underwent surgical stabilization. Of the 117 patients, 12 suffered a perioperative infection; two had a staphylococcal infection, and 10 had a polymicrobial infection with gram-negative and gram-positive organisms. There was a statistically higher infection rate

in completely neurologically injured patients compared to those with no deficit or incomplete injuries. The authors concluded that aggressive and earlier intervention is required in this patient population. In critique, the study was designed to assess the incidence of spinal infection in a spine trauma population and does not state the duration of follow-up. It offers Level III prognostic evidence the infection rate in spinal surgery for trauma in patients receiving antibiotic prophylaxis is 10%. With neurologic injury, the infection rate is higher and the infections are polymicrobial. The critical evidence is the epidemiologic fact that polymicrobial infections are most common in the neurologically injured as opposed to non-injured patients and antibiotic selection to include gram-negative coverage in this subset should be considered.

Fang et al⁹ reported a retrospective case control study analyzing preoperative and intraoperative risk factors for spinal infection after surgery, with characterization of the nature and timing of the infections. A first generation cephalosporin was given unless the patient had a history of a significant allergy, in which case vancomycin was given. Antibiotics were redosed during prolonged cases (greater than six hours) or after significant blood loss. Antibiotics were continued for 48 hours after the procedure, except for simple decompressions, which only received antibiotics until discharge. A review of three month follow-up data on 1629 procedures performed on 1095 patients revealed that a postoperative infection developed in 48 patients (4.4%). Data regarding preoperative and intraoperative risk factors were gathered from patient charts for these and a randomly selected control group of 95 uninfected patients. For analysis, these patient groups were further divided into adult and pediatric subgroups, with an age cutoff of 18 years. Preoperative risk factors reviewed included smoking, diabetes, previous surgery, previous infection, steroid use, body mass index and alcohol abuse. Intraoperative factors reviewed included staging of procedures, estimated blood loss, operating time and use of allograft or instrumentation. The majority of infections occurred during the early postoperative period (less than three months). Age greater than 60 years, smoking, diabetes, previous surgical infection, increased body mass index and alcohol abuse were statistically significant preoperative risk factors. The most likely procedure to be complicated by an infection was a combined anterior/posterior spinal fusion performed in a staged manner under separate anesthesia. Infections were primarily monomicrobial, although five patients had more than four organisms identified. The most common organism cultured from the wounds was *Staphylococcus aureus*. All patients were treated with surgical irrigation and debridement and appropriate antibiotics to treat the cultured organism. The authors concluded that the 4.4% infection risk in patients with diabetes requires aggressive treatment of patients undergoing complex or prolonged spinal procedures to prevent and treat infections. Understanding a patient's preoperative risk factors may help the physician to optimize a patient's preoperative condition. Additionally, awareness of critical intraoperative parameters will help to optimize surgical treatment. It may be appropriate to increase the duration of prophylactic antibiotics or implement other measures to decrease the incidence of infection for high risk patients. Because of lack of standardized follow-up, this potential Level III study provides Level IV evi-

dence that diabetes is a specific risk factor for infection in instrumented lumbar fusion patients.

Liao et al¹⁰ described a retrospective case control study examining infection risk in patients with diabetes undergoing instrumented lumbar fusion. Intravenous cefamezine (500 mg) was administered 30 minutes before surgery and the antibiotics were continued for three days (intravenous cefamezine 500 mg every six hours). Spinal procedures that became infected after surgery were analyzed to identify the significance of preoperative and intraoperative risk factors. Characterization of the nature and timing of the infections was also performed. Of 337 patients who underwent posterior spinal instrumented fusion between 1995 and 1997, 39 were diabetic. Plasma glucose concentration, body mass index, type of instrument, operation time, blood loss, hospital stay and complications were recorded. The pathogenic organism and treatments for infection were also described. Wound infection characterized by wound erythematous changes, partial wound dehiscence with purulent discharge and wound culture data was obtained from the charts at one year minimum follow-up (average 2.75 years). The rate of wound infection in diabetic patients was 10.3% compared with 0.7% in non-diabetic patients ($p = 0.003$). Body mass index and preoperative blood sugar were also significantly different between the two groups ($p = 0.02$, $p < 0.001$). The authors concluded that patients with a diabetic history or preoperative hyperglycemia had a higher infection rate after posterior spinal instrumented fusion when compared with non-diabetic patients. Due to the small sample size of patients not enrolled at the same point in their disease, this potential Level III study provides Level IV prognostic evidence that diabetic history or hyperglycemia preoperatively increases the risk of infection in complex spinal surgery.

Mastronardi (2005) et al¹¹ reported a retrospective comparative study evaluating the efficacy of two intraoperative antibiotic prophylaxis protocols in a large series of lumbar microdiscectomies performed in two different neurosurgical centers. Of the 1167 patients included in the study, 450 received a single intravenous dose of cefazoline 1 g at induction of general anesthesia (Group A) and 717 received a single dose of intravenous ampicillin 1 g and sulbactam 500 mg at induction of anesthesia (Group P). At six months, a diagnosis of postoperative spondylodiscitis was made in three out of 450 patients in Group A (0.67%) and in five out of 717 patients in Group P (0.69%). In all cases, treatment consisted of rigid thoracolumbar orthosis and four to six week administration of amoxicillin/clavulanate compound (500/125 mg). The authors concluded that the low incidence of postoperative spondylodiscitis obtained with both protocols seems to confirm that intraoperative antibiotic prophylaxis is associated with the same rate of discitis seen with prolonged prophylaxis still adopted in many centers, but is more advantageous both in terms of welfare and comfort for patients and in economic terms. However, at the moment it is not possible to identify the ideal antibiotic for this purpose. A 0.7% infection risk can be expected despite prophylaxis. Although a comparative study by design, this study provides Level IV (case series) prognostic evidence that a 0.7% infection rate can be expected despite prophylactic antibiotic use.

Mastronardi (2004) et al¹² presented a retrospective case series evaluating the safety and efficacy of a specific intraoperative

antibiotic protocol for a variety of spinal surgeries. Over a three year period 973 patients received 1.5 g intravenous ampicillin/sulbactam on induction or intravenous 400 mg Teicoplanin on induction (if surgery longer than two hours) with redosing of teicoplanin at four hours or 1500 mL blood loss. Data was gathered at six weeks to one year regarding drainage from the wound, wound abscess or positive culture. Wound infection occurred in nine cases (1%) and discitis in four of 657 (0.06%) patients. This study provides Level IV prognostic evidence that a 1% infection rate with 0.6% rate of discitis can be expected despite the use of prophylaxis.

Despite appropriate prophylaxis, diabetes carries an increased infection rate compared with non-diabetic patients.

Level of Evidence: III

Chen et al¹ performed a retrospective case control study to determine the role diabetes plays in spinal infection risk. Of the 195 spinal infection patients included in the study, 30 had diabetes and 165 did not. Prophylactic protocols varied and the spinal surgeries were heterogeneous with instrumented and uninstrumented procedures at all levels. Outcomes were reviewed at 30 days for all patients and at one year for patients with fixation. Known risk factors for surgical site infection in spinal surgery were examined: age, gender, tobacco use, body mass index, American Society of Anesthesiologists (ASA) class, intraoperative antibiotic redosing, surgical time, bone allograft use, estimated blood loss (EBL) and drain use. The adjusted relative risk of having diabetes for developing surgical site infection was 4.10 (95% C.I. = 1.37–12.32). Other factors did not appear as risk factors for surgical site infections. The data confirm that diabetes is a risk factor for surgical site infections in spinal arthrodesis surgery. This study provides Level II prognostic evidence that diabetes alone, and not body habitus or other risk factors, increases the risk of infection after spinal surgery.

Olsen (2008) et al⁷ described a retrospective case control study designed to determine independent risk factors for surgical site infection following orthopedic spinal operations. All patient received standard prophylaxis with cephalosporin or vancomycin in penicillin sensitive patients. Of 2316 patients, 46 patients with superficial, deep or organ-space surgical site infections were identified and compared with 227 uninfected control patients. The overall rate of spinal surgical site infection during the five years of the study was 2.0% (46/2316). Univariate analyses showed serum glucose levels, preoperatively and within five days after the operation, to be significantly higher in patients in whom surgical site infection developed than in uninfected control patients. Independent risk factors for surgical site infection that were identified by multivariate analysis were diabetes (odds ratio = 3.5, 95% confidence interval = 1.2, 10.0), suboptimal timing of prophylactic antibiotic therapy (odds ratio = 3.4, 95% confidence interval = 1.5, 7.9), a preoperative serum glucose level of >125 mg/dL (>6.9 mmol/L) or a postoperative serum glucose level of >200 mg/dL (>11.1 mmol/L) (odds ratio

= 3.3, 95% confidence interval = 1.4, 7.5), obesity (odds ratio = 2.2, 95% confidence interval = 1.1, 4.7), and two or more surgical residents participating in the operative procedure (odds ratio = 2.2, 95% confidence interval = 1.0, 4.7). A decreased risk of surgical site infection was associated with operations involving the cervical spine (odds ratio = 0.3, 95% confidence interval = 0.1, 0.6). The authors concluded that diabetes was associated with the highest independent risk of spinal surgical site infection, and an elevated preoperative or postoperative serum glucose level was also independently associated with an increased risk of surgical site infection. The role of hyperglycemia as a risk factor for surgical site infection in patients not previously diagnosed with diabetes should be investigated further. Administration of prophylactic antibiotics within one hour before the operation and increasing the antibiotic dosage to adjust for obesity are also important strategies to decrease the risk of surgical site infection after spinal operations. This study provides Level III prognostic evidence that diabetes is the highest independent risk factor, and infection occurred at a 2% overall rate in all patients in the face of prophylactic antibiotics.

Fang et al⁹ reported a retrospective case control study analyzing preoperative and intraoperative risk factors for spinal infection after surgery, with characterization of the nature and timing of the infections. A first generation cephalosporin was given unless the patient had a history of a significant allergy, in which case vancomycin was given. Antibiotics were redosed during prolonged cases (greater than six hours) or after significant blood loss. Antibiotics were continued for 48 hours after the procedure, except for simple decompressions, which only received antibiotics until discharge. A review of three month follow-up data on 1629 procedures performed on 1095 patients revealed that a postoperative infection developed in 48 patients (4.4%). Data regarding preoperative and intraoperative risk factors were gathered from patient charts for these and a randomly selected control group of 95 uninfected patients. For analysis, these patient groups were further divided into adult and pediatric subgroups, with an age cutoff of 18 years. Preoperative risk factors reviewed included smoking, diabetes, previous surgery, previous infection, steroid use, body mass index and alcohol abuse. Intraoperative factors reviewed included staging of procedures, estimated blood loss, operating time and use of allograft or instrumentation. The majority of infections occurred during the early postoperative period (less than three months). Age greater than 60 years, smoking, diabetes, previous surgical infection, increased body mass index and alcohol abuse were statistically significant preoperative risk factors. The most likely procedure to be complicated by an infection was a combined anterior/posterior spinal fusion performed in a staged manner under separate anesthesia. Infections were primarily monomicrobial, although five patients had more than four organisms identified. The most common organism cultured from the wounds was *Staphylococcus aureus*. All patients were treated with surgical irrigation and debridement and appropriate antibiotics to treat the cultured organism. The authors concluded that the 4.4% infection risk in patients with diabetes requires aggressive treatment of patients undergoing complex or prolonged spinal procedures to prevent and treat infections. Understanding a patient's preoperative risk factors may help the physician to optimize a patient's preopera-

tive condition. Additionally, awareness of critical intraoperative parameters will help to optimize surgical treatment. It may be appropriate to increase the duration of prophylactic antibiotics or implement other measures to decrease the incidence of infection for high risk patients. Because of lack of standardized follow-up, this potential Level III study provides Level IV evidence that diabetes is a specific risk factor for infection in instrumented lumbar fusion patients.

Liao et al¹⁰ described a retrospective case control study examining infection risk in patients with diabetes undergoing instrumented lumbar fusion. Intravenous cefamezine (500 mg) was administered 30 minutes before surgery and the antibiotics were continued for three days (intravenous cefamezine 500 mg every six hours). Spinal procedures that became infected after surgery were analyzed to identify the significance of preoperative and intraoperative risk factors. Characterization of the nature and timing of the infections was also performed. Of 337 patients who underwent posterior spinal instrumented fusion between 1995 and 1997, 39 were diabetic. Plasma glucose concentration, body mass index, type of instrument, operation time, blood loss, hospital stay and complications were recorded. The pathogenic organism and treatments for infection were also described. Wound infection characterized by wound erythematous changes, partial wound dehiscence with purulent discharge and wound culture data was obtained from the charts at one year minimum follow-up (average 2.75 years). The rate of wound infection in diabetic patients was 10.3% compared with 0.7% in non-diabetic patients ($p = 0.003$). Body mass index and preoperative blood sugar were also significantly different between the two groups ($p = 0.02$, $p < 0.001$). The authors concluded that patients with a diabetic history or preoperative hyperglycemia had a higher infection rate after posterior spinal instrumented fusion when compared with non-diabetic patients. Due to the small sample size of patients not enrolled at the same point in their disease, this potential Level III study provides Level IV prognostic evidence that diabetic history or hyperglycemia preoperatively increases the risk of infection in complex spinal surgery.

There is insufficient evidence to make a statement regarding the impact of obesity on the rate of surgical site infection in prophylaxed patients.

Level of Evidence: I (Insufficient)

Chen et al¹ performed a retrospective case control study to determine the role that diabetes and other risk factors play in the development of surgical site infection in spinal surgery patients. Of the 195 spinal infection patients included in the study, 30 had diabetes and 165 did not. Prophylactic protocols varied and the spinal surgeries were heterogeneous with instrumented and uninstrumented procedures at all levels. Outcomes were reviewed at 30 days for all patients and at one year for patients with fixation. In addition to diabetes, known risk factors for surgical site infection in spinal surgery were examined including: age, gender, tobacco use, body mass index >35 (morbid obesity), American

Society of Anesthesiologists (ASA) class >3, intraoperative antibiotic redosing, surgical time, bone allograft use, estimated blood loss (EBL) and drain use. The adjusted relative risk of having diabetes for developing surgical site infection was significant (RR 4.10, 95% C.I. = 1.37–12.32); however, the other factors did not appear as significant risk factors in univariate or multivariate analysis. This study provides Level II prognostic evidence that diabetes alone, and not body habitus or other risk factors, increases the risk of infection after spinal surgery.

Olsen (2003) et al⁶ performed a retrospective case control study to identify the specific independent risk factors for surgical site infections occurring after laminectomy or spinal fusion. All patients received standard prophylaxis with cephalosporin or vancomycin in penicillin sensitive patients. Infection was defined using the CDC guideline definition, with infections identified between two and 83 days (median time from surgery to infection was 14 days). Of the 53/1918 patients who experienced surgical site infections, 12 were excluded due to missing data. These patients were compared with 179 noninfected matched controls. Infection rate even with prophylaxis was 2.76% with no significant variation in the infection rate during the four-year period. Through multivariate analysis, the authors identified postoperative incontinence, morbid obesity, tumor resection and posterior approach as independent risk factors for the development of surgical site infection. This study provides Level III prognostic evidence that morbid obesity is associated with a fivefold increased risk of surgical site infection after spinal surgery (OR 5.2, 95% C.I.=1.9-14.2).

Olsen (2008) et al⁷ described a retrospective case control study designed to determine independent risk factors for surgical site infection following orthopedic spinal operations. All patients received standard prophylaxis with cephalosporin or vancomycin in penicillin sensitive patients. Of 2316 patients, 46 patients with superficial, deep or organ-space surgical site infections were identified and compared with 227 uninfected control patients. The overall rate of spinal surgical site infection during the five years of the study was 2.0% (46/2316). Independent risk factors for surgical site infection that were identified by multivariate analysis were diabetes (odds ratio = 3.5, 95% confidence interval = 1.2, 10.0), suboptimal timing of prophylactic antibiotic therapy (odds ratio = 3.4, 95% confidence interval = 1.5, 7.9), a preoperative serum glucose level of >125 mg/dL (>6.9 mmol/L) or a postoperative serum glucose level of >200 mg/dL (>11.1 mmol/L) (odds ratio = 3.3, 95% confidence interval = 1.4, 7.5), obesity (odds ratio = 2.2, 95% confidence interval = 1.1, 4.7), and two or more surgical residents participating in the operative procedure (odds ratio = 2.2, 95% confidence interval = 1.0, 4.7). A decreased risk of surgical site infection was associated with operations involving the cervical spine (odds ratio = 0.3, 95% confidence interval = 0.1, 0.6). The authors suggest that increasing the antibiotic dosage to adjust for obesity is an important strategy to decrease the risk of surgical site infection after spinal operations. This study provides Level III prognostic evidence that obesity is an independent risk factor for surgical site infection in spinal surgery patients, and infection occurred at a 2% overall rate in all patients in the face of prophylactic antibiotics.

Fang et al⁹ reported a retrospective case control study analyzing preoperative and intraoperative risk factors for spinal infec-

tion after surgery, with characterization of the nature and timing of the infections. A first generation cephalosporin was given unless the patient had a history of a significant allergy, in which case vancomycin was given. Antibiotics were redosed during prolonged cases (greater than six hours) or after significant blood loss. Antibiotics were continued for 48 hours after the procedure, except for simple decompressions, which only received antibiotics until discharge. A review of three month follow-up data on 1629 procedures performed on 1095 patients revealed that a postoperative infection developed in 48 patients (4.4%). Data regarding preoperative and intraoperative risk factors were gathered from patient charts for these and a randomly selected control group of 95 uninfected patients. For analysis, these patient groups were further divided into adult and pediatric subgroups, with an age cutoff of 18 years. Preoperative risk factors reviewed included smoking, diabetes, previous surgery, previous infection, steroid use, body mass index and alcohol abuse. Intraoperative factors reviewed included staging of procedures, estimated blood loss, operating time and use of allograft or instrumentation. The majority of infections occurred during the early postoperative period (less than three months). Age greater than 60 years, smoking, diabetes, previous surgical infection and alcohol abuse were statistically significant preoperative risk factors. Infected patients also had increased BMI in comparison to control patients; however, this factor was not statistically significant when pediatric patients were excluded from the analysis. The most likely procedure to be complicated by an infection was a combined anterior/posterior spinal fusion performed in a staged manner under separate anesthesia. Infections were primarily monomicrobial, although five patients had more than four organisms identified. The most common organism cultured from the wounds was *Staphylococcus aureus*. All patients were treated with surgical irrigation and debridement and appropriate antibiotics to treat the cultured organism. Understanding a patient's preoperative risk factors may help the physician to optimize a patient's preoperative condition. Additionally, awareness of critical intraoperative parameters will help to optimize surgical treatment. It may be appropriate to increase the duration of prophylactic antibiotics or implement other measures to decrease the incidence of infection for high risk patients. Because of lack of standardized follow-up, this potential Level III study provides Level IV evidence that age greater than 60 years, smoking, diabetes, previous surgical infection and alcohol abuse are statistically significant preoperative risk factors for infection in instrumented lumbar fusion patients; however, increased BMI did not prove to be a significant risk factor when analyzing adult patients only.

Liao et al¹⁰ described a retrospective case control study examining infection risk in patients with diabetes undergoing instrumented lumbar fusion. Intravenous cefamezine (500 mg) was administered 30 minutes before surgery and the antibiotics were continued for three days (intravenous cefamezine 500 mg every six hours). Spinal procedures that became infected after surgery were analyzed to identify the significance of preoperative and intraoperative risk factors. Of 337 patients who underwent posterior spinal instrumented fusion between 1995 and 1997, 39 were diabetic. Plasma glucose concentration, body mass index, type of instrument, operation time, blood loss, hospital stay and com-

plications were recorded. When comparing preoperative patient characteristics, mean body mass index was significantly higher in the diabetic group versus non-diabetic group, 27.11 vs. 25.59, $p=0.02$, respectively. Diabetic patients also had significantly higher preoperative blood sugar levels ($p<0.001$). Wound infection characterized by wound erythematous changes, partial wound dehiscence with purulent discharge and wound culture data was obtained from the charts at one year minimum follow-up (average 2.75 years). The rate of wound infection in diabetic patients was 10.3% compared with 0.7% in non-diabetic patients ($p = 0.003$). The authors concluded that patients with a diabetic history or preoperative hyperglycemia had a higher infection rate after posterior spinal instrumented fusion when compared with non-diabetic patients. Due to the small sample size of patients not enrolled at the same point in their disease, this potential Level III study provides Level IV prognostic evidence that diabetic history or hyperglycemia preoperatively increases the risk of infection in complex spinal surgery.

Future Directions for Research

For purposes of comparative effectiveness, well-designed prognostic studies defining the rate of surgical site infections in patients with and without comorbidities need to be performed.

To optimize outcomes for patients with comorbidities, evidence is needed regarding specific antibiotic regimens, dosing and route of administration for patients with comorbidities.

Rate of Surgical Site Infections References

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B. Protocol

For patients receiving antibiotic prophylaxis prior to open spine surgery, what are the recommended drugs, their dosages, administration routes and timing resulting in decreased postoperative infection rates?

Preoperative antibiotic prophylaxis is suggested to decrease infection rates in patients undergoing spine surgery. In typical, uncomplicated spinal procedures, the superiority of one agent, dose or route of administration over any other has not been clearly demonstrated. When determining the appropriate drug choice, the patient's risk factors, allergies, length and complexity of the procedure and issues of antibiotic resistance should be considered.

Grade of Recommendation: B

Petignat et al¹ conducted a prospective, randomized controlled trial assessing the efficacy of one preoperative 1.5 g dose of cefuroxime in preventing surgical site infection after lumbar laminotomy and discectomy for herniated disc. Of the 1237 patients included in the study, 613 received 1.5 g intravenous cefuroxime on induction and 624 received placebo. Presence of infection, as defined by the Centers for Disease Control (CDC) guidelines, was assessed at six weeks, three months and six months. Baseline characteristics were similar in patients allocated to cefuroxime (n = 613) or placebo (n=624). Eight (1.3%) patients in the cefuroxime group and 18 patients (2.8%) in the placebo group developed a surgical site infection (p =0.073). A diagnosis of spondylodiscitis or epidural abscess was made in nine patients in the placebo group, but none in the cefuroxime group (p < 0.01), which corresponded to a number necessary to treat of 69 patients to prevent one of these infections. There were no significant adverse events attributed to either cefuroxime or placebo. Overall surgical site infection rate was 1.3% with antibiotics versus 2.8% with placebo (p=0.073), and discitis rate was 0/613 versus 9/624 (p<0.01), respectively. The authors concluded that a single, preoperative dose of cefuroxime significantly reduces the risk of organ-space infection, most notably spondylodiscitis, after surgery for herniated disc. Cefuroxime is protective against spondylodiscitis. This study provides Level I therapeutic evidence that for uncomplicated lumbar microdiscectomy, a single preoperative 1.5 g dose of cefuroxime relative to placebo,

with a documented trend for reduced post op infection and significantly reduces the incidence of spondylodiscitis specifically.

Barker et al² performed a retrospective meta-analysis of 451 prophylaxed patients compared with 392 controls to examine the efficacy of antibiotic prophylaxis in spinal surgery combining orthopaedic and neurosurgery trials (one spinal trial, four neurosurgical trials, one orthopedic trial). Types of prophylaxis and protocols varied across the 451 patients receiving prophylaxis. Duration of follow-up varied with infection confirmed by masked observer assessment of bacteriological cultures and presence of purulent draining. All six trials reported lower infection rates but significance was not achieved for any one trial (odds ration=0-0.74), p values ranged from 0.07 to 1.0. On meta-analysis, the random effects model demonstrated significant effects for efficacy, with an odds ratio of 0.37 (0.17-0.78, p<0.01). The fixed effects model yielded similar results (odds ratio=0.35, p<0.006). Three trials used antibiotics with both gram-positive and gram-negative coverage and three trials used gram-positive coverage alone. There was no evidence of different treatment effects with the inclusion of gram-negative coverage. Investigation of the optimal timing of administration was not possible. The authors concluded that prophylactic antibiotic therapy for spinal operations is effective under a wide range of clinical conditions. No difference in the efficacies of differing antibiotic regimens was observed, provided at least one preoperative dose of gram-positive coverage was administered. Investigation of optimal

This clinical guideline should not be construed as including all proper methods of care or excluding or other acceptable methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific procedure or treatment is to be made by the physician and patient in light of all circumstances presented by the patient and the needs and resources particular to the locality or institution

timing of administration was not possible. This study provides Level II therapeutic evidence that prophylactic antibiotic therapy with gram-positive coverage is effective in reducing the risk of infection after spinal surgery. The superiority of one agent or regimen was not demonstrated.

Pons et al³ described a prospective, randomized trial comparing perioperative antibiotic protocols that included either 2 g ceftizoxime or 1 g vancomycin plus 80 mg gentamicin in 291 patients who underwent various clean spine surgeries. Of the 291 patients, 142 received ceftizoxime and 149 vancomycin/gentamicin one hour prior to incision. Infections were confirmed using bacterial cultures for deep infections, urinary tract infection, or catheter infections; pneumonia diagnosed by purulent sputum and/or new infiltrate on CXR; and cellulitis was diagnosed by presence of spreading induration or erythema. Primary infections were reported in 2.8% (4/142) of the ceftizoxime patients and 2.7% (4/149) of the vancomycin-gentamicin patients. Secondary infections were reported in 4.2% (6/142) and 4.0% (6/149) patients, respectively. The authors concluded that the design of the trial does not allow for statistical analysis of subgroups, however, an overview of the data does not suggest a relationship between postoperative infection and any of the technical or clinical variables. Ceftizoxime is less toxic than vancomycin/gentamicin and equally as effective in preventing infections after clean neurosurgical procedures. Because the study design does not permit subgroup analysis, this potential Level I study provides Level II evidence that ceftizoxime and vancomycin-gentamicin are equally effective in reducing infections with ceftizoxime being less toxic. However, the study was not designed for subgroup analysis. The superiority of one agent or regimen was not demonstrated.

Rubinstein et al⁴ performed a prospective, randomized controlled trial to investigate the efficacy of a single dose of 1 g of cephazolin in reducing postoperative infections in patients undergoing 'clean' operations on the lumbar spine. Of the 141 patients included in the study, 70 received 1 g intravenous cephalosporin upon arrival to the operative room (approximately two hours prior to surgery) and 71 received placebo. Presence of infection was assessed at 30 days, with surgical site infection defined as drainage of purulent material from the operative site and a positive bacteriological culture, or inflammation of an area more than 20 mm in diameter; for urinary tract infection, more than 100,000 colony forming units/mL on culture; and for pneumonia, the clinical diagnosis was made by the treating physician. There were 21 wound or urinary infections in the 71 patients who received placebo and nine in the 70 who received cephazolin ($p < 0.05$). Nine patients (12.7%) who received placebo and three (4.3%) who received cephazolin developed wound infections ($p = 0.07$). All but three of the infections in the placebo group were confirmed by bacterial culture. All the organisms isolated from the patients who received placebo (except the group-D streptococci which are inherently resistant) were sensitive to cephazolin whereas in the cephazolin prophylactic group 43% of the organisms isolated were resistant or had reduced sensitivity to the drug. The authors concluded that the administration of a single dose of cephazolin preoperatively is recommended for patients undergoing lumbar spinal surgery. In critique, the sample size was small and the study's follow-up

period was short. In addition, the authors expanded the definition of infection to include wound, urinary tract infection and pneumonia in order to achieve statistical significance. Due to these limitations, this potential Level I study provides Level II therapeutic evidence that for uncomplicated spine surgery, a single preoperative dose of cephazolin decreases infection rate; however, it does not significantly decrease the rate of wound infection. The use of cephazolin appears to be associated with an increase in development of resistant organisms.

Dobzyniak et al⁵ described a retrospective comparative study examining the efficacy of single versus multiple dosing for lumbar disc surgery. The antibiotics used for prophylaxis consisted of cephazolin 1 g, 525 patients; clindamycin 600 mg, 15 patients; vancomycin 1 g plus clindamycin 600 mg, 46 patients; and vancomycin 1 g alone, 24 patients. The choice of an antibiotic other than cephazolin was based on a patient allergy to penicillin or cephalosporin and surgeons preference when these allergies were encountered. Of the 635 consecutive patients included in the study, 418 received the multidose regimen, 192 received the single dose and 25 patients were eliminated from the study as no preoperative dose was documented. Infection was confirmed at six weeks via cultures and attending physician's assessment. The infection rate was 1.56% (3/192) with single dosing versus 1.20% (5/418) with multiple dosing, $p=0.711$, Fisher exact test. The authors concluded that a single preoperative dose of prophylactic antibiotics is as effective as preoperative plus postoperative antibiotics in the prevention of wound infections in lumbar disc surgery. They recommend preoperative antibiotics alone, citing no advantage in prolonging a patient's discharge following lumbar disc excision to administer postoperative antibiotics. This study provides Level III therapeutic evidence that single dosing is as effective as multiple dosing; however, different antibiotics do not appear to affect the rate of wound infection. The superiority of one agent or regimen was not demonstrated.

Hellbusch et al⁶ conducted a prospective, randomized controlled trial examining the effects of multiple dosing regimens on the postoperative infection rate in instrumented lumbar spinal fusion. Two hundred sixty-nine patients were randomized into either a preoperative only protocol or preoperative with an extended postoperative antibiotic protocol. Patients in the preoperative only protocol group received a single dose of intravenous cefazolin 1 g or 2 g based on weight 30 minutes before incision. The extended postoperative antibiotic protocol group received the same preoperative dose plus postoperative intravenous cefazolin every eight hours for three days followed by oral cephalexin every six hours for seven days. Because of untoward drug reaction or deviation from the antibiotic protocol, 36 of the 269 patients were eliminated from the study. Therefore, 233 patients completed the entire study; 117 received preoperative antibiotics only and 116 received pre- and postoperative antibiotics. At 21 days follow-up, there was no significant difference in infection rates between the two antibiotic protocols. The postoperative infection rates were 4.3% for the preoperative only protocol and 1.7% for the preoperative with extended antibiotic protocol. The overall postoperative infection rate was 3%. However, the study did identify five variables that appeared to demonstrate a trend toward increase in infection rate: blood transfusion, electrophysiological monitoring, increased height,

increased weight and increased body mass index. Increased tobacco use trended toward a lower infection rate. Statistical significance was not achieved, and the authors suggested that a larger sample size of 700 patients per group was needed to prove statistical superiority or equivalency between treatment groups. The authors concluded that preoperative prophylactic antibiotic use in instrumented lumbar spinal fusion is generally accepted and has been shown consistently to decrease postoperative infection rates. Prolonged postoperative antibiotic dosing carries with it an increased cost and potential complications. Due to questions about the method of randomization and lack of validated outcome measures, this potential Level II study provides Level III therapeutic evidence that preoperative prophylactic antibiotic use in instrumented lumbar spinal fusion is effective in reducing the risk of infection. The superiority of one agent or regimen was not demonstrated.

Kakimaru et al⁷ reported results from a retrospective comparative study comparing the infection rates following spinal surgery with and without postoperative antimicrobial prophylaxis. Of the 284 patients included in the study, 141 received preoperative and postoperative dosing while 143 received preoperative and intraoperative dosing. The antibiotics used included cefazolin 1 g in 108 patients, flomoxef 1 g in 26 patients, and piperacillin 1 g in 7 patients for the postoperative group. For the no postoperative dosing group, cefazolin 1 g was given to 142 patients and minocycline 100 mg was given to 1 patient. Patients in the postoperative dosing group had an intravenous dose within 30 minutes of skin incision, a dose postoperatively intravenously, and oral antibiotics for an average of 2.7 days, or the preoperative dose with intraoperative redosing at three hour intervals and a single postoperative dose. Patients in the no postoperative dosing group received a preoperative dose within 30 minutes of skin incision followed by intraoperative dosing at three hour intervals until skin closure. Infection was confirmed via bacterial cultures and inspection of wound for redness, heat, swelling and pain. In the postoperative dosing group, 2.8% (4/141) developed infections (three superficial and one deep); in the no postoperative dosing group, 1.4% (2/143) developed infections ($p=0.335$). The authors concluded that the duration of antimicrobial prophylaxis does not influence the rate of surgical site infections. Postoperative administration of antimicrobials appears unnecessary. This study provides Level III evidence that the duration of antimicrobial prophylaxis does not influence the incidence of surgical site infections. The superiority of one agent or regimen was not demonstrated.

Kanayama et al⁸ performed a retrospective comparative study to compare the rate of surgical site infections in lumbar spine surgeries for two different antibiotic prophylaxis protocols. A first-generation cephalosporin was administered unless the patient had a history of a significant allergy such as anaphylactic shock, systemic skin eruption, or toxic liver dysfunction. The postoperative group received antibiotics for five to seven days after surgery. The no postoperative dose group received antibiotics only on the day of surgery; antibiotics were given 30 minutes before skin incision. An additional dose was administered every three hours to maintain therapeutic levels throughout surgery. The rate of surgical site infection was compared between the two prophylaxis groups. At a maximum of six months, a positive

wound culture and/or typical infectious signs including a purulent exudate, surrounding erythema, and wound fluctuance detected infections. Laboratory studies were also referenced, such as prolonged elevation in the C-reactive protein value. There were 1133 patients in the postoperative-dose group and 464 patients in the no postoperative-dose group. The rate of instrumentation surgery was not statistically different between the postoperative-dose group (43%) and the no postoperative-dose group (39%). The overall rate of surgical site infection was 0.7%. The infection rate was 0.8% (9/1133) in the postoperative-dose group and 0.4% (2/464) in the no postoperative-dose group; the difference between the two was not significant. Regarding the organisms of surgical site infection, resistant strains of bacteria were cultured in five (83.3%) of six patients in the multiple-dose group, whereas none was cultured in the single-dose group. The authors concluded there was no statistical difference was observed between protocols. The CDC protocol of preoperative dosing prevents development of resistant strains while reducing the risk of surgical site infections. This study provides Level III therapeutic evidence that postoperative dosing is unnecessary and that preoperative plus intraoperative dosing only is efficacious in preventing surgical site infection. Also, extended dosing may induce resistant strains. Suction drains were left in place in fusions for two to three days. Accordingly, multidosing of antibiotics until drains are removed may not be beneficial. The superiority of one agent or regimen was not demonstrated.

Luer et al⁹ described a retrospective case control study comparing postoperative infections after laminectomy/discectomy to examine variables that may be associated with infection. The antibiotic protocol included a single intravenous dose of 1 g cefazolin with varied timing (within one hour preoperatively, to within two hours, to greater than two hours, to postincision). Infection was confirmed via bacterial cultures. The clinical evaluation for infection was not described. Of the 22 patients with documented wound infection, 12 had received prophylactic antibiotics with 33% (4/12) having received cefazolin within two hours of incision versus 57% (8/14) of the uninfected matched controls, $p=0.001$. The surgical incision was closed less than two hours after incision in 43% (6/14) of uninfected patients and 17% (2/12) with infection ($p<0.001$). The authors reported that wound culture data did not indicate infection by organisms resistant to cefazolin. They concluded that the choice of cefazolin appears adequate but administration needs to occur in the appropriate time frame. This small study provides Level III therapeutic evidence that antibiotic prophylaxis with cephalosporin more than two hours prior to incision appears to yield a higher infection rate, and dosing within two hours of incision may improve infection rate.

Mastronardi (2005) et al¹⁰ reported a retrospective comparative study evaluating the efficacy of two intraoperative antibiotic prophylaxis protocols in a large series of lumbar microdiscectomies performed in two different neurosurgical centers. Of the 1167 patients included in the study, 450 received a single intravenous dose of cefazoline 1 g at induction of general anesthesia (Group A) and 717 received a single dose of intravenous ampicillin 1 g and sulbactam 500 mg at induction of anesthesia (Group P). At six months, a diagnosis of postoperative spondylodiscitis was confirmed via lumbar MRI and sedimentation

rate in three out of 450 patients in Group A (0.67%) and in five out of 717 patients in Group P (0.69%). In all cases, treatment consisted of rigid thoracolumbar orthosis and four to six week administration of amoxicillin/clavulanate compound (500/125 mg). The authors concluded that administration of a single dose of antibiotic at time of induction appears safe and effective. Multicenter trials would be needed to assess superiority of an agent. This study provides Level III therapeutic evidence both cefazolin and ampicillin/sulbactam are effective agents when given at the time of induction for prevention of discitis following lumbar discectomy. The superiority of one agent or regimen was not demonstrated.

Rohde et al¹¹ described a retrospective comparative study designed to report the incidence of postoperative spondylodiscitis in 1642 consecutive cases in which no antibiotic prophylaxis was used and to define the value of a collagenous sponge containing gentamicin in preventing disc space infections. No topical or systemic antibiotics were administered in the first 508 patients. A 4 cm × 4 cm collagenous sponge containing 8 mg of gentamicin was placed in the cleared disc space in the subsequent 1134 patients. Surgery was performed for 1584 primary lumbar disc herniations (two-level discectomy in 39 cases, three-level discectomy in one case) and 169 operations for recurrent herniations. In all patients, the erythrocyte sedimentation rate (ESR) was obtained before surgery and on the first day after surgery. Beginning in January 1992, C-reactive protein (CRP) also was analyzed before surgery, one day after surgery and six days after surgery. All patients were clinically re-examined on days 10-14 after surgery (day of discharge). Final follow-up was at 60 days. In 19 of these 508 patients, a postoperative spondylodiscitis developed, accounting for an incidence rate of 3.7%. None of the 1134 patients receiving antibiotic prophylaxis developed a postoperative spondylodiscitis during the follow-up period of 60 days. Therefore, the incidence of postoperative spondylodiscitis was 0%. Using the Fisher exact test, the difference in the incidence rates between the patient groups with and without antibiotic prophylaxis during lumbar discectomy was highly significant ($p < 0.00001$). The authors observed no complications related to the use of a collagenous sponge containing gentamicin for antibiotic prophylaxis. The authors concluded that a 3.7% incidence of postoperative spondylodiscitis was found in the absence of prophylactic antibiotics. Gentamicin-containing collagenous sponges placed in the cleared disc space were effective in preventing postoperative spondylodiscitis. This study provides Level III therapeutic evidence that for uncomplicated lumbar microdiscectomy, topical administration of a gentamicin soaked collagen sponge is more effective than placebo in preventing clinically significant discitis.

Sweet et al¹² performed a retrospective comparative study to evaluate the safety and efficacy of adjunctive local application of vancomycin for infection prophylaxis in posterior instrumented thoracic and lumbar spine wounds compared to intravenous cephalixin alone. Since 2000, 1732 consecutive thoracic and lumbar posterior instrumented spinal fusions have been performed with routine 24 hours of perioperative intravenous antibiotic prophylaxis with cephalixin. Since 2006, 911 of these instrumented thoracic and lumbar cases had 2 g of vancomycin powder applied to the wound prior to closure in addition to in-

travenous antibiotics. A retrospective review for infection rates and complications was performed with an average follow-up of 2.5 years (range: 1-7 years). If wound infection was suspected based on clinical and constitutional symptoms, aspiration was completed. If aspiration demonstrated purulent material or the wound was clinically suspicious for subfascial infection, the wound was explored and aerobic, anaerobic and fungal cultures were obtained. Posterior instrumented thoracic and lumbar fusions were performed in 821 patients using intravenous cephalixin prophylaxis with a total of 21 resulting deep wound infections (2.6%). Coag negative staph was the most commonly isolated organism. Posterior instrumented thoracic and lumbar fusions were performed in 911 patients with intravenous cephalixin plus adjunctive local vancomycin powder with two ensuing deep wound infections (0.2%). The reduction in wound infections was statistically significant ($p < 0.0001$). There were no adverse clinical outcomes or wound complications related to the local application of vancomycin. The authors concluded that adjunctive local application of vancomycin powder decreases the post surgical wound infection rate with statistical significance in posterior instrumented thoracolumbar spine fusions. This study provides Level III therapeutic evidence that adjunctive local application of vancomycin powder decreases the post surgical wound infection rate compared with intravenous cephalixin in posterior instrumented thoracolumbar fusion.

Takahashi et al¹³ performed a retrospective comparative study to compare the effectiveness of preoperative cephalosporin with various postoperative dosing schedules in reducing infection rates following a variety of spinal surgeries including decompression with or without fusion, with or without fixation. Group 1 received first- or second-generation cephalosporin or penicillin administered by intravenous drip infusion for seven days (4 g/day) after the operation. After the drip infusion, cephalosporin was administered orally for one week. Group 2 received first- or second- generation cephalosporin administered by intravenous drip infusion. The initial dose was given at the time of anesthesia induction. When the operating time exceeded five hours, an additional dose was given intraoperatively. The administration was continued for five days (2 g/day) after the operation, including the day of the operation. After the drip infusion, a cephalosporin was given orally for one week. Group 3 received first- or second-generation cephalosporin administered by intravenous drip infusion, with the initial dose given at the time of anesthesia induction. Additional doses were administered every three hours during the operation. The administration was then continued for three days (2 g/day) after the operation, including the day of the operation. After the drip infusion, a cephalosporin was given orally for one week. Group 4 received first generation cephalosporin administered by intravenous drip infusion with the initial dose given at the time of anesthesia induction. Additional doses were given every three hours during the operation. The administration was then continued for two days (2 g/day) after the operation, including the day of the operation. Of the 1415 patients included in the study, 539 were included in Group 1, 536 in Group 2, 257 in Group 3 and 83 in Group 4. Adopting the CDC guideline criteria, surgical site infections involving only the skin and/or subcutaneous tissues at the site of the incision were designated superficial infections, and those involving

deeper soft tissues (e.g., fascial and muscle layers) at the site of the incision were designated deep infections. The overall frequency of surgical site infections for the different groups were: Group 1, 2.6% (14/539); Group 2, 0.9% (5/536); Group 3 and 4, 0/257 and 0/83, respectively. Comparison using Tukey's multiple comparison test showed $p < 0.05$ for comparing infection rates between Groups 1, 2 and 3. The authors concluded that when thorough prophylactic countermeasures are undertaken against perioperative surgical site infections, the frequency of these infections can be decreased, with a decrease in the duration of antimicrobial prophylaxis administration from seven days to two days. This study provides Level III therapeutic evidence that shorter duration of antimicrobial prophylaxis is more effective, and two days of antibiotic administration is recommended compared to longer durations.

In typical, uncomplicated spinal procedures, a single dose of preoperative prophylactic antibiotics with intraoperative redosing as needed is suggested.

Grade of Recommendation: B

A single preoperative dose of prophylaxis with intraoperative redosing as needed was demonstrated to be equivalent to extended protocols for typical, uncomplicated spinal procedures. Extended protocols of more than three days have been shown to result in increased risk of antibiotic resistance.

Dobzyniak et al⁵ described a retrospective comparative study examining the efficacy of single versus multiple dosing for lumbar disc surgery. The antibiotics used for prophylaxis consisted of cephazolin 1 g, 525 patients; clindamycin 600 mg, 15 patients; vancomycin 1 g plus clindamycin 600 mg, 46 patients; and vancomycin 1 g alone, 24 patients. The choice of an antibiotic other than cephazolin was based on a patient allergy to penicillin or cephalosporin and surgeons preference when these allergies were encountered. Of the 635 consecutive patients included in the study, 418 received the multidose regimen, 192 received the single dose, and 25 patients were eliminated from the study since no preoperative dose was documented. Infection was confirmed at six weeks via cultures and attending physician's assessment. The infection rate was 1.56% (3/192) with single dosing versus 1.20% (5/418) with multiple dosing, $p = 0.711$, Fisher exact test. The authors concluded that a single preoperative dose of prophylactic antibiotics is as effective as preoperative plus postoperative antibiotics in the prevention of wound infections in lumbar disc surgery. They recommend preoperative antibiotics alone, citing no advantage in prolonging a patient's discharge following lumbar disc excision to administer postoperative antibiotics. This study provides Level III therapeutic evidence that single dosing is as effective as multiple dosing; however, different antibiotics do not appear to affect the rate of wound infection. The superiority of one agent or regimen was not demonstrated.

Hellbusch et al⁶ conducted a prospective, randomized controlled trial examining the effects of multiple dosing regimens on the postoperative infection rate in instrumented lumbar spi-

nal fusion. Two hundred sixty-nine patients were randomized into either a preoperative only protocol or preoperative with an extended postoperative antibiotic protocol. Patients in the preoperative only protocol group received a single dose of intravenous cefazolin 1 g or 2 g based on weight 30 minutes before incision. The extended postoperative antibiotic protocol group received the same preoperative dose plus postoperative intravenous cefazolin every eight hours for three days followed by oral cephalexin every six hours for seven days. Because of untoward drug reaction or deviation from the antibiotic protocol, 36 of the 269 patients were eliminated from the study. Therefore, 233 patients completed the entire study; 117 received preoperative antibiotics only and 116 received pre- and postoperative antibiotics. At 21 day follow-up there was no significant difference in infection rates between the two antibiotic protocols, and the superiority of one agent or regimen was not demonstrated. The postoperative infection rates were 4.3% for the preoperative only protocol and 1.7% for the preoperative with extended antibiotic protocol. The overall postoperative infection rate was 3%. However, the study did identify five variables that appeared to demonstrate a trend toward increase in infection rate: blood transfusion, electrophysiological monitoring, increased height, increased weight and increased body mass index. Increased tobacco use trended toward a lower infection rate. The authors concluded that preoperative prophylactic antibiotic use in instrumented lumbar spinal fusion is generally accepted and has been shown consistently to decrease postoperative infection rates. Prolonged postoperative antibiotics increase cost and potential complications. Due to questions about the method of randomization and lack of validated outcome measures, this potential Level II study provides Level III therapeutic evidence that preoperative prophylactic antibiotic use in instrumented lumbar spinal fusion is effective at reducing the risk of infection.

Kakimaru et al⁷ reported results from a retrospective comparative study comparing the infection rates following spinal surgery with and without postoperative antimicrobial prophylaxis. Of the 284 patients included in the study, 141 received preoperative and postoperative dosing while 143 received preoperative and intraoperative dosing. The antibiotics used included cefazolin 1 g in 108 patients, flomoxef 1 g in 26 patients, and piperacillin 1 g in 7 patients for the postoperative group. For the no postoperative dosing group, cefazolin 1 g was given to 142 patients and minocycline 100 mg was given to 1 patient. Patients in the postoperative dosing group had an intravenous dose within 30 minutes of skin incision, a dose postoperatively intravenously, and oral antibiotics for an average of 2.7 days, or the preoperative dose with intraoperative redosing at three hour intervals and a single postoperative dose. For the no postoperative dosing group, patients received a preoperative dose within 30 minutes of skin incision with intraoperative dosing at three hour intervals until skin closure. Infection was confirmed via bacterial cultures and inspection of wound for redness, heat, swelling and pain. In the postoperative dosing group, 2.8% (4/141) developed infections (three superficial and one deep); in the no postoperative dosing group, 1.4% (2/143) developed infections ($p = 0.335$). The authors concluded that the duration of antimicrobial prophylaxis does not influence the rate of surgical site infections, and the superiority of one agent or regimen was not

demonstrated. This study provides Level III evidence that the duration of antimicrobial prophylaxis does not influence the incidence of surgical site infections, and postoperative administration of antimicrobials appears unnecessary.

Kanayama et al⁸ performed a retrospective comparative study to compare the rate of surgical site infections in lumbar spine surgeries for two different antibiotic prophylaxis protocols. A first-generation cephalosporin was administered unless the patient had a history of a significant allergy such as anaphylactic shock, systemic skin eruption or toxic liver dysfunction. The postoperative dose group received antibiotics for five to seven days after surgery. The no postoperative dose group received antibiotics only on the day of surgery; antibiotics were given 30 minutes before skin incision and an additional dose was administered every three hours to maintain therapeutic levels throughout surgery. The rate of surgical site infection was compared between the two prophylaxis groups. At a maximum of six months, a positive wound culture and/or typical infectious signs including a purulent exudate, surrounding erythema and wound fluctuance detected infections. Laboratory studies were also referenced, such as prolonged elevation in the C-reactive protein value. There were 1133 patients in the postoperative dose group and 464 patients in the no postoperative dose group. The rate of instrumentation surgery was not statistically different between the postoperative dose group (43%) and the no postoperative dose group (39%). The overall rate of surgical site infection was 0.7%. The infection rate was 0.8% (9/1133) in the postoperative dose group and 0.4% (2/464) in the no postoperative dose group; the difference between the two was not significant. Regarding the organisms of surgical site infection, resistant strains of bacteria were cultured in five (83.3%) of six patients in the postoperative dose group, whereas none were cultured in the no postoperative dose group. The authors concluded there was no statistical difference was observed between protocols, and the superiority of one agent or regimen was not demonstrated. The CDC protocol of preoperative dosing prevents development of resistant strains while reducing the risk of surgical site infections. This study provides Level III therapeutic evidence that preoperative plus intraoperative redosing is efficacious in preventing surgical site infection. Also, extended dosing may induce resistant strains. Suction drains were left in place in fusions for two to three days. Accordingly, extended dosing of antibiotics until drains are removed may not be beneficial.

Takahashi et al¹³ performed a retrospective comparative study to compare the effectiveness of preoperative cephalosporin with various postoperative dosing schedules in reducing infection rates following a variety of spinal surgeries including decompression with or without fusion, with or without fixation. Group 1 received first- or second-generation cephalosporin or penicillin administered by intravenous drip infusion for seven days (4 g/day) after the operation. After the drip infusion, cephalosporin was administered orally for one week. Group 2 received first- or second-generation cephalosporin administered by intravenous drip infusion. The initial dose was given at the time of anesthesia induction. When the operating time exceeded five hours, an additional dose was given intraoperatively. The administration continued for five days (2 g/day) after the operation, including the day of the operation. After the drip infusion, a cephalosporin was given orally for one week. Group 3 received

first- or second-generation cephalosporin administered by intravenous drip infusion, with the initial dose given at the time of anesthesia induction. Additional doses were administered every three hours during the operation. The administration was then continued for three days (2 g/day) after the operation, including the day of the operation. After the drip infusion, a cephalosporin was given orally for one week. Group 4 received first-generation cephalosporin administered by intravenous drip infusion with the initial dose given at the time of anesthesia induction. Additional doses were given every three hours during the operation. The administration was then continued for two days (2 g/day) after the operation, including the day of the operation. Of the 1415 patients included in the study, 539 were included in Group 1, 536 in Group 2, 257 in Group 3 and 83 in Group 4. Adopting the CDC guideline criteria, surgical site infections involving only the skin and/or subcutaneous tissues at the site of the incision were designated superficial infections, and those involving deeper soft tissues (eg, fascial and muscle layers) at the site of the incision were designated deep infections. The overall frequency of surgical site infections for the different groups were: Group 1, 2.6% (14/539); Group 2, 0.9% (5/536); Group 3 and 4, 0/257 and 0/83, respectively. Comparison using Tukey's multiple comparison test showed $p < 0.05$ for comparing infections rates between Groups 1, 2 and 3. The authors concluded that when thorough prophylactic countermeasures are undertaken against perioperative surgical site infections, the frequency of these infections can be decreased, with a decrease in the duration of antimicrobial prophylaxis administration from seven days to two days. This study provides Level III therapeutic evidence that a shorter duration of antimicrobial prophylaxis is more effective compared to longer durations.

CONSENSUS STATEMENT: In patients with comorbidities or for those undergoing complicated spine surgery, alternative prophylactic regimens including redosing, gram-negative coverage or the addition of intrawound application of vancomycin or gentamicin, are suggested to decrease the incidence of surgical site infections when compared to standard prophylaxis regimens.

CONSENSUS STATEMENT: Comorbidities and risk factors reviewed in the literature include obesity, diabetes, neurologic deficits, incontinence, preoperative serum glucose level of >125 mg/dL or a postoperative serum glucose level of >200 mg/dL, trauma and prolonged multilevel instrumented surgery. Olsen (2003) et al¹⁴ and Olsen (2008) et al¹⁵ are provided as support studies below to further define the risk factors associated with surgical site infection in spine surgery patients.

Olsen (2003) et al¹⁴ performed a retrospective case control study to identify the specific independent risk factors for surgical site infections occurring after laminectomy or spinal fusion. All patients received standard prophylaxis with cephalosporin or vancomycin in penicillin sensitive patients. Infection was defined using the CDC guideline definition, with infections identified between two and 83 days (median time from surgery to infection was 14 days). Of the 53 of 1918 patients who experienced surgical site infections, 12 were excluded due to missing data. These patients were compared with 179 noninfected matched controls. The infection rate, even with prophylaxis, was 2.76% with no significant variation in the infection rate during the four-year period. Cultures were obtained from infected patients and gram-negative rods and/or anaerobes were present in 17 of 39 (44%) cultures. Additionally, gram-negative rods and/or anaerobes were isolated significantly more often in patients who underwent lumbar or lumbosacral procedures (15/24) compared to patients who underwent thoracic or cervical procedures (2/15, $p < 0.001$). The authors identified postoperative incontinence, obesity, tumor resection and posterior approach as significant risk factors. The length of stay was significantly longer in patients with a surgical site infection compared to those without infection. This study provides Level III prognostic evidence that incontinence (resulting from neurologic injury), obesity, tumor resection (related to neurologic deficits) and posterior approach increase risk of infection and gram-negative bacteria and/or anaerobes are likely to be isolated from a portion of infected patients. In the face of antibiotic prophylaxis with all comers and comorbidities represented, a 2.76% infection rate can be expected. Alternative prophylactic regimens may be necessary to further reduce the infection rate in patients with risk factors for surgical site infection.

Olsen (2008) et al¹⁵ described a retrospective case control study designed to determine independent risk factors for surgical site infection following orthopedic spinal operations. All patients received standard prophylaxis with cephalosporins or vancomycin in penicillin sensitive patients. Of 2316 patients, 46 patients with superficial, deep or organ-space surgical site infections were identified and compared with 227 uninfected control patients. In the face of prophylactic antibiotics, the overall rate of spinal surgical site infection during the five years of the study was 2.0% (46/2316). Univariate analyses showed serum glucose levels, preoperatively and within five days after the operation, to be significantly higher in patients in whom surgical site infection developed than in uninfected control patients. Independent risk factors for surgical site infection that were identified by multivariate analysis were diabetes (odds ratio = 3.5, 95% confidence interval = 1.2, 10.0), suboptimal timing of prophylactic antibiotic therapy (odds ratio = 3.4, 95% confidence interval = 1.5, 7.9), a preoperative serum glucose level of >125 mg/dL (>6.9 mmol/L) or a postoperative serum glucose level of >200 mg/dL (>11.1 mmol/L) (odds ratio = 3.3, 95% confidence interval = 1.4, 7.5), obesity (odds ratio = 2.2, 95% confidence interval = 1.1, 4.7) and two or more surgical residents participating in the operative procedure (odds ratio = 2.2, 95% confidence interval = 1.0, 4.7). A decreased risk of surgical site infection was associated with operations involving the cervical spine (odds ratio = 0.3, 95% confidence interval = 0.1, 0.6). The authors concluded that dia-

betes was associated with the highest independent risk of spinal surgical site infection, and an elevated preoperative or postoperative serum glucose level was also independently associated with an increased risk of surgical site infection. The role of hyperglycemia as a risk factor for surgical site infection in patients not previously diagnosed with diabetes should be investigated further. Administration of prophylactic antibiotics within one hour before the operation and increasing the antibiotic dosage to adjust for obesity are also important strategies to decrease the risk of surgical site infection after spinal operations. This study provides Level III prognostic evidence that diabetes, suboptimal timing of antibiotic prophylaxis, preoperative glucose level of >125 mg/dL, postoperative glucose level of >200 mg/dL and obesity are independent risk factors for surgical site infection following orthopaedic spinal operations. Alternative prophylactic regimens, including higher dosages for obese patients, may be necessary to further reduce the risk of infection in patients with risk factors for surgical site infection.

Kakimaru et al⁷ reported results from a retrospective comparative study comparing the infection rates following spinal surgery without instrumentation. Of the 284 patients included in the study, 141 received preoperative and postoperative dosing and 143 received preoperative and intraoperative dosing. The antibiotics used included cefazolin 1 g in 108 patients, flomoxef 1 g in 26 patients and piperacillin 1 g in 7 patients for the postoperative group. For the no postoperative group, cefazolin 1 g was given to 142 patients and minocycline 100 mg was given to one patient. Patients in the postoperative dosing group had an intravenous dose within 30 minutes of skin incision, a dose postoperatively intravenously and oral antibiotics for an average of 2.7 days, or the preoperative dose with intraoperative redosing at three hour intervals and a single postoperative dose. For the no postoperative dosing group, patients had a preoperative dose within 30 minutes of skin incision with intraoperative dosing at three hour intervals until skin closure. Infection was confirmed via bacterial cultures and inspection of wound for redness, heat, swelling and pain. The authors found no statistically significant difference in infection rates between the protocols, and the superiority of one agent or regimen was not demonstrated. In the postoperative dosing group, 2.8% (4/141) developed infections (three superficial and one deep); in the no postoperative dosing group, 1.4% (2/143) developed infections ($p = 0.335$). Altogether, 28 patients had diabetes including 10.6% (15/141) of patients the postoperative group and 9% (13/143) of patients in the no postoperative group. None of the diabetic patients developed surgical site infections. The authors concluded that the duration of antimicrobial prophylaxis does not influence the incidence of surgical site infections and postoperative administration of antimicrobials appears unnecessary. This study provides Level III evidence that preoperative administration of antimicrobial prophylaxis plus intraoperative redosing at three hour intervals is effective at preventing surgical site infection.

Kanayama et al⁸ performed a retrospective comparative study to compare the rate of surgical site infections in lumbar spine surgeries for two different antibiotic prophylaxis protocols. A first-generation cephalosporin was administered unless the patient had a history of a significant allergy such as anaphylactic shock, systemic skin eruption or toxic liver dysfunction.

The postoperative dose group patients received antibiotics for five to seven days after surgery. The no postoperative dose group patients received antibiotics only on the day of surgery; antibiotics were given 30 minutes before skin incision. An additional dose was administered every three hours to maintain therapeutic levels throughout surgery. Infection was defined as a positive wound culture and/or typical infectious signs including a purulent exudate, surrounding erythema and wound fluctuance detected at a maximum of six months. Laboratory studies were also referenced, such as prolonged elevation in the C-reactive protein value. For the purposes of this study, the surgical site infection incidence rate was determined according to the number of wound infection requiring additional surgical infections. There were 1133 patients in the postoperative-dose group and 464 patients in the no postoperative group. The rate of instrumentation surgery was not statistically different between the postoperative-dose group (43%) and the no postoperative-dose group (39%). The overall rate of surgical site infection was 0.7%. The infection rate was 0.8% (9/1133) in the postoperative-dose group and 0.4% (2/464) in the no postoperative-dose group; the difference between the two was not significant. Regarding the organisms of surgical site infection, resistant strains of bacteria were cultured in five (83.3%) of six patients in the postoperative-dose group, whereas none was cultured in the no postoperative-dose group. The authors concluded there was no statistical difference was observed between protocols and the superiority of one agent or regimen was not demonstrated. The CDC protocol of preoperative dosing prevents development of resistant strains while reducing the risk of surgical site infections. This study provides Level III therapeutic evidence that preoperative plus intraoperative dosing at three hour intervals throughout surgery is efficacious in preventing surgical site infection. Also, extended dosing may induce resistant strains. Suction drains were left in place in fusions for two to three days. Accordingly, multidosing of antibiotics until drains are removed may not be beneficial.

Rohde et al¹¹ described a retrospective comparative study designed to report the incidence of postoperative spondylodiscitis in 1642 consecutive cases in which no antibiotic prophylaxis was used and to define the value of single dose administration of a collagenous sponge containing gentamicin as an antibiotic prophylaxis alternative for preventing disc space infections. No topical or systemic antibiotics were administered in the first 508 patients. A 4 cm × 4 cm collagenous sponge containing 8 mg of gentamicin was placed in the cleared disc space in the subsequent 1134 patients. Surgery was performed for 1584 primary lumbar disc herniations (two-level discectomy in 39 cases, three-level discectomy in one case) and 169 operations for recurrent herniations. In all patients, the erythrocyte sedimentation rate (ESR) was obtained before surgery and on the first day after surgery. Beginning in January 1992, C-reactive protein (CRP) also was analyzed before surgery, one day after surgery and six days after surgery. All patients were clinically re-examined on days 10-14 after surgery (day of discharge). Final follow-up was at 60 days. In 19 of these 508 patients, a postoperative spondylodiscitis developed, accounting for an incidence rate of 3.7%. None of the 1134 patients receiving antibiotic prophylaxis developed a postoperative spondylodiscitis during the follow-up period of 60 days resulting in an incidence of 0%. Using the

Fisher exact test, the difference in the incidence rates between the patient groups with and without antibiotic prophylaxis during lumbar discectomy was highly significant ($p < 0.00001$). The authors observed no complications related to the use of a collagenous sponge containing gentamicin for antibiotic prophylaxis. The authors concluded that a 3.7% incidence of postoperative spondylodiscitis was found in the absence of prophylactic antibiotics. Gentamicin-containing collagenous sponges placed in the cleared disc space were effective in preventing postoperative spondylodiscitis. This study provides Level III therapeutic evidence that for uncomplicated lumbar microdiscectomy, topical administration of gentamicin soaked collagen sponge is more effective than placebo in preventing clinically significant discitis.

Sweet et al¹² performed a retrospective comparative study to evaluate the safety and efficacy of adjunctive local application of vancomycin for infection prophylaxis in posterior instrumented thoracic and lumbar spine wounds compared to intravenous cephalexin alone. Since 2000, 1732 consecutive thoracic and lumbar posterior instrumented spinal fusions have been performed with routine 24 hours of perioperative intravenous antibiotic prophylaxis with cephalexin. Since 2006, 911 of these instrumented thoracic and lumbar cases had 2 g of vancomycin powder applied to the wound prior to closure in addition to intravenous antibiotics. A retrospective review for infection rates and complications was performed with an average follow-up of 2.5 years (range: 1-7 years). If wound infection was suspected based on clinical and constitutional symptoms, aspiration was completed. If aspiration demonstrated purulent material or the wound was clinically suspicious for subfascial infection, the wound was explored and aerobic, anaerobic and fungal cultures were obtained. Posterior instrumented thoracic and lumbar fusions were performed in 821 patients using intravenous cephalexin prophylaxis with a total of 21 resulting deep wound infections (2.6%). Coag negative staph was the most commonly isolated organism. Posterior instrumented thoracic and lumbar fusions were performed in 911 patients with intravenous cephalexin plus adjunctive local vancomycin powder with two ensuing deep wound infections (0.2%). The reduction in wound infections was statistically significant ($p < 0.0001$). There were no adverse clinical outcomes or wound complications related to the local application of vancomycin. The authors concluded that adjunctive local application of vancomycin powder decreases the post surgical wound infection rate with statistical significance in posterior instrumented thoracolumbar spine fusions. This study provides Level III therapeutic evidence that adjunctive local application of vancomycin powder decreases the post surgical wound infection rate compared with intravenous cephalexin in posterior instrumented thoracolumbar fusion.

Takahashi et al¹³ performed a retrospective comparative study to compare the effectiveness of preoperative cephalosporin with various postoperative dosing schedules in reducing infection rates following a variety of spinal surgeries including decompression with or without fusion, with or without fixation. Group 1 (n=539) received first- or second-generation cephalosporin or penicillin administered by intravenous drip infusion for seven days (4 g/day) after the operation followed by oral cephalosporin for one week. Group 2 (n=536) received first- or second-generation cephalosporin administered by intravenous drip infusion at

the time of anesthesia induction. When the operating time exceeded five hours, an additional dose was given intraoperatively. The administration was continued for five days (2 g/day) after the operation, including the day of the operation. After the drip infusion, a cephalosporin was given orally for one week. Group 3 (n=257) received first- or second-generation cephalosporin administered by intravenous drip infusion, with the initial dose given at the time of anesthesia induction. Additional doses were administered every three hours during the operation. The administration was then continued for three days (2 g/day) after the operation, including the day of the operation. After the drip infusion, a cephalosporin was given orally for one week. Group 4 (n=83) received first generation cephalosporin administered by intravenous drip infusion with the initial dose given at the time of anesthesia induction. Additional doses were given every three hours during the operation. The administration was then continued for two days (2 g/day) after the operation, including the day of the operation. Patients with diabetes mellitus, metastatic spinal tumors, on dialysis, or receiving daily steroid administration of 5 mg or more for at least 90 days were defined as compromised hosts and included 19.1%, 16.0%, 19.1%, and 28.9% of patients in groups 1-4. Adopting the CDC guideline criteria, surgical site infections involving only the skin and/or subcutaneous tissues at the site of the incision were designated superficial infections, and those involving deeper soft tissues (eg, fascial and muscle layers) at the site of the incision were designated deep infections. The overall frequency of surgical site infections for the different groups were: Group 1, 2.6% (14/539); Group 2, 0.9% (5/536); Group 3 and 4, 0/257 and 0/83, respectively. Comparison using Tukey's multiple comparison test showed $p < 0.05$ for comparing infections rates between Groups 1, 2 and 3. In addition, there was no significant difference in the frequency of surgical site infection between the compromised hosts and rest of the patients. The authors concluded that when thorough prophylactic countermeasures are undertaken against surgical site infections, the frequency of these infections can be decreased, with a decrease in the duration of antimicrobial prophylaxis administration from seven days to two days. This study provides Level III therapeutic evidence that shorter duration of antimicrobial prophylaxis is more effective at preventing infection in patients undergoing spinal surgery with and without instrumentation compared to longer durations.

Future Directions for Research

Large multicenter randomized controlled trials assessing the efficacy of various protocols should be tailored to specific patient populations (eg, obesity, diabetes, trauma, neuromuscular injury or disease, prolonged multilevel instrumented surgery) at increased risk for surgical site infections.

Protocol (Mixed Groups) References

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For patients receiving antibiotic prophylaxis prior to open spine surgery without spinal implants, what are the recommended drugs, their dosages, administration routes and timing resulting in decreased postoperative infections rates?

Preoperative antibiotic prophylaxis is suggested to decrease infection rates in patients undergoing spine surgery without spinal implants. In these typical, uncomplicated spinal procedures, the superiority of one agent, dose or route of administration over any other has not been clearly demonstrated. When determining the appropriate drug choice, the patient's risk factors, allergies, length and complexity of the procedure and issues of antibiotic resistance should be considered.

Grade of Recommendation: B

Petignat et al¹ conducted a prospective, randomized controlled trial assessing the efficacy of one preoperative 1.5 g dose of cefuroxime in preventing surgical site infection after lumbar laminotomy and discectomy for herniated disc. Of the 1237 patients included in the study, 613 received 1.5 g intravenous cefuroxime on induction and 624 received placebo. Presence of infection, as defined by the Centers for Disease Control (CDC) guidelines, was assessed at six weeks, three months and six months. Baseline characteristics were similar in patients allocated to cefuroxime (n = 613) or placebo (n=624). Eight (1.3%) patients in the cefuroxime group and 18 patients (2.8%) in the placebo group developed a surgical site infection (p =0.073). A diagnosis of spondylodiscitis or epidural abscess was made in nine patients in the placebo group, but none in the cefuroxime group (p < 0.01), which corresponded to a number necessary to treat of 69 patients to prevent one of these infections. There were no significant adverse events attributed to either cefuroxime or placebo. Overall surgical site infection rate was 1.3% with antibiotics versus 2.8% with placebo (p=0.073), and discitis rate was 0/613 versus 9/624 (p<0.01), respectively. The authors concluded that a single, preoperative dose of cefuroxime significantly reduces the risk of organ-space infection, most notably spondylodiscitis, after surgery for herniated disc. Cefuroxime is protective against spondylodiscitis. This study provides Level I therapeutic evidence that for uncomplicated lumbar microdiscectomy, a single preoperative 1.5 g dose of cefuroxime is more effective in preventing infection than placebo.

Pons et al² described a prospective, randomized trial comparing perioperative antibiotic protocols that included either 2 g ceftizoxime or 1 g vancomycin plus 80 mg gentamicin in 291

patients who underwent various clean spine surgeries. Of the 291 patients, 142 received ceftizoxime and 149 vancomycin/gentamicin one hour prior to incision. Infections were confirmed using bacterial cultures for deep infections, urinary tract infection, or catheter infections; pneumonia diagnosed by purulent sputum and/or new infiltrate on CXR; and cellulitis was diagnosed by presence of spreading induration or erythema. Primary infections were reported in 2.8% (4/142) of the ceftizoxime patients and 2.7% (4/149) of the vancomycin-gentamicin patients. Secondary infections were reported in 4.2% (6/142) and 4.0% (6/149) patients, respectively. The authors concluded that the design of the trial does not allow for statistical analysis of subgroups, however, an overview of the data does not suggest a relationship between postoperative infection and any of the technical or clinical variables. Ceftizoxime is less toxic than vancomycin/gentamicin and equally as effective in preventing infections after clean neurosurgical procedures. Because the study design does not permit subgroup analysis, this potential Level I study provides Level II evidence that ceftizoxime and vancomycin-gentamicin are equally effective in reducing infections with ceftizoxime being less toxic. However, the study was not designed for subgroup analysis. The superiority of one agent or regimen was not demonstrated.

Rubinstein et al³ performed a prospective, randomized controlled trial to investigate the efficacy of a single dose of 1 g of cephazolin in reducing postoperative infections in patients undergoing 'clean' operations on the lumbar spine. Of the 141 patients included in the study, 70 received 1 g intravenous cephalazolin upon arrival to the operative room (approximately two hours prior to surgery) and 71 received placebos. Presence of

infection was assessed at 30 days, with surgical site infection defined as drainage of purulent material from the operative site and a positive bacteriological culture, or inflammation of an area more than 20 mm in diameter; for urinary tract infection, more than 100,000 colony forming units/mL on culture; and for pneumonia, the clinical diagnosis was made by the treating physician. There were 21 wound or urinary infections in the 71 patients who received placebo and nine in the 70 who received cephazolin ($p < 0.05$). Nine patients (12.7%) who received placebo and three (4.3%) who received cephazolin developed wound infections ($p = 0.07$). All but three of the infections in the placebo group were confirmed by bacterial culture. All the organisms isolated from the patients who received placebo (except the group-D streptococci which are inherently resistant) were sensitive to cephazolin whereas in the cephazolin prophylactic group 43% of the organisms isolated were resistant or had reduced sensitivity to the drug. The authors concluded that the administration of a single dose of cephazolin preoperatively is recommended for patients undergoing lumbar spinal surgery. In critique, the sample size was small and the study's follow-up period was short. In addition, the authors expanded the definition of infection to include wound, urinary tract infection and pneumonia in order to achieve statistical significance. Due to these limitations, this potential Level I study provides Level II therapeutic evidence that for uncomplicated spine surgery, a single preoperative dose of cephazolin decreases infection rate; however, it does not significantly decrease the rate of wound infection. The use of cephazolin appears to be associated with an increase in development of resistant organisms.

Dobzyniak et al⁴ described a retrospective comparative study examining the efficacy of single versus multiple dosing for lumbar disc surgery. The antibiotics used for prophylaxis consisted of cephazolin 1 g, 525 patients; clindamycin 600 mg, 15 patients; vancomycin 1 g plus clindamycin 600 mg, 46 patients; and vancomycin 1 g alone, 24 patients. The choice of an antibiotic other than cephazolin was based on a patient allergy to penicillin or cephalosporins and surgeons preference when these allergies were encountered. Of the 635 consecutive patients included in the study, 418 received the multidose regimen, 192 received the single dose, and 25 patients were eliminated from the study as no preoperative dose was documented. Infection was confirmed at six weeks via cultures and attending physician's assessment. The infection rate was 1.56% (3/192) with single dosing versus 1.20% (5/418) with multiple dosing, $p=0.711$, Fisher exact test. The authors concluded that a single preoperative dose of prophylactic antibiotics is as effective as preoperative plus postoperative antibiotics in the prevention of wound infections in lumbar disc surgery. They recommend preoperative antibiotics alone, citing no advantage in prolonging a patient's discharge following uncomplicated lumbar disc excision to administer postoperative antibiotics. This study provides Level III therapeutic evidence that single dosing is as effective as multiple dosing; however, different antibiotics do not appear to affect the rate of wound infection. The superiority of one agent or regimen was not demonstrated.

Kakimaru et al⁵ reported results from a retrospective comparative study comparing the infection rates following uninstrumented spinal surgery with and without postoperative antimicrobial prophylaxis. Of the 284 patients included in the study,

141 received preoperative and postoperative dosing while 143 received preoperative and intraoperative dosing. The antibiotics used included cefazolin 1 g in 108 patients, flomoxef 1 g in 26 patients, and piperacillin 1 g in seven patients for the postoperative group. For the no postoperative dosing group, cefazolin 1 g was given to 142 patients and minocycline 100 mg was given to one patient. Patients in the postoperative dosing group had an intravenous dose within 30 minutes of skin incision, a dose postoperatively intravenously and oral antibiotics for 2.7 days average, or the preoperative dose with intraoperative redosing at three hour intervals and a single postoperative dose. For the no postoperative group, patients received a preoperative dose within 30 minutes of skin incision with intraoperative dosing at three hour intervals until skin closure. Infection was confirmed via bacterial cultures and inspection of wound for redness, heat, swelling and pain. In the postoperative dosing group, 2.8% (4/141) developed infections (three superficial and one deep); in the no postoperative dosing group, 1.4% (2/143) developed infections ($p=0.335$). The authors concluded that the duration of antimicrobial prophylaxis does not influence the rate of surgical site infections. This study provides Level III evidence that the duration of antimicrobial prophylaxis does not influence the incidence of surgical site infections and postoperative administration of antimicrobials appears unnecessary. The superiority of one agent or regimen was not demonstrated.

Luer et al⁶ described a retrospective case control study comparing postoperative infections after laminectomy/discectomy to examine variables that may be associated with infection. The antibiotic protocol included a single intravenous dose of 1 g cefazolin with varied timing (within one hour preoperatively, to within two hours, to greater than two hours, to postincision). Infection was confirmed via bacterial cultures. The clinical evaluation for infection was not described. Of the 22 patients with documented wound infection, 12 had received prophylactic antibiotics with 33% (4/12) having received cefazolin within two hours of incision versus 57% (8/14) of the uninfected matched controls, $p=0.001$. The surgical incision was closed less than two hours after incision in 43% (6/14) of uninfected patients and 17% (2/12) with infection ($p<0.001$). The authors reported that wound culture data did not indicate infection by organisms resistant to cefazolin. They concluded that the choice of cefazolin appears adequate but administration needs to occur in the appropriate time frame. This small study provides Level III therapeutic evidence that antibiotic prophylaxis with cephalosporin more than two hours prior to incision appears to yield a higher infection rate, and dosing within two hours of incision may improve infection rate.

Mastrorandi (2005) et al⁷ reported a retrospective comparative study evaluating the efficacy of two intraoperative antibiotic prophylaxis protocols in a large series of lumbar microdiscectomies performed in two different neurosurgical centers. Of the 1167 patients included in the study, 450 received a single intravenous dose of cefazolin 1 g at induction of general anesthesia (Group A) and 717 received a single dose of intravenous ampicillin 1 g and sulbactam 500 mg at induction of anesthesia (Group P). At six months, a diagnosis of postoperative spondylodiscitis was confirmed via lumbar MRI and sedimentation rate in three out of 450 patients in Group A (0.67%) and in five

out of 717 patients in Group P (0.69%). In all cases, treatment consisted of rigid thoracolumbar orthosis and four to six week administration of amoxicillin/clavulanate compound (500/125 mg). The authors concluded that administration of a single dose of antibiotic at time of induction appears safe and effective. Multicenter trials would be needed to assess superiority of an agent. This study provides Level III therapeutic evidence both cefazolin and ampicillin/sulbactam are effective agents when given at the time of induction for prevention of discitis following lumbar discectomy. The superiority of one agent or regimen was not demonstrated.

Rohde et al⁸ described a retrospective comparative study designed to report the incidence of postoperative spondylodiscitis in 1642 consecutive cases in which no antibiotic prophylaxis was used and to define the value of a collagenous sponge containing gentamicin in preventing disc space infections. No topical or systemic antibiotics were administered in the first 508 patients. A 4 cm × 4 cm collagenous sponge containing 8 mg of gentamicin was placed in the cleared disc space in the subsequent 1134 patients. Surgery was performed for 1584 primary lumbar disc herniations (two-level discectomy in 39 cases, three-level discectomy in one case) and 169 operations for recurrent herniations. In all patients, the erythrocyte sedimentation rate (ESR) was obtained before surgery and on the first day after surgery. Beginning in January 1992, C-reactive protein (CRP) also was analyzed before surgery, one day after surgery and six days after surgery. All patients were clinically re-examined on days 10-14 after surgery (day of discharge). Final follow-up was at 60 days. In 19 of these 508 patients, a postoperative spondylodiscitis developed, accounting for an incidence rate of 3.7%. None of the 1134 patients receiving antibiotic prophylaxis developed a postoperative spondylodiscitis during the follow-up period of 60 days. Therefore, the incidence of postoperative spondylodiscitis was 0%. Using the Fisher exact test, the difference in the incidence rates between the patient groups with and without antibiotic prophylaxis during lumbar discectomy was highly significant ($p < 0.00001$). The authors observed no complications related to the use of a collagenous sponge containing gentamicin for antibiotic prophylaxis. This study provides Level III therapeutic evidence that for uncomplicated lumbar microdiscectomy, topical administration of a gentamicin soaked collagen sponge is more effective than placebo in preventing clinically significant discitis.

Takahashi et al⁹ performed a retrospective comparative study to compare the effectiveness of preoperative cephalosporin with various postoperative dosing schedules in reducing infection rates following a variety of spinal surgeries including decompression with or without fusion, with or without fixation. Group 1 received first- or second-generation or penicillin administered by intravenous drip infusion for seven days (4 g/day) after the operation. After the drip infusion, cephalosporin was administered orally for one week. Group 2 received first- or second-generation cephalosporin administered by intravenous drip infusion. The initial dose was given at the time of anesthesia induction. When the operating time exceeded five hours, an additional dose was given intraoperatively. The administration was continued for five days (2 g/day) after the operation, including the day of the operation. After the drip infusion, a cephalosporin

was given orally for one week. Group 3 received first- or second-generation cephalosporin administered by intravenous drip infusion, with the initial dose given at the time of anesthesia induction. Additional doses were administered every three hours during the operation. The administration was then continued for three days (2 g/day) after the operation, including the day of the operation. After the drip infusion, a cephalosporin was given orally for one week. Group 4 received first generation cephalosporin administered by intravenous drip infusion with the initial dose given at the time of anesthesia induction. Additional doses were given every three hours during the operation. The administration was then continued for two days (2 g/day) after the operation, including the day of the operation. Of the 1415 patients included in the study, 539 were included in Group 1, 536 in Group 2, 257 in Group 3 and 83 in Group 4. Adopting the CDC guideline criteria, surgical site infections involving only the skin and/or subcutaneous tissues at the site of the incision were designated superficial infections, and those involving deeper soft tissues (eg, fascial and muscle layers) at the site of the incision were designated deep infections. The overall frequency of surgical site infections for the different groups were: Group 1, 2.6% (14/539); Group 2, 0.9% (5/536); Group 3 and 4, 0/257 and 0/83, respectively. Comparison using Tukey's multiple comparison test showed $p < 0.05$ for comparing infections rates between Groups 1, 2 and 3. The authors concluded that when thorough prophylactic countermeasures are undertaken against perioperative surgical site infections, the frequency of these infections can be decreased, with a decrease in the duration of antimicrobial prophylaxis administration from seven days to two days. This study provides Level III therapeutic evidence that shorter duration of antimicrobial prophylaxis is more effective compared to longer durations.

In typical, uncomplicated open spine surgery without spinal implants, a single dose of preoperative prophylactic antibiotics with intraoperative redosing as needed is suggested.

Grade of Recommendation: B

Dobzyniak et al⁴ described a retrospective comparative study examining the efficacy of single versus multiple dosing for lumbar disc surgery. The antibiotics used for prophylaxis consisted of cephazolin 1 g, 525 patients; clindamycin 600 mg, 15 patients; vancomycin 1 g plus clindamycin 600 mg, 46 patients; and vancomycin 1 g alone, 24 patients. The choice of an antibiotic other than cephazolin was based on a patient allergy to penicillin or cephalosporins and surgeons preference when these allergies were encountered. Of the 635 consecutive patients included in the study, 418 received the multidose regimen, 192 received the single dose, and 25 patients were eliminated from the study since no preoperative dose was documented. Infection was confirmed at six weeks via cultures and attending physician's assessment. The infection rate was 1.56% (3/192) with single dosing versus 1.20% (5/418) with multiple dosing, $p=0.711$, Fisher exact test. The authors concluded that a single preoperative dose of prophylaxis

lactic antibiotics is as effective as preoperative plus postoperative antibiotics in the prevention of wound infections in lumbar disc surgery. They recommend preoperative antibiotics alone, citing no advantage in prolonging a patient's discharge following lumbar disc excision to administer postoperative antibiotics. This study provides Level III therapeutic evidence that single dosing is as effective as multiple dosing; however, different antibiotics do not appear to affect the rate of wound infection. The superiority of one agent or regimen was not demonstrated.

Kakimaru et al⁵ reported results from a retrospective comparative study comparing the infection rates following uninstrumented spinal surgery with and without postoperative antimicrobial prophylaxis. Of the 284 patients included in the study, 141 received preoperative and postoperative dosing and 143 received preoperative and intraoperative dosing. The antibiotics used included cefazolin 1 g in 108 patients, flomoxef 1 g in 26 patients, and iperacillin 1 g in 7 patients for the postoperative group. For the no postoperative group, cefazolin 1 g was given to 142 patients and minocycline 100 mg was given to 1 patient. Patients in the postoperative dosing group had an intravenous dose within 30 minutes of skin incision, a dose postoperatively intravenously, and oral antibiotics for 2.7 days average, or the preoperative dose with intraoperative redosing at three hour intervals and a single postoperative dose. No postoperative dosing group patients received a preoperative dose within 30 minutes of skin incision with intraoperative dosing at three hour intervals until skin closure. Infection was confirmed via bacterial cultures and inspection of wound for redness, heat, swelling and pain. In the postoperative dosing group, 2.8% (4/141) developed infections (three superficial and one deep); in the no postoperative dosing group, 1.4% (2/143) developed infections ($p=0.335$). The authors concluded that the duration of antimicrobial prophylaxis does not influence the rate of surgical site infections and postoperative administration of antimicrobials appears unnecessary. This study provides Level III therapeutic evidence that preoperative administration of antimicrobial prophylaxis plus intraoperative redosing at three hour intervals is effective at preventing surgical site infection in patients undergoing spinal surgery without instrumentation. The superiority of one agent or regimen was not demonstrated.

Takahashi et al⁹ performed a retrospective comparative study to compare the effectiveness of preoperative cephalosporin with various postoperative dosing schedules in reducing infection rates following a variety of spinal surgeries including decompression with or without fusion, with or without fixation. Group 1 received first- or second-generation cephalosporin or penicillin administered by intravenous drip infusion for seven days (4 g/day) after the operation. After the drip infusion, cephalosporin was administered orally for one week. Group 2 received first- or second-generation cephalosporin administered by intravenous drip infusion. The initial dose was given at the time of anesthesia induction. When the operating time exceeded five hours, an additional dose was given intraoperatively. The administration was continued for five days (2 g/day) after the operation, including the day of the operation. After the drip infusion, a cephalosporin was given orally for one week. Group 3 received first- or second-generation cephalosporin administered by intravenous drip infusion, with the initial dose given at the time of anesthesia

induction. Additional doses were administered every three hours during the operation. The administration was then continued for three days (2 g/day) after the operation, including the day of the operation. After the drip infusion, a cephalosporin was given orally for one week. Group 4 received first-generation cephalosporin administered by intravenous drip infusion with the initial dose given at the time of anesthesia induction. Additional doses were given every three hours during the operation. The administration was then continued for two days (2 g/day) after the operation, including the day of the operation. Of the 1415 patients included in the study, 539 were included in Group 1, 536 in Group 2, 257 in Group 3 and 83 in Group 4. Adopting the CDC guideline criteria, surgical site infections involving only the skin and/or subcutaneous tissues at the site of the incision were designated superficial infections, and those involving deeper soft tissues (eg, fascial and muscle layers) at the site of the incision were designated deep infections. The overall frequency of surgical site infections for the different groups were: Group 1, 2.6% (14/539); Group 2, 0.9% (5/536); Group 3 and 4, 0/257 and 0/83, respectively. Comparison using Tukey's multiple comparison test showed $p<0.05$ for comparing infections rates between Groups 1, 2 and 3. The authors concluded that when thorough prophylactic countermeasures are undertaken against perioperative surgical site infections, the frequency of these infections can be decreased, with a decrease in the duration of antimicrobial prophylaxis administration from seven days to two days. This study provides Level III therapeutic evidence that shorter duration of antimicrobial prophylaxis is more effective at preventing surgical site infection in spinal surgery patients compared to longer durations.

Future Directions for Research

Large multicenter randomized controlled trials assessing the efficacy of various protocols should be tailored to specific patient populations (eg, obesity, diabetes, trauma, neuromuscular injury or disease, prolonged multilevel instrumented surgery) at increased risk for surgical site infections.

Protocol (Noninstrumented) References

1. Petignat C, Francioli P, Harbarth S, et al. Cefuroxime prophylaxis is effective in noninstrumented spine surgery: a double-blind, placebo-controlled study. *Spine (Phila Pa 1976)*. Aug 15 2008;33(18):1919-1924.
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This clinical guideline should not be construed as including all proper methods of care or excluding or other acceptable methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific procedure or treatment is to be made by the physician and patient in light of all circumstances presented by the patient and the needs and resources particular to the locality or institution

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For patients receiving antibiotic prophylaxis prior to open spine surgery with spinal implants, what are the recommended drugs, their dosages, administration routes and timing resulting in decreased postoperative infections rates?

Preoperative antibiotic prophylaxis is suggested to decrease infection rates in patients undergoing spine surgery with spinal implants. In these complex spinal procedures, the superiority of one agent, dose or route of administration over any other has not been clearly demonstrated. When determining the appropriate drug choice, the patient's risk factors, allergies, length and complexity of the procedure and issues of antibiotic resistance should be considered.

Grade of Recommendation: B

Hellbusch et al¹ conducted a prospective, randomized controlled trial examining the effects of multiple dosing regimens on the postoperative infection rate in instrumented lumbar spinal fusion. Two hundred sixty-nine patients were randomized into either a preoperative only protocol or preoperative with an extended postoperative antibiotic protocol. Patients in the preoperative only protocol group received a single dose of intravenous cefazolin 1 g or 2 g based on weight 30 minutes before incision. The extended postoperative antibiotic protocol group received the same preoperative dose plus postoperative intravenous cefazolin every eight hours for three days followed by oral cephalixin every six hours for seven days. Because of untoward drug reaction or deviation from the antibiotic protocol, 36 of the 269 patients were eliminated from the study. Therefore, 233 patients completed the entire study; 117 receiving preoperative antibiotics only, and 116 receiving pre- and postoperative antibiotics. At 21 days follow-up, there was no significant difference in infection rates between the two antibiotic protocols. The postoperative infection rates were 4.3% for the preoperative only protocol and 1.7% for the preoperative with extended antibiotic protocol. The overall postoperative infection rate was 3%. However, the study did identify five variables that appeared to demonstrate a trend toward increase in infection rate: blood transfusion, elec-

trophysiological monitoring, increased height, increased weight, and increased body mass index. Increased tobacco use trended toward a lower infection rate. Statistical significance was not achieved. The authors concluded that preoperative prophylactic antibiotic use in instrumented lumbar spinal fusion is generally accepted and has been shown consistently to decrease postoperative infection rates. Prolonged postoperative antibiotic dosing increases cost and potential complications. Due to questions about the method of randomization and lack of validated outcome measures, this potential Level II study provides Level III therapeutic evidence that preoperative prophylactic antibiotic use in instrumented lumbar spinal fusion is effective at reducing the risk of infection. The superiority of one agent or regimen was not demonstrated.

Sweet et al² performed a retrospective comparative study to evaluate the safety and efficacy of adjunctive local application of vancomycin for infection prophylaxis in posterior instrumented thoracic and lumbar spine wounds compared to intravenous cephalixin alone. Since 2000, 1732 consecutive thoracic and lumbar posterior instrumented spinal fusions have been performed with routine 24 hours of perioperative intravenous antibiotic prophylaxis with cephalixin. Since 2006, 911 of these instrumented thoracic and lumbar cases had 2 g of vancomycin

powder applied to the wound prior to closure in addition to intravenous antibiotics. A retrospective review for infection rates and complications was performed with an average follow-up of 2.5 years (range: 1-7 years). If wound infection was suspected based on clinical and constitutional symptoms, aspiration was completed. If aspiration demonstrated purulent material or the wound was clinically suspicious for subfascial infection, the wound was explored and aerobic, anaerobic and fungal cultures were obtained. Posterior instrumented thoracic and lumbar fusions were performed in 821 patients using intravenous cephalexin prophylaxis with a total of 21 resulting deep wound infections (2.6%). Coag negative staph was the most commonly isolated organism. Posterior instrumented thoracic and lumbar fusions were performed in 911 patients with intravenous cephalexin plus adjunctive local vancomycin powder with two ensuing deep wound infections (0.2%). The reduction in wound infections was statistically significant ($p < 0.0001$). There were no adverse clinical outcomes or wound complications related to the local application of vancomycin. The authors concluded that adjunctive local application of vancomycin powder decreases the post surgical wound infection rate with statistical significance in posterior instrumented thoracolumbar spine fusions. This study provides Level III therapeutic evidence that adjunctive local application of vancomycin powder decreases the post surgical wound infection rate compared with intravenous cephalexin in posterior instrumented thoracolumbar fusion.

CONSENSUS STATEMENT. In patients with risk factors for polymicrobial infection, appropriate broad-spectrum antibiotics are suggested to decrease the risk of infection when instrumented fusion is performed.

Kanafani et al³ described a case control study comparing risk factors in patients who did or did not develop infections. All patients received antibiotics, although patients with infections more frequently received first-generation as opposed to second-generation cephalosporins. Also, there was a higher percentage of patients with instrumentation in the infection group. This paper offers Level III evidence that patients who require instrumented fusions have a higher rate of infection than patients who do not require such extensive procedures.

Olsen (2003) et al⁴ performed a retrospective case control study to identify the specific independent risk factors for surgical site infections occurring after laminectomy or spinal fusion. All patients received standard prophylaxis with cephalosporins or vancomycin in penicillin sensitive patients. Infection was defined using the CDC guideline definition, with infections identified between two and 83 days (median time from surgery to infection was 14 days). Of the 53 of 1918 patients who experienced surgical site infections, 12 were excluded due to missing data. These patients were compared with 179 noninfected matched controls. Infection rate even with prophylaxis was 2.76% with no significant variation in the infection rate during the four-year period. Cultures were obtained from infected patients and gram-negative rods and/or anaerobes were present in 17 of 39 (44%) cultures. Additionally, gram-negative rods and/or

anaerobes were isolated significantly more often in patients who underwent lumbar or lumbosacral procedures (15/24) compared to patients who underwent thoracic or cervical procedures (2/15, $p < 0.001$). The authors identified postoperative incontinence, obesity, tumor resection and posterior approach as risk factors. This study provides Level III prognostic evidence that incontinence (resulting from neurologic injury), obesity, tumor resection (related to neurologic deficits) and posterior approach increase risk of infection. Alternative prophylactic regimens, such as broad-spectrum antibiotics, may be necessary to further reduce this infection rate.

Olsen (2008) et al⁵ described a retrospective case control study designed to determine independent risk factors for surgical site infection following orthopaedic spinal operations. All patients received standard prophylaxis with cephalosporins or vancomycin in penicillin sensitive patients. Of 2316 patients, 46 patients with superficial, deep or organ-space surgical site infections were identified and compared with 227 uninfected control patients. The overall rate of spinal surgical site infection during the five years of the study was 2.0% (46/2316). Univariate analyses showed serum glucose levels, preoperatively and within five days after the operation, to be significantly higher in patients in whom surgical site infection developed than in uninfected control patients. Independent risk factors for surgical site infection that were identified by multivariate analysis were diabetes (odds ratio = 3.5, 95% confidence interval = 1.2, 10.0), suboptimal timing of prophylactic antibiotic therapy (odds ratio = 3.4, 95% confidence interval = 1.5, 7.9), a preoperative serum glucose level of >125 mg/dL (>6.9 mmol/L) or a postoperative serum glucose level of >200 mg/dL (>11.1 mmol/L) (odds ratio = 3.3, 95% confidence interval = 1.4, 7.5), obesity (odds ratio = 2.2, 95% confidence interval = 1.1, 4.7) and two or more surgical residents participating in the operative procedure (odds ratio = 2.2, 95% confidence interval = 1.0, 4.7). A decreased risk of surgical site infection was associated with operations involving the cervical spine (odds ratio = 0.3, 95% confidence interval = 0.1, 0.6). The authors concluded that diabetes was associated with the highest independent risk of spinal surgical site infection, and an elevated preoperative or postoperative serum glucose level was also independently associated with an increased risk of surgical site infection. The role of hyperglycemia as a risk factor for surgical site infection in patients not previously diagnosed with diabetes should be investigated further. Administration of prophylactic antibiotics within one hour before the operation and increasing the antibiotic dosage to adjust for obesity are also important strategies to decrease the risk of surgical site infection after spinal operations. This study provides Level III prognostic evidence that diabetes, preoperative glucose level of >125 mg/dL, postoperative glucose level of >200 mg/dL, and obesity are independent risk factors for surgical site infection following orthopaedic spinal operations. Alternative prophylactic regimens, such as broad-spectrum antibiotics, may be necessary to further reduce this infection rate.

Rechtine et al⁶ described a retrospective case control study of 235 consecutive fracture patients. Of the 235 patients, 117 underwent surgical stabilization. Of the 117 patients, 12 suffered a perioperative infection, two had a staphylococcal infection and 10 had a polymicrobial infection with gram-negative and gram-

positive organisms. There was a statistically higher infection rate in completely neurologically injured patients compared to those with no deficit or incomplete injuries. The authors concluded that aggressive and earlier intervention is required in this patient population. In critique, the study was designed to assess the incidence of spinal infection in a spine trauma population and does not state the duration of follow-up. It offers Level III therapeutic evidence supporting the efficacy of prophylactic antibiotics in instrumented spinal surgery in patients with incomplete cord injury or in spinal fractures without cord injury. However, in the subgroup with spinal cord injury, infections were more likely a result of multiple organisms including gram-negative species. This study raises compelling questions about antibiotic choice for prophylaxis in spinal cord injury patients.

Sweet et al² performed a retrospective comparative study to evaluate the safety and efficacy of adjunctive local application of vancomycin for infection prophylaxis in posterior instrumented thoracic and lumbar spine wounds compared to intravenous cephalexin alone. Since 2000, 1732 consecutive thoracic and lumbar posterior instrumented spinal fusions have been performed with routine 24 hours of perioperative intravenous antibiotic prophylaxis with cephalexin. Since 2006, 911 of these instrumented thoracic and lumbar cases had 2 g of vancomycin powder applied to the wound prior to closure in addition to intravenous antibiotics. A retrospective review for infection rates and complications was performed with an average follow-up of 2.5 years (range: 1-7 years). If wound infection was suspected based on clinical and constitutional symptoms, aspiration was completed. If aspiration demonstrated purulent material or the wound was clinically suspicious for subfascial infection, the wound was explored and aerobic, anaerobic and fungal cultures were obtained. Posterior instrumented thoracic and lumbar fusions were performed in 821 patients using intravenous cephalexin prophylaxis with a total of 21 resulting deep wound infections (2.6%). Coag negative staph was the most commonly isolated organism. Posterior instrumented thoracic and lumbar fusions were performed in 911 patients with intravenous cephalexin plus adjunctive local vancomycin powder with two ensuing deep wound infections (0.2%). The reduction in wound in-

fections was statistically significant ($p < 0.0001$). There were no adverse clinical outcomes or wound complications related to the local application of vancomycin. The authors concluded that adjunctive local application of vancomycin powder decreases the post surgical wound infection rate with statistical significance in posterior instrumented thoracolumbar spine fusions. This study provides Level III therapeutic evidence that adjunctive local application of the broad spectrum antibiotic, vancomycin powder, decreases the post surgical wound infection rate compared with intravenous cephalexin in posterior instrumented thoracolumbar fusion.

Future Directions for Research

Large multicenter randomized controlled trials assessing the efficacy of various protocols should be tailored to specific patient populations (eg, obesity, diabetes, trauma, neuromuscular injury or disease, prolonged multilevel instrumented surgery) at increased risk for surgical site infections.

Protocol (Instrumented) References

1. Hellbusch LC, Helzer-Julien M, Doran SE, et al. Single-dose vs. multiple-dose antibiotic prophylaxis in instrumented lumbar fusion--a prospective study. *Surg Neurol*. Dec 2008;70(6):622-627; discussion 627.
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What is a reasonable algorithmic approach for antibiotic selection for a given patient?

CONSENSUS STATEMENT: Simple uncomplicated spine surgery (without instrumentation or comorbidities) => one single preoperative dose of antibiotic of choice with intraoperative redosing as needed

CONSENSUS STATEMENT: Instrumented spine surgery, prolonged procedures, comorbidities (eg, diabetes, neuromuscular disease, cord injury or general spine trauma) => one single preoperative dose of antibiotic of choice + consideration of additional gram-negative coverage and/or the application of intrawound vancomycin or gentamicin

Future Directions for Research

Large multicenter randomized controlled trials assessing the efficacy of various protocols should be tailored to specific patient populations (eg, obesity, diabetes, trauma, neuromuscular injury or disease, prolonged multilevel instrumented surgery) at increased risk for surgical site infections.

C. Redosing

For patients receiving antibiotic prophylaxis prior to open spine surgery, what are the intraoperative redosing recommendations for the recommended drugs (including dosages and time of administration) resulting in decreased postoperative infection rates?

CONSENSUS STATEMENT: Intraoperative redosing within 3-4 hours may be considered to maintain therapeutic antibiotic levels throughout the procedure. The superiority of one drug has not been demonstrated in the literature. When determining the appropriate drug choice, the patient's risk factors, allergies, length and complexity of the procedure and issues of antibiotic resistance should be considered.

There is no study directly comparing redosing to not redosing. However, several studies did use redosing in their cohorts, and are consistent with the consensus statement.

Hellbusch et al¹ conducted a prospective, randomized controlled trial examining the effects of multiple dosing regimens on the postoperative infection rate in instrumented lumbar spinal fusion. Two hundred sixty-nine patients were randomized into either a preoperative only protocol or preoperative with an extended postoperative antibiotic protocol. Patients in the preoperative only protocol group received a single dose of intravenous cefazolin 1 g or 2 g based on weight 30 minutes before incision. The extended postoperative antibiotic protocol group received the same preoperative dose plus postoperative intravenous cefazolin every eight hours for three days followed by oral cephalexin every six hours for seven days. Because of untoward drug reaction or deviation from the antibiotic protocol, 36 of the 269 patients were eliminated from the study. Therefore, 233 patients completed the entire study; 117 receiving preoperative antibiotics only, and 116 receiving pre- and postoperative antibiotics. At 21 days follow-up, there was no significant difference in infection rates between the two antibiotic protocols. The postoperative infection rates were 4.3% for the preoperative only protocol and 1.7% for the preoperative with extended antibiotic protocol. The overall postoperative infection rate was 3%. However, the study did identify five variables that appeared to demonstrate a trend toward increase in infection rate: blood transfusion, electrophysiological monitoring, increased height, increased weight and increased body mass index. Increased tobacco use trended toward a lower infection rate. Although a

comparative study by design, this study provides Level IV therapeutic evidence that patients with prolonged procedures that are redosed have a similar infection rate to simpler procedures without a redosing regimen.

Kakimaru et al² reported results from a retrospective comparative study comparing the infection rates following spinal surgery with and without postoperative antimicrobial prophylaxis. Of the 284 patients included in the study, 141 received preoperative and postoperative dosing and 143 received preoperative and intraoperative dosing. The antibiotics used included cefazolin 1 g in 108 patients, flomoxef 1 g in 26 patients, and piperacillin 1 g in seven patients for the postoperative group. For the preoperative plus intraoperative dosing group, cefazolin 1 g was given to 142 patients and minocycline 100 mg was given to one patient. Patients in the postoperative dosing group had an intravenous dose within 30 minutes of skin incision, a dose postoperatively intravenously, and oral antibiotics for 2.7 days average, or the preoperative dose with intraoperative redosing at three hour intervals and a single postoperative dose. Preoperative plus intraoperative dosing patients had a preoperative dose within 30 minutes of skin incision with intraoperative dosing at three hour intervals until skin closure. Infection was confirmed via bacterial cultures and inspection of wound for redness, heat, swelling and pain. In the postoperative dosing group, 2.8% (4/141) developed infections (three superficial and one deep); in the preoperative plus intraoperative dosing group, 1.4% (2/143) developed infections ($p=0.335$). The authors concluded that the duration of antimicrobial prophylaxis does not influence the rate of surgical site infections and postoperative administration

of antimicrobials appears unnecessary. Although a comparative study by design, this study provides Level IV therapeutic evidence that intraoperative redosing resulted in similar infection rates as single dosing in shorter cases.

Kanayama et al³ performed a retrospective case control study to compare the rate of surgical site infections in lumbar spine surgeries for two different antibiotic prophylaxis protocols. A first-generation cephalosporin was administered unless the patient had a history of a significant allergy such as anaphylactic shock, systemic skin eruption or toxic liver dysfunction. Postoperative group patients received antibiotics for five to seven days after surgery. No postoperative dose group patients received antibiotics only on the day of surgery; antibiotics were given 30 minutes before skin incision. An additional dose was administered every three hours to maintain therapeutic levels throughout surgery. The rate of surgical site infection was compared between the two prophylaxis groups. At a maximum of six months, a positive wound culture and/or typical infectious signs including a purulent exudate, surrounding erythema, and wound fluctuance defined infections. Laboratory studies were also referenced, such as prolonged elevation in the C-reactive protein value. There were 1133 patients in the postoperative-dose group and 464 patients in the no postoperative-dose group. The rate of instrumentation surgery was not statistically different between the postoperative-dose group (43%) and the no postoperative-dose group (39%). The overall rate of surgical site infection was 0.7%. The infection rate was 0.8% (9/1133) in the postoperative-dose group and 0.4% (2/464) in the no postoperative-dose group; the difference between the two was not significant. Regarding the organisms of surgical site infection, resistant strains of bacteria were cultured in five (83.3%) of six patients in the postoperative-dose group, whereas none was cultured in the no postoperative-dose group. The authors concluded there was no statistical difference was observed between protocols. Although a comparative study by design, this study provides Level IV therapeutic evidence that intraoperative redosing resulted in similar infection rates as single dosing in shorter cases.

Mastronardi (2004) et al⁴ presented a retrospective case series evaluating the safety and efficacy of a specific intraoperative antibiotic protocol for a variety of spinal surgeries. Over a three-year period, 973 patients received ampicillin/sulbactam 1.5 g intravenous on induction or Teicoplanin 400 mg intravenous on induction (if surgery longer than two hours) with redosing of teicoplanin at four hours or 1500 mL blood loss. Data was gathered at six weeks to one year regarding drainage from the wound, wound abscess or positive culture. Wound infection occurred in nine cases (1%) and discitis in four of 657 (0.06%) patients. This study provides Level IV therapeutic evidence that intraoperative redosing resulted in similar infection rates as single dosing in shorter cases.

Riley et al⁵ described a retrospective study of one year's patients (40) who had either simple discectomy or instrumented procedures. Patients received 1.5 g cefuroxime preoperatively and every four hours for a 48-hour duration. Intravenous gentamicin (80 mg) was administered preoperatively, with redosing every six hours intraoperatively and every eight hours postoperatively for a 48-hour duration. No infections occurred in the 40 patients. The study provides a good discussion of the basic

science behind the use of cefuroxime and gentamicin as readily disc eluting antibiotics as compared with cephalosporin as a less disc-eluting antibiotic. In critique of this study, it was a retrospective chart review evaluating postoperative infection in an extremely small cohort of patients. With such a small sample size, no conclusions regarding efficacy of a specific regimen can be drawn. This is an extension of a basic science study looking at the penetration of cephalosporin, gentamicin and cefuroxime into disc tissue. It provides Level IV therapeutic evidence that redosing resulted in similar infection rates as single dosing in shorter cases.

Takahashi et al⁶ performed a retrospective comparative study to compare the effectiveness of preoperative cephalosporin with various postoperative dosing schedules in reducing infection rates following a variety of spinal surgeries including decompression with or without fusion, with or without fixation. Group 1 received first- or second-generation cephalosporin or penicillin administered by intravenous drip infusion for seven days (4 g/day) after the operation. After the drip infusion, cephalosporin was administered orally for one week. Group 2 received first- or second- generation cephalosporin administered by intravenous drip infusion. The initial dose was given at the time of anesthesia induction. When the operating time exceeded five hours, an additional dose was given intraoperatively. The administration was continued for five days (2 g/day) after the operation, including the day of the operation. After the drip infusion, a cephalosporin was given orally for one week. Group 3 received first- or second-generation cephalosporin administered by intravenous drip infusion, with the initial dose given at the time of anesthesia induction. Additional doses were administered every three hours during the operation. The administration was then continued for three days (2 g/day) after the operation, including the day of the operation. After the drip infusion, a cephalosporin was given orally for one week. Group 4 received first-generation cephalosporin administered by intravenous drip infusion with the initial dose given at the time of anesthesia induction. Additional doses were given every three hours during the operation. The administration was then continued for two days (2 g/day) after the operation, including the day of the operation. Of the 1415 patients included in the study, 539 were included in Group 1, 536 in Group 2, 257 in Group 3 and 83 in Group 4. Adopting the CDC guideline criteria, surgical site infections involving only the skin and/or subcutaneous tissues at the site of the incision were designated superficial infections, and those involving deeper soft tissues (eg, fascial and muscle layers) at the site of the incision were designated deep infections. The overall frequency of surgical site infections for the different groups were: Group 1, 2.6% (14/539); Group 2, 0.9% (5/536); Group 3 and 4, 0/257 and 0/83, respectively. Comparison using Tukey's multiple comparison test showed $p < 0.05$ for comparing infections rates between Groups 1, 2 and 3. The authors concluded that when thorough prophylactic countermeasures are undertaken against perioperative surgical site infections, the frequency of these infections can be decreased, with a decrease in the duration of antimicrobial prophylaxis administration from seven days to two days. Although a comparative study by design, this study provides Level IV therapeutic evidence that intraoperative redosing resulted in similar infection rates as single dosing in shorter cases.

Future Directions for Research

Recommendation #1:

A case controlled study is suggested utilizing available national databases to determine the relative efficacy of redosing antibiotic prophylaxis in specific patient populations undergoing spine surgery.

Recommendation #2:

A series of randomized controlled studies evaluating dosing regimens is recommended; each study could address a specific sub-population defined by diagnosis, procedure and comorbidity.

Redosing References

1. Hellbusch LC, Helzer-Julien M, Doran SE, et al. Single-dose vs. multiple-dose antibiotic prophylaxis in instrumented lumbar fusion--a prospective study. *Surg Neurol.* Dec 2008;70(6):622-627; discussion 627.
2. Kakimaru H, Kono M, Matsusaki M, Iwata A, Uchio Y. Postoperative antimicrobial prophylaxis following spinal decompression surgery: is it necessary? *J Orthop Sci.* May;15(3):305-309.
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6. Takahashi H, Wada A, Iida Y, et al. Antimicrobial prophylaxis for spinal surgery. *J Orthop Sci.* Jan 2009;14(1):40-44.

D. Discontinuation

For patients receiving antibiotic prophylaxis prior to open spine surgery, does discontinuation of prophylaxis at 24 hours result in decreased or increased postoperative infection rates as compared to longer periods of administration?

For typical, uncomplicated cases, a single dose of preoperative prophylactic antibiotics with intraoperative redosing as needed is suggested to decrease the risk of surgical site infection.

Grade of Recommendation: B

Dobzyniak et al¹ described a retrospective comparative study examining the efficacy of single versus multiple dosing for lumbar disc surgery. The antibiotics used for prophylaxis consisted of cephazolin 1 g, 525 patients; clindamycin 600 mg, 15 patients; vancomycin 1 g plus clindamycin 600 mg, 46 patients; and vancomycin 1 g alone, 24 patients. The choice of an antibiotic other than cephazolin was based on a patient allergy to penicillin or cephalosporins and surgeons preference when these allergies were encountered. Of the 635 consecutive patients included in the study, 418 received the multidose regimen, 192 received the single dose and 25 patients were eliminated from the study since no preoperative dose was documented. Infection was confirmed at six weeks via cultures and attending physician's assessment. The infection rate was 1.56% (3/192) with single dosing versus 1.20% (5/418) with multiple dosing, $p=0.711$, Fisher exact test. The authors concluded that a single preoperative dose of prophylactic antibiotics is as effective as preoperative plus postoperative antibiotics in the prevention of wound infections in lumbar disc surgery. They recommend preoperative antibiotics alone, citing no advantage in prolonging a patient's discharge following lumbar disc excision to administer postoperative antibiotics. This study provides Level III therapeutic evidence that single dosing is as effective as multiple dosing; however, different antibiotics do not appear to affect the rate of wound infection. The superiority of one agent or regimen was not demonstrated.

Hellbusch et al² conducted a prospective, randomized controlled trial examining the effects of multiple dosing regimens on the postoperative infection rate in instrumented lumbar spinal fusion. Two hundred sixty-nine patients were randomized into either a preoperative only protocol or preoperative with an

extended postoperative antibiotic protocol. Patients in the preoperative only protocol group received a single dose of intravenous cefazolin 1 g or 2 g based on weight 30 minutes before incision. The extended postoperative antibiotic protocol group received the same preoperative dose plus postoperative intravenous cefazolin every eight hours for three days followed by oral cephalexin every six hours for seven days. Because of untoward drug reaction or deviation from the antibiotic protocol, 36 of the 269 patients were eliminated from the study. Therefore, 233 patients completed the entire study; 117 receiving preoperative antibiotics only and 116 receiving pre- and postoperative antibiotics. At 21 days follow-up, there was no significant difference in infection rates between the two antibiotic protocols. The postoperative infection rates were 3% overall, 4.3% for the preoperative only protocol and 1.7% for the preoperative with extended antibiotic protocol. Statistical significance was not achieved, and the authors suggested that a larger sample size of 700 patients per group was needed to prove statistical superiority or equivalency between treatment groups. The authors concluded that preoperative prophylactic antibiotic use in instrumented lumbar spinal fusion is generally accepted and has been shown consistently to decrease postoperative infection rates. Prolonged postoperative antibiotic dosing carries with it an increased cost and potential complications. Due to questions about the method of randomization and lack of validated outcome measures, this potential Level II study provides Level III therapeutic evidence that preoperative prophylactic antibiotic use in instrumented lumbar spinal fusion is effective at reducing the risk of infection. Antibiotic prophylaxis can be discontinued within 24 hours with no significant change in infection rate.

This clinical guideline should not be construed as including all proper methods of care or excluding or other acceptable methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific procedure or treatment is to be made by the physician and patient in light of all circumstances presented by the patient and the needs and resources particular to the locality or institution

Kakimaru et al³ reported results from a retrospective comparative study comparing the infection rates following spinal surgery with and without postoperative antimicrobial prophylaxis. Of the 284 patients included in the study, 141 received preoperative and postoperative dosing and 143 received a preoperative and intraoperative dosing. The antibiotics used included cefazolin 1 g in 108 patients, flomoxef 1 g in 26 patients and piperacillin 1 g in seven patients for the postoperative group. For the no postoperative dosing group, cefazolin 1 g for was given to 142 patients and minocycline 100 mg for was given to one patient. Patients in the postoperative dosing group had an intravenous dose within 30 minutes of skin incision, a dose postoperatively intravenously, and oral antibiotics for 2.7 days average, or the preoperative dose with intraoperative redosing at three hour intervals and a single postoperative dose. No postoperative dosing patients had a preoperative dose within 30 minutes of skin incision with intraoperative dosing at three hour intervals until skin closure. Infection was confirmed via bacterial cultures and inspection of wound for redness, heat, swelling and pain. In the postoperative dosing group, 2.8% (4/141) developed infections (three superficial and one deep); in the no postoperative dosing group, 1.4% (2/143) developed infections ($p=0.335$). The authors concluded that the duration of antimicrobial prophylaxis does not influence the rate of surgical site infections and postoperative administration of antimicrobials appears unnecessary. This study provides Level III evidence that preoperative plus intraoperative redosing of antimicrobial prophylaxis as needed is effective at preventing surgical site infection in spinal surgery patients. The superiority of one agent or regimen was not demonstrated.

Kanayama et al⁴ performed a retrospective comparative study to compare the rate of surgical site infections in lumbar spine surgeries for two different antibiotic prophylaxis protocols. A first-generation cephalosporin was administered unless the patient had a history of a significant allergy such as anaphylactic shock, systemic skin eruption or toxic liver dysfunction. Postoperative-dose group patients received antibiotics for five to seven days after surgery. No postoperative-dose group patients received antibiotics only on the day of surgery; antibiotics were given 30 minutes before skin incision. An additional dose was administered every three hours to maintain therapeutic levels throughout surgery. Infection was defined as a positive wound culture and/or typical infectious signs including a purulent exudate, surrounding erythema and wound fluctuance detected within six months of surgery. Laboratory studies were also referenced, such as prolonged elevation in the C-reactive protein value. There were 1133 patients in the postoperative-dose group, and 464 patients in the no postoperative-dose group. The rate of instrumentation surgery was not statistically different between the postoperative-dose group (43%) and the no postoperative-dose group (39%). The overall rate of surgical site infection was 0.7%. The infection rate was 0.8% (9/1133) in the postoperative-dose group and 0.4% (2/464) in the no postoperative-dose group; the difference between the two was not significant. Regarding the organisms of surgical site infection, resistant strains of bacteria were cultured in five (83.3%) of six patients in the postoperative-dose group, whereas none was cultured in the no postoperative-dose group. The authors concluded there was no

statistical difference was observed between protocols. The CDC protocol of preoperative dosing prevents development of resistant strains while reducing the risk of surgical site infections. This study provides Level III therapeutic evidence that preoperative and intraoperative redosing is efficacious in preventing surgical site infection. Also, extended dosing may induce resistant strains. Suction drains were left in place in fusions for two to three days. Accordingly, multidosing of antibiotics until drains are removed may not be beneficial. The superiority of one agent or regimen was not demonstrated.

Takahashi et al⁵ performed a retrospective comparative study to compare the effectiveness of preoperative cephalosporin with various postoperative dosing schedules in reducing infection rates following a variety of spinal surgeries including decompression with or without fusion, with or without fixation. Group 1 received first- or second-generation cephalosporin or penicillin administered by intravenous drip infusion for seven days (4 g/day) after the operation. After the drip infusion, cephalosporin was administered orally for one week. Group 2 received first- or second-generation cephalosporin administered by intravenous drip infusion. The initial dose was given at the time of anesthesia induction. When the operating time exceeded five hours, an additional dose was given intraoperatively. The administration was continued for five days (2 g/day) after the operation, including the day of the operation. After the drip infusion, a cephalosporin was given orally for one week. Group 3 received first- or second-generation cephalosporin administered by intravenous drip infusion, with the initial dose given at the time of anesthesia induction. Additional doses were administered every three hours during the operation. The administration was then continued for three days (2 g/day) after the operation, including the day of the operation. After the drip infusion, a cephalosporin was given orally for one week. Group 4 received first-generation cephalosporin administered by intravenous drip infusion with the initial dose given at the time of anesthesia induction. Additional doses were given every three hours during the operation. The administration was then continued for two days (2 g/day) after the operation, including the day of the operation. Of the 1415 patients included in the study, 539 were included in Group 1, 536 in Group 2, 257 in Group 3 and 83 in Group 4. Adopting the CDC guideline criteria, surgical site infections involving only the skin and/or subcutaneous tissues at the site of the incision were designated superficial infections, and those involving deeper soft tissues (eg, fascial and muscle layers) at the site of the incision were designated deep infections. The overall frequency of surgical site infections for the different groups were: Group 1, 2.6% (14/539); Group 2, 0.9% (5/536); Group 3 and 4, 0/257 and 0/83, respectively. Comparison using Tukey's multiple comparison test showed $p<0.05$ for comparing infections rates between Groups 1, 2 and 3. The authors concluded that when thorough prophylactic countermeasures are undertaken against perioperative surgical site infections, the frequency of these infections can be decreased, with a decrease in the duration of antimicrobial prophylaxis administration from seven days to two days. This study provides Level III therapeutic evidence that shorter duration of antimicrobial prophylaxis is more effective compared to longer durations.

Prolonged postoperative regimens may be considered in complex situations (ie, trauma, cord injury, neuromuscular disease, diabetes or other comorbidities). Comorbidities and complex situations reviewed in the literature include obesity, diabetes, neurologic deficits, incontinence, preoperative serum glucose level of >125 mg/dL or a postoperative serum glucose level of >200 mg/dL, trauma, prolonged multilevel instrumented surgery and other comorbidities.

Grade of Recommendation: C

While there appear to be clinical scenarios where prolonged antibiotics may be helpful, at this time the evidence is weak, and the specific indications are not completely clear. Until better data is available, the surgeon should make this decision based on their experience, the regional historical profile of infections in their centers, the complexity of the surgery and the specific comorbidities of the patient.

Olsen (2003) et al⁶ performed a retrospective case control study to identify the specific independent risk factors for surgical site infections occurring after laminectomy or spinal fusion. All patients received standard prophylaxis with cephalosporins or vancomycin in penicillin sensitive patients. Infection was defined using the CDC guideline definition, with infections identified between two and 83 days (median time from surgery to infection was 14 days). Of the 53 of 1918 patients who experienced surgical site infections, 12 were excluded due to missing data. These patients were compared with 179 noninfected matched controls. Infection rate, even with prophylaxis, was 2.76% with no significant variation in the infection rate during the four-year period. The authors identified postoperative incontinence, obesity, tumor resection and posterior approach as risk factors. This study provides Level III prognostic evidence that incontinence (resulting from neurologic injury), obesity, tumor resection (related to neurologic deficits) and posterior approach increase risk of infection. Prolonged prophylactic regimens may be necessary to further reduce the infection rate in patients with risk factors for surgical site infection.

Olsen (2008) et al⁷ described a retrospective case control study designed to determine independent risk factors for surgical site infection following orthopedic spinal operations. All patients received standard prophylaxis with cephalosporins or vancomycin in penicillin sensitive patients. Of 2316 patients, 46 patients with superficial, deep or organ-space surgical site infections were identified and compared with 227 uninfected control patients. The overall rate of spinal surgical site infection during the five years of the study was 2.0% (46/2316). Univariate analyses showed serum glucose levels, preoperatively and within five days after the operation, to be significantly higher in patients in whom surgical site infection developed than in uninfected control patients. Independent risk factors for surgical site infection that were identified by multivariate analysis were

diabetes (odds ratio = 3.5, 95% confidence interval = 1.2, 10.0), suboptimal timing of prophylactic antibiotic therapy (odds ratio = 3.4, 95% confidence interval = 1.5, 7.9), a preoperative serum glucose level of >125 mg/dL (>6.9 mmol/L) or a postoperative serum glucose level of >200 mg/dL (>11.1 mmol/L) (odds ratio = 3.3, 95% confidence interval = 1.4, 7.5), obesity (odds ratio = 2.2, 95% confidence interval = 1.1, 4.7) and two or more surgical residents participating in the operative procedure (odds ratio = 2.2, 95% confidence interval = 1.0, 4.7). A decreased risk of surgical site infection was associated with operations involving the cervical spine (odds ratio = 0.3, 95% confidence interval = 0.1, 0.6). The authors concluded that diabetes was associated with the highest independent risk of spinal surgical site infection and an elevated preoperative or postoperative serum glucose level was also independently associated with an increased risk of surgical site infection. The role of hyperglycemia as a risk factor for surgical site infection in patients not previously diagnosed with diabetes should be investigated further. Administration of prophylactic antibiotics within one hour before the operation and increasing the antibiotic dosage to adjust for obesity are also important strategies to decrease the risk of surgical site infection after spinal operations. This study provides Level III prognostic evidence that diabetes, suboptimal timing of antibiotic prophylaxis, preoperative glucose level of >125 mg/dL, postoperative glucose level of >200mg/dL and obesity are independent risk factors for surgical site infection following orthopedic spinal operations. Prolonged prophylactic regimens may be necessary to further reduce the infection rate in patients with risk factors for surgical site infection.

Hellbusch et al² conducted a prospective, randomized controlled trial examining the effects of multiple dosing regimens on the postoperative infection rate in instrumented lumbar spinal fusion. Two hundred sixty-nine patients were randomized into either a preoperative only protocol or preoperative with an extended postoperative antibiotic protocol. Patients in the preoperative only protocol group received a single dose of intravenous cefazolin 1 g or 2 g based on weight 30 minutes before incision. The extended postoperative antibiotic protocol group received the same preoperative dose plus postoperative intravenous cefazolin every eight hours for three days followed by oral cephalexin every six hours for seven days. Because of untoward drug reaction or deviation from the antibiotic protocol, 36 patients were eliminated from the study. Therefore, 233 patients completed the entire study; 117 receiving preoperative antibiotics only and 116 receiving pre- and postoperative antibiotics. At 21 days follow-up, there was no significant difference in infection rates between the two antibiotic protocols. The postoperative infection rates were 4.3% for the preoperative only protocol and 1.7% for the preoperative with extended antibiotic protocol. The overall postoperative infection rate was 3%. Although not statistically significant, the study identified five variables that appeared to demonstrate a trend toward increased infection rate: blood transfusion, electrophysiological monitoring, increased height, increased weight and increased body mass index. The authors concluded that there were no significant differences in infection rates between the antibiotic protocols. Preoperative prophylactic antibiotic use in instrumented lumbar spinal fusion is generally accepted and has been shown consistently to decrease postop-

erative infection rates, but the ideal duration could be variable in patients at high risk for infection. Although a comparative study by design, this study provides Level IV therapeutic evidence that prolonged postoperative regimens decrease the infection rate.

Future Directions for Research

Controlled studies are suggested comparing infection rates in spinal surgical patients with trauma, neuromuscular disease, diabetes, or other comorbidities who received antibiotics, which were discontinued within 24 hours, as compared with groups who received antibiotics for a longer period of time.

Discontinuation References

1. Dobzyniak MA, Fischgrund JS, Hankins S, Herkowitz HN. Single versus multiple dose antibiotic prophylaxis in lumbar disc surgery. *Spine*. Nov 1 2003;28(21):E453-455.
2. Hellbusch LC, Helzer-Julien M, Doran SE, et al. Single-dose vs. multiple-dose antibiotic prophylaxis in instrumented lumbar fusion--a prospective study. *Surg Neurol*. Dec 2008;70(6):622-627; discussion 627.
3. Kakimaru H, Kono M, Matsusaki M, Iwata A, Uchio Y. Postoperative antimicrobial prophylaxis following spinal decompression surgery: is it necessary? *J Orthop Sci*. May 2010;15(3):305-309.
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5. Takahashi H, Wada A, Iida Y, et al. Antimicrobial prophylaxis for spinal surgery. *J Orthop Sci*. Jan 2009;14(1):40-44.
6. Olsen MA, Mayfield J, Laurysen C, et al. Risk factors for surgical site infection in spinal surgery. *J Neurosurg*. Mar 2003;98(2 Suppl):149-155.
7. Olsen MA, Nepple JJ, Riew KD, et al. Risk factors for surgical site infection following orthopaedic spinal operations. *J Bone Joint Surg Am*. Jan 2008;90(1):62-69.

E. Wound Drains

For patients receiving antibiotic prophylaxis prior to open spine surgery and who receive placement of wound drains at wound closure, does discontinuation of prophylaxis at 24 hours result in decreased or increased postoperative infection rates as compared to discontinuation of antibiotics at time of drain removal?

A comprehensive review of the literature did not yield evidence to address the question related to the effect on postoperative infection rates of the duration of prophylaxis in the presence of a wound drain.

There is insufficient evidence to make a recommendation for or against the early discontinuation of antibiotic prophylaxis in patients with wound drains.

Grade of Recommendation: I (Insufficient Evidence)

Kanayama et al¹ performed a retrospective comparative study to compare the rate of surgical site infections in lumbar spine surgeries for two different antibiotic prophylaxis protocols. Although the purpose of this study was not to evaluate the optimal duration of antibiotic prophylaxis in the presence of drains, this was the only study identified in the literature review to address a drain removal protocol. A first-generation cephalosporin was administered unless the patient had a history of a significant allergy such as anaphylactic shock, systemic skin eruption or toxic liver dysfunction. Postoperative-dose group patients (n=1133) received antibiotics for five to seven days after surgery. No postoperative dose group patients (n=464) received antibiotics only on the day of surgery; antibiotics were given 30 minutes before skin incision. An additional dose was administered every three hours to maintain therapeutic levels throughout surgery. Infection was defined as a positive wound culture and/or typical infectious signs including a purulent exudate, surrounding erythema, and wound fluctuance detected within six months after surgery. The rate of instrumentation surgery was not statistically different between the multiple-dose group (43%) and the single-dose group (39%). The overall rate of surgical site infection was 0.7%. The infection rate was 0.8% (9/1133) in the postoperative-dose group and 0.4% (2/464) in the no postoperative-dose group; the difference between the two was not significant. Regarding the organisms of surgical site infection, resistant strains of bacteria were cultured in five (83.3%) of six patients in the postoperative-

dose group, whereas none was cultured in the no postoperative-dose group. This study provides Level III therapeutic evidence that the protocol of preoperative antibiotic prophylaxis plus intraoperative redosing every three hours is as effective as preoperative plus postoperative dosing of antibiotics. Also, extended dosing may induce resistant strains. Suction drains were left in place in fusions for two to three days. Accordingly, multidosing of antibiotics until drains are removed may not be beneficial.

The use of drains is not recommended as a means to reduce infection rates following single level surgical procedures.

Grade of Recommendation: I (Insufficient Evidence)

Payne et al² described a randomized controlled trial of drain use in 205 patients undergoing a single level laminectomy without fusion. The patients were randomized to determine whether they would receive a wound drain. There was no difference between the groups in terms of infection rates. In critique, this study appears on the surface to provide Level I evidence. However, it was downgraded to Level II because it was substantially underpowered. It provides Level II therapeutic evidence that drains have

This clinical guideline should not be construed as including all proper methods of care or excluding or other acceptable methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific procedure or treatment is to be made by the physician and patient in light of all circumstances presented by the patient and the needs and resources particular to the locality or institution

no effect on infection rates. For a single level nonfusion spine procedure, a drain neither decreases nor increases the infection rate.

Future Directions for Research

Recommendation #1:

Controlled studies are suggested comparing infection rates in nonfusion and nonimplanted spinal surgical patients with drains and discontinuation at 24 hours as compared with longer duration prophylaxis.

Recommendation #2:

Controlled studies are suggested comparing infection rates in

spinal surgical patients receiving spinal implants with drains and discontinuation at 24 hours as compared with longer duration prophylaxis.

Wound Drains References

1. Kanayama M, Hashimoto T, Shigenobu K, Oha F, Togawa D. Effective prevention of surgical site infection using a Centers for Disease Control and Prevention guideline-based antimicrobial prophylaxis in lumbar spine surgery. *J Neurosurg Spine*. Apr 2007;6(4):327-329.
2. Pavel A, Smith RL, al e. Prophylactic antibiotics in elective orthopedic surgery: A prospective study of 1591 cases. *South Med J*. 1977;Suppl 1:50-55.

F. Body Habitus

For patients receiving antibiotic prophylaxis prior to spine surgery, should the recommended protocol differ based upon body habitus (eg, body mass index)?

Obese patients are at higher risk for postoperative infection, when given a standardized dose of antibiotic prophylaxis. In spite of this conclusion, there is insufficient evidence to make a recommendation for or against recommending a different protocol for patients based upon body habitus.

Grade of Recommendation: I (Insufficient Evidence)

Chen et al¹ performed a retrospective case control study to determine the role that diabetes and other known risk factors play in the development of surgical site infection in spinal surgery patients. Of the 195 spinal infection patients included in the study, 30 had diabetes and 165 did not. Prophylactic protocols varied and the spinal surgeries were heterogeneous with instrumented and uninstrumented procedures at all levels. Outcomes were reviewed at 30 days for all patients and at one year for patients with fixation. In addition to diabetes, known risk factors for surgical site infection in spinal surgery were examined: age, gender, tobacco use, body mass index > 35 (morbid obesity), American Society of Anesthesiologists (ASA) class, intraoperative antibiotic redosing, surgical time, bone allograft use, estimated blood loss (EBL) and drain use. The adjusted relative risk of having diabetes for developing surgical site infection was significant (RR 4.10, 95% C.I. = 1.37–12.32); however, the other factors did not appear as significant risk factors. This study provides Level IV prognostic evidence that body mass index was not found to be a risk for developing an infection after spinal surgery.

Olsen (2003) et al² performed a retrospective case control study to identify the specific independent risk factors for surgical site infections occurring after laminectomy or spinal fusion. All patients received standard prophylaxis with cephalosporins or vancomycin in penicillin sensitive patients. Infection was defined using the CDC guideline definition, with infections identified between two and 83 days (median time from surgery to infection was 14 days). Of the 53 of 1918 patients who experienced surgical site infections, 12 were excluded due to missing data. These patients were compared with 179 noninfected matched controls. Infection rate even with prophylaxis was 2.76% with no significant variation in the infection rate during the four-year period. Through multivariate analysis, the authors identified postoperative incontinence, morbid obesity, tumor resection and posterior approach as independent risk factors for the development of surgical site infection. This study provides

Level IV prognostic evidence that morbid obesity is associated with a five-fold increased risk of surgical site infection after spinal surgery (OR 5.2, 95% C.I.=1.9-14.2).

Olsen (2008) et al³ described a retrospective case control study designed to determine independent risk factors for surgical site infection following orthopedic spinal operations. All patients received standard prophylaxis with cephalosporins or vancomycin in penicillin sensitive patients. Of 2316 patients, 46 patients with superficial, deep, or organ-space surgical site infections were identified and compared with 227 uninfected control patients. Univariate analyses showed serum glucose levels, preoperatively and within five days after the operation, to be significantly higher in patients in whom surgical site infection developed than in uninfected control patients. Independent risk factors for surgical site infection that were identified by multivariate analysis were diabetes (odds ratio = 3.5, 95% confidence interval = 1.2, 10.0), suboptimal timing of prophylactic antibiotic therapy (odds ratio = 3.4, 95% confidence interval = 1.5, 7.9), a preoperative serum glucose level of >125 mg/dL (>6.9 mmol/L) or a postoperative serum glucose level of >200 mg/dL (>11.1 mmol/L) (odds ratio = 3.3, 95% confidence interval = 1.4, 7.5), obesity (odds ratio = 2.2, 95% confidence interval = 1.1, 4.7) and two or more surgical residents participating in the operative procedure (odds ratio = 2.2, 95% confidence interval = 1.0, 4.7). A decreased risk of surgical site infection was associated with operations involving the cervical spine (odds ratio = 0.3, 95% confidence interval = 0.1, 0.6). The authors suggest that increasing the antibiotic dosage to adjust for obesity is an important strategy to decrease the risk of surgical site infection after spinal operations. This study provides Level IV prognostic evidence that obesity is an independent risk factor for surgical site infection in spinal surgery patients, and infection occurred at a 2% overall rate in all patients in the face of prophylactic antibiotics.

Wimmer et al⁴ performed a retrospective study of 850 spinal procedures, in which all patients received 2 gm of cefazolin in-

travenous perioperatively and a single additional injection if the surgery lasted more than three hours. In an analysis of the 22 patients who developed an infection, six were obese. Analyzed as a subgroup, obesity was found to be a risk factor with a p-value ($p < 0.04$). In critique of this study, there was no analysis of adjustments made to the antibiotic regimen in relation to the patients' BMI. While other risk factors were considered more important, obesity was found to be an independent risk factor for postoperative infection in this retrospective review despite the use of prophylactic antibiotics. This study offers Level III prognostic evidence that obesity is a risk factor for perioperative infection, but does not offer clear evidence for a specific adjustment of antibiotic prophylaxis in obese patients.

Future Directions for Research

Prospective, randomized clinical trials are suggested to evaluate the effect of antibiotic choice and altered dosing on infection rates in obese patients.

Body Habitus References

1. Chen S, Anderson MV, Cheng WK, Wongworawat MD. Diabetes associated with increased surgical site infections in spinal arthrodesis. *Clin Orthop Relat Res.* Jul 2009;467(7):1670-1673.
2. Olsen MA, Mayfield J, Laurysen C, et al. Risk factors for surgical site infection in spinal surgery. *J Neurosurg.* Mar 2003;98(2 Suppl):149-155.
3. Olsen MA, Nepple JJ, Riew KD, et al. Risk factors for surgical site infection following orthopaedic spinal operations. *J Bone Joint Surg Am.* Jan 2008;90(1):62-69.
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G. Comorbidities

For patients receiving antibiotic prophylaxis prior to open spine surgery, do comorbidities (other than obesity) such as diabetes, smoking, nutritional depletion, immunodeficiencies and concurrent use of antithrombotic therapies alter the recommendations for antibiotic prophylaxis?

CONSENSUS STATEMENT: In patients with comorbidities or for those undergoing complicated spine surgery, alternative prophylactic regimens are suggested to decrease the incidence of surgical site infections when compared to standard prophylaxis regimens.

There is insufficient evidence to make a recommendation for or against the specific alternative regimens that are efficacious. However, promising alternative regimens that have been studied include redosing, gram-negative coverage and the addition of intrawound application of vancomycin or gentamicin.

Grade of Recommendation: I (Insufficient Evidence)

Kanafani et al¹ described a case control study comparing risk factors in patients who did or did not develop infections. This study reported the incidence of postoperative infection after spinal surgeries at a single institution. They also compared infected cases with control samples from the same population in order to identify risk factors. The presence of diabetes, older age and implants (spinal hardware) were the only three variables that were significantly higher in the infected group. Both cases and controls received preoperative antibiotic prophylaxis, but infected cases received a first generation cephalosporin more often. The authors documented infection rates for patients who received first-generation cephalosporin, second-generation, third-generation or a glycopeptide. The average duration of antibiotic administration was 2.2 days in infected cases and 1.5 hours in controls. In critique of this study, the efficacy of antibiotic prophylaxis could not be analyzed for instrumented versus noninstrumented cases. The study offers Level III prognostic evidence that diabetes, older age and the use of instrumentation are risk factors for postoperative wound infection despite the use of preoperative antibiotic prophylaxis. This study does not offer any evidence suggesting alterations in antibiotic prophylaxis in the presence of specific co-morbidities.

Olsen (2003) et al² performed a retrospective case control study to identify the specific independent risk factors for surgical site infections occurring after laminectomy or spinal fusion. All patients received standard prophylaxis with cephalosporins or vancomycin in penicillin sensitive patients. Infection was defined using the CDC guideline definition, with infections identified between two and 83 days (median time from surgery to infection was 14 days). Of the 53 of 1918 patients who experienced surgical site infections, 12 were excluded due to missing data. These patients were compared with 179 noninfected matched controls. Infection rate even with prophylaxis was 2.76% with no significant variation in the infection rate during the four-year period. Cultures were obtained from infected patients and gram-negative rods and/or anaerobes were present in 17/39 (44%) of the cultures. Additionally, gram-negative rods and/or anaerobes were isolated significantly more often in patients who underwent lumbar or lumbosacral procedures (15/24) compared to patients who underwent thoracic or cervical procedures (2/15, $p < 0.001$). The authors identified postoperative incontinence, obesity, tumor resection and posterior approach as risk factors. This study provides Level III prognostic evidence that incontinence, tumor resection and posterior approach increase risk of infection and

This clinical guideline should not be construed as including all proper methods of care or excluding or other acceptable methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific procedure or treatment is to be made by the physician and patient in light of all circumstances presented by the patient and the needs and resources particular to the locality or institution

gram-negative bacteria and/or anaerobes are likely to be isolated from a portion of infected patients. Alternative prophylactic regimens may be necessary to further reduce the infection rate in patients with risk factors for surgical site infection.

Olsen (2008) et al³ described a retrospective case control study designed to determine independent risk factors for surgical site infection following orthopedic spinal operations. All patients received standard prophylaxis with cephalosporins or vancomycin in penicillin sensitive patients. Of 2316 patients, 46 patients with superficial, deep or organ-space surgical site infections were identified and compared with 227 uninfected control patients. The overall rate of spinal surgical site infection during the five years of the study was 2.0% (46/2316). Univariate analyses showed serum glucose levels, preoperatively and within five days after the operation, to be significantly higher in patients in whom surgical site infection developed than in uninfected control patients. Independent risk factors for surgical site infection that were identified by multivariate analysis were diabetes (odds ratio = 3.5, 95% confidence interval = 1.2, 10.0), suboptimal timing of prophylactic antibiotic therapy (odds ratio = 3.4, 95% confidence interval = 1.5, 7.9), a preoperative serum glucose level of >125 mg/dL (>6.9 mmol/L) or a postoperative serum glucose level of >200 mg/dL (>11.1 mmol/L) (odds ratio = 3.3, 95% confidence interval = 1.4, 7.5), obesity (odds ratio = 2.2, 95% confidence interval = 1.1, 4.7) and two or more surgical residents participating in the operative procedure (odds ratio = 2.2, 95% confidence interval = 1.0, 4.7). A decreased risk of surgical site infection was associated with operations involving the cervical spine (odds ratio = 0.3, 95% confidence interval = 0.1, 0.6). The authors concluded that diabetes was associated with the highest independent risk of spinal surgical site infection and an elevated preoperative or postoperative serum glucose level was also independently associated with an increased risk of surgical site infection. The role of hyperglycemia as a risk factor for surgical site infection in patients not previously diagnosed with diabetes should be investigated further. Administration of prophylactic antibiotics within one hour before the operation and increasing the antibiotic dosage to adjust for obesity are also important strategies to decrease the risk of surgical site infection after spinal operations. This study provides Level III prognostic evidence that diabetes is the highest independent risk factor, and infection occurred at a 2% overall rate in all patients in the face of prophylactic antibiotics. Alternative prophylactic regimens may be necessary to further reduce the infection rate in patients with diabetes and other risk factors for surgical site infection.

Takahashi et al⁴ performed a retrospective comparative study to compare the effectiveness of preoperative cephalosporin with various postoperative dosing schedules in reducing infection rates following a variety of spinal surgeries including decompression with or without fusion, with or without fixation. Group 1 received first- or second-generation cephalosporin or penicillin administered by intravenous drip infusion for seven days (4 g/day) after the operation. After the drip infusion, cephalosporin was administered orally for one week. Group 2 received first- or second-generation cephalosporin administered by intravenous drip infusion. The initial dose was given at the time of anesthesia induction. When the operating time exceeded five hours, an additional dose was given intraoperatively. The administration was

continued for five days (2 g/day) after the operation, including the day of the operation. After the drip infusion, a cephalosporin was given orally for one week. Group 3 received first- or second-generation cephalosporin administered by intravenous drip infusion, with the initial dose given at the time of anesthesia induction. Additional doses were administered every three hours during the operation. The administration was then continued for three days (2 g/day) after the operation, including the day of the operation. After the drip infusion, a cephalosporin was given orally for one week. Group 4 received first generation cephalosporin administered by intravenous drip infusion with the initial dose given at the time of anesthesia induction. Additional doses were given every three hours during the operation. The administration was then continued for two days (2 g/day) after the operation, including the day of the operation. Patients with diabetes mellitus, metastatic spinal tumors, on dialysis or receiving daily steroid administration of 5 mg or more for at least 90 days were defined as compromised hosts and included 19.1%, 16.0%, 19.1% and 28.9% of patients in groups 1-4. Adopting the CDC guideline criteria, surgical site infections involving only the skin and/or subcutaneous tissues at the site of the incision were designated superficial infections and those involving deeper soft tissues (eg, fascial and muscle layers) at the site of the incision were designated deep infections. The overall frequency of surgical site infections for the different groups were: Group 1, 2.6% (14/539); Group 2, 0.9% (5/536); Group 3 and 4, 0/257 and 0/83, respectively. Comparison using Tukey's multiple comparison test showed $p < 0.05$ for comparing infections rates between Groups 1, 2 and 3. In addition, there was no significant difference in the frequency of surgical site infection between the compromised hosts and rest of the patients. The authors concluded that when thorough prophylactic countermeasures are undertaken against perioperative surgical site infections, the frequency of these infections can be decreased, with a decrease in the duration of antimicrobial prophylaxis administration from seven days to two days. This study provides Level III therapeutic evidence that shorter duration of antimicrobial prophylaxis is more effective, and two days of antibiotic administration is recommended compared to longer durations.

Hellbusch et al⁵ conducted a prospective, randomized controlled trial examining the effects of multiple dosing regimens on the postoperative infection rate in instrumented lumbar spinal fusion. Two hundred sixty-nine patients were randomized into either a preoperative only protocol or preoperative with an extended postoperative antibiotic protocol. Patients in the preoperative only protocol group received a single dose of intravenous cefazolin 1 g or 2 g based on weight 30 minutes before incision. The extended postoperative antibiotic protocol group received the same preoperative dose plus postoperative intravenous cefazolin every eight hours for three days followed by oral cephalexin every six hours for seven days. Because of untoward drug reaction or deviation from the antibiotic protocol, 36 patients were eliminated from the study. Therefore, 233 patients completed the entire study; 117 receiving preoperative antibiotics only, and 116 receiving pre- and postoperative antibiotics. At 21 days follow-up, there was no significant difference in infection rates between the two antibiotic protocols. The postoperative infection rates were 4.3% for the preoperative only protocol

and 1.7% for the preoperative with extended antibiotic protocol. The overall postoperative infection rate was 3%. Although not statistically significant, the study identified five variables that appeared to demonstrate a trend toward increased infection rate: blood transfusion, electrophysiological monitoring, increased height, increased weight and increased body mass index. Increased tobacco use trended toward a lower infection rate. The authors concluded that preoperative prophylactic antibiotic use in instrumented lumbar spinal fusion is generally accepted and has been shown consistently to decrease postoperative infection rates, but the ideal duration could be variable in patients at high risk for infection. Although a comparative study by design, this study provides Level IV therapeutic evidence that prolonged postoperative regimens decrease the infection rate.

Rohde et al⁶ described a retrospective comparative study designed to report the incidence of postoperative spondylodiscitis in 1642 consecutive cases in which no antibiotic prophylaxis was used and to define the value of a collagenous sponge containing gentamicin in preventing disc space infections. No topical or systemic antibiotics were administered in the first 508 patients. A 4 cm × 4 cm collagenous sponge containing 8 mg of gentamicin was placed in the cleared disc space in the subsequent 1134 patients. Surgery was performed for 1584 primary lumbar disc herniations (two-level discectomy in 39 cases, three-level discectomy in one case) and 169 operations for recurrent herniations. In all patients, the erythrocyte sedimentation rate (ESR) was obtained before surgery and on the first day after surgery. Beginning in January 1992, C-reactive protein (CRP) was also analyzed before surgery, one day after surgery and six days after surgery. All patients were clinically re-examined on days 10-14 after surgery (day of discharge). Final follow-up was at 60 days. In 19 of these 508 patients, a postoperative spondylodiscitis developed, accounting for an incidence rate of 3.7%. None of the 1134 patients receiving antibiotic prophylaxis developed a postoperative spondylodiscitis during the follow-up period of 60 days. Therefore, the incidence of postoperative spondylodiscitis was 0%. Using the Fisher exact test, the difference in the incidence rates between the patient groups with and without antibiotic prophylaxis during lumbar discectomy was highly significant ($p < 0.00001$). The authors observed no complications related to the use of a collagenous sponge containing gentamicin for antibiotic prophylaxis. The authors concluded that a 3.7% incidence of postoperative spondylodiscitis was found in the absence of prophylactic antibiotics. Gentamicin-containing collagenous sponges placed in the cleared disc space, used as an alternative to traditional antibiotic prophylaxis, were effective in preventing postoperative spondylodiscitis. This study provides Level III therapeutic evidence that for uncomplicated lumbar microdiscectomy, topical administration of a gentamicin soaked collagen sponge is more effective than placebo in preventing clinically significant discitis.

Sweet et al⁷ performed a retrospective comparative study to evaluate the safety and efficacy of adjunctive local application of vancomycin for infection prophylaxis in posterior instrumented thoracic and lumbar spine wounds compared to intravenous cephalexin alone. Since 2000, 1732 consecutive thoracic and lumbar posterior instrumented spinal fusions have been performed with routine 24 hours of perioperative intravenous

antibiotic prophylaxis with cephalexin. Since 2006, 911 of these instrumented thoracic and lumbar cases had 2 g of vancomycin powder applied to the wound prior to closure in addition to intravenous antibiotics. A retrospective review for infection rates and complications was performed with an average follow-up of 2.5 years (range: 1-7 years). If wound infection was suspected based on clinical and constitutional symptoms, aspiration was completed. If aspiration demonstrated purulent material or the wound was clinically suspicious for subfascial infection, the wound was explored and aerobic, anaerobic and fungal cultures were obtained. Posterior instrumented thoracic and lumbar fusions were performed in 821 patients using intravenous cephalexin prophylaxis with a total of 21 resulting deep wound infections (2.6%). Coag negative staph was the most commonly isolated organism. Posterior instrumented thoracic and lumbar fusions were performed in 911 patients with intravenous cephalexin plus adjunctive local vancomycin powder with two ensuing deep wound infections (0.2%). The reduction in wound infections was statistically significant ($p < 0.0001$). There were no adverse clinical outcomes or wound complications related to the local application of vancomycin. The authors concluded that adjunctive local application of vancomycin powder, used as an alternative to traditional antibiotic prophylaxis, decreases the post surgical wound infection rate with statistical significance in posterior instrumented thoracolumbar spine fusions. This study provides Level III therapeutic evidence that adjunctive local application of vancomycin powder decreases the post surgical wound infection rate compared with intravenous cephalexin in posterior instrumented thoracolumbar fusion.

Future Directions for Research

Large multicenter randomized controlled trials assessing the efficacy of various protocols should be tailored to specific patient populations (eg, diabetes, trauma, neuromuscular injury or disease, prolonged multilevel instrumented surgery) at increased risk for surgical site infections.

Comorbidities References

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For patients with a history of MRSA infection, does prophylaxis with vancomycin reduce infections with MRSA compared to other antimicrobial agents?

Although no literature was available to address this specific question about patients with a history of MRSA, the search did identify studies that addressed prophylaxis to reduce infections with MRSA.

There is insufficient evidence to make a recommendation for or against the prophylactic use of vancomycin compared with other antimicrobial agents to reduce infections with MRSA.

Grade of Recommendation: I (Insufficient Evidence)

Klekamp et al¹ performed a retrospective review to determine the risk factors associated with methicillin resistant staphylococcus aurea (MRSA) wound infection after spinal surgery. The study compared 35 patients with postoperative methicillin-resistant Staphylococcus aureas (MRSA) infection to 35 uninfected control patients in order to determine risk factors. Regarding antibiotic prophylaxis, 19% of patients in the MRSA group received vancomycin at the time of index surgery, while 46% of the control group patients did not. The authors found that lymphopenia, history of chronic infections, alcohol abuse, recent hospitalization and prolonged postoperative wound drainage were significant risk factors for MRSA infection. In critique of this study, the authors did not state which prophylaxis regimen was used if vancomycin was not administered; the reader is left to assume that it is cephazolin or a similar agent. There was an equivalent rate of instrumented cases in the infected and noninfected groups; however, conclusions regarding the efficacy of vancomycin prophylaxis based only on the presence of instrumented fusion are difficult to draw. The authors concluded that there is potential for resistance to develop with increased use of vancomycin. This study offers Level III prognostic evidence that if intravenous vancomycin prophylaxis is to be considered, it should be utilized in patients at risk for MRSA and not the general population.

Sweet et al² performed a retrospective comparative study to evaluate the safety and efficacy of adjunctive local application of vancomycin for infection prophylaxis in posterior instrumented thoracic and lumbar spine wounds compared to intravenous cephalixin alone. Since 2000, 1732 consecutive thoracic and lumbar posterior instrumented spinal fusions have been performed with routine 24 hours of perioperative intravenous antibiotic prophylaxis with cephalixin. Since 2006, 911 of these instrumented thoracic and lumbar cases had 2 g of vancomycin powder applied to the wound prior to closure in addition to intravenous antibiotics. A retrospective review for infection rates and complications was performed with an average follow-up of 2.5 years (range: 1-7 years). If wound infection was suspected based on clinical and constitutional symptoms, aspiration was completed. If aspiration demonstrated purulent material or the wound was clinically

suspicious for subfascial infection, the wound was explored and aerobic, anaerobic and fungal cultures were obtained. Posterior instrumented thoracic and lumbar fusions were performed in 821 patients using intravenous cephalixin prophylaxis with a total of 21 resulting deep wound infections (2.6%). Coag negative staph was the most commonly isolated organism. Posterior instrumented thoracic and lumbar fusions were performed in 911 patients with intravenous cephalixin plus adjunctive local vancomycin powder with two ensuing deep wound infections (0.2%). The reduction in wound infections was statistically significant ($p < 0.0001$). There were no adverse clinical outcomes or wound complications related to the local application of vancomycin. The authors concluded that adjunctive local application of vancomycin powder decreases the post surgical wound infection rate with statistical significance in posterior instrumented thoracolumbar spine fusions. This study provides Level III therapeutic evidence that adjunctive local application of vancomycin powder decreases the post surgical wound infection rate compared with intravenous cephalixin in posterior instrumented thoracolumbar fusion.

Future Directions for Research

Recommendation #1:

Large multicenter randomized controlled trials assessing the efficacy of various protocols should be tailored to present subgroup analyses on patients with a history of MRSA.

Recommendation #2:

Additional studies should be performed to assess the efficacy of intravenous versus intrawound vancomycin and other antimicrobial agents in reducing the rate of MRSA infections.

MRSA References

1. Klekamp J, Spengler DM, McNamara MJ, Haas DW. Risk factors associated with methicillin-resistant staphylococcal wound infection after spinal surgery. *J Spinal Disord.* Jun 1999;12(3):187-191.
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H. Complications

What are the incidence and severity of complications/adverse events resulting from the use of prophylactic antibiotics?

CONSENSUS STATEMENT: Reported isolated complications related to prophylactic antibiotics include flushing, hypotension, rashes, intramembranous colitis and, most seriously, Stevens-Johnson syndrome.

Petignat et al¹ conducted a prospective, randomized controlled trial to compare infection rates and adverse events in those patients who received 1.5 g cefuroxime versus placebo for lumbar discectomy. Of the 1237 patients included in the study, 613 received 1.5 g intravenous cefuroxime on induction and 624 received placebo. Presence of infection, as defined by the Centers for Disease Control (CDC) guidelines, was assessed at six weeks, three months and six months. There were no significant adverse events attributed to either cefuroxime or placebo. This study provides Level I prognostic evidence that there are no significant side effects attributable to cefuroxime or placebo.

Pons et al² described a prospective, randomized trial comparing perioperative antibiotic protocols that included either 2 g Ceftizoxime or 1 g vancomycin plus 80 mg gentamicin in 291 patients who underwent various clean spine surgeries. Of the 291 patients, 142 received Ceftizoxime and 149 vancomycin/gentamicin one hour prior to incision. No patients in the ceftizoxime group experienced drug reactions, however six of the 404 patients who received the vancomycin / gentamicin protocol had clinically significant hypotension and/or flushing ('red-man syndrome') even though the antibiotics were infused over 45 minutes to minimize this effect. The authors concluded that flushing/hypotension is a reported adverse reaction which resolved by slowing or stopping the antibiotics until the symptoms resolved. This study provides Level II prognostic evidence that flushing/hypotension have been reported upon infusion with vancomycin/gentamicin.

Sweet et al³ performed a retrospective comparative study to evaluate the safety and efficacy of adjunctive local application of vancomycin for infection prophylaxis in posterior instrumented thoracic and lumbar spine wounds compared to intravenous cephalexin alone. Since 2000, 1732 consecutive thoracic and lumbar posterior instrumented spinal fusions have been performed with routine 24 hours of perioperative intravenous antibiotic prophylaxis with cephalexin. Since 2006, 911 of these instrumented thoracic and lumbar cases had 2 g of vancomycin powder applied to the wound prior to closure in addition to in-

travenous antibiotics. A retrospective review for infection rates and complications was performed with an average follow-up of 2.5 years (range: 1-7 years). There were no adverse clinical outcomes or wound complications related to the local application of vancomycin. This study provides Level II prognostic evidence that there are no adverse clinical outcomes or wound complications related to the intrawound application of vancomycin.

Kakimaru et al⁴ reported results from a retrospective comparative study comparing the infection rates following spinal surgery with and without postoperative antimicrobial prophylaxis. Of the 284 patients included in the study, 141 received preoperative and postoperative dosing and 143 received preoperative and intraoperative dosing. The antibiotics used included cefazolin 1 g in 108 patients, flomoxef 1 g in 26 patients, and piperacillin 1 g in seven patients for the postoperative group. Two cases of pseudomembranous colitis were seen in the postoperative dosing group. Although a comparative study by design, this study provides Level IV prognostic evidence that pseudomembranous colitis is a potential complication resulting from the use of prophylactic antibiotics.

Kanayama et al⁵ performed a retrospective comparative study to compare the rate of surgical site infections in lumbar spine surgeries for two different antibiotic prophylaxis protocols. A first-generation cephalosporin was administered unless the patient had a history of a significant allergy such as anaphylactic shock, systemic skin eruption or toxic liver dysfunction. Postoperative-dose group patients received antibiotics for five to seven days after surgery. No postoperative-dose group patients received antibiotics only on the day of surgery; antibiotics were given 30 minutes before skin incision. An additional dose was administered every three hours to maintain therapeutic levels throughout surgery. Resistant strains of bacteria were cultured in five (83.3%) of six patients in the multiple-dose group, whereas none was cultured in the no postoperative-dose group. Although a comparative study by design, this study provides Level IV prognostic evidence that extended antibiotic prophylaxis protocols may lead to antibiotic resistance.

This clinical guideline should not be construed as including all proper methods of care or excluding or other acceptable methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific procedure or treatment is to be made by the physician and patient in light of all circumstances presented by the patient and the needs and resources particular to the locality or institution

Laurencin et al⁶ described a single case of Stevens-Johnson syndrome caused by vancomycin. The complication presented on day 29 following instrumented occipitocervical fusion. The study provides Level IV prognostic evidence that vancomycin treatment may result in Stevens-Johnson syndrome.

Mastronardi (2005) et al⁷ reported a retrospective comparative study evaluating the efficacy of two intraoperative antibiotic prophylaxis protocols in a large series of lumbar microdiscectomies performed in two different neurosurgical centers. Of the 1167 patients included in the study, 450 received a single intravenous dose of cefazoline 1 g at induction of general anesthesia (Group A) and 717 received a single dose of intravenous ampicillin 1 g and sulbactam 500 mg at induction of anesthesia (Group P). Rash was seen in 0.89% of the cefazolin group and 0.84% in the ampicillin and sulbactam group. Although a comparative study by design, this study provides Level IV prognostic evidence that skin rash is a minor adverse reaction that may result from antibiotic prophylaxis.

Mastronardi (2004) et al⁸ presented a retrospective case series evaluating the safety and efficacy of a specific intraoperative antibiotic protocol for a variety of spinal surgeries. Over a three-year period 973 patients received ampicillin/sulbactam 1.5 g intravenous on induction or Teicoplanin 400 mg intravenous on induction (if surgery longer than two hours) with redosing of teicoplanin at four hours or 1500 mL blood loss. Rash was seen in 0.7% of patients. This study provides Level IV prognostic evidence that skin rash is a minor transient side effect that may result from antibiotic prophylaxis.

Future Directions for Research

As new antibiotic prophylaxis protocols are investigated, complications should be accurately reported.

Incidence of Complications References

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What strategies can be implemented to minimize complications/adverse events resulting from the use of prophylactic antibiotics in spine surgery?

CONSENSUS STATEMENT: In typical, uncomplicated spinal procedures, a single dose of preoperative prophylactic antibiotics with intraoperative redosing as needed is suggested to reduce the risk of complications/adverse events.

Reported isolated complications/adverse events related to prophylactic antibiotics are discussed in the previous section and include: flushing, hypotension, rashes, intramembranous colitis and, most seriously, Stevens-Johnson Syndrome.

Kakimaru et al¹ reported results from a retrospective comparative study comparing the infection rates following spinal surgery with and without postoperative antimicrobial prophylaxis. Of the 284 patients included in the study, 141 received preoperative and postoperative dosing and 143 received preoperative and intraoperative dosing. The antibiotics used included cefazolin 1 g in 108 patients, flomoxef 1 g in 26 patients, and piperacillin 1 g in 7 patients for the postoperative group. For the preoperative only group, cefazolin 1 g for 142 patients and minocycline 100 mg for one patient. Patients in the postoperative dosing group had an intravenous dose within 30 minutes of skin incision, a dose postoperatively intravenously and oral antibiotics for 2.7 days average, or the preoperative dose with intraoperative redosing at three hour intervals and a single postoperative dose. No postoperative dose patients had a preoperative dose within 30 minutes of skin incision with intraoperative dosing at three hour intervals. Infection was confirmed via bacterial cultures and inspection of wound for redness, heat, swelling and pain. In the postoperative dosing group, 2.8% (4/141) developed infections (three superficial and one deep); in the no postoperative dosing group, 1.4% (2/143) developed infections ($p=0.335$). The authors concluded that the duration of antimicrobial prophylaxis does not influence the rate of surgical site infections. This study provides Level III evidence that postoperative administration of antimicrobials appears unnecessary and preoperative plus intraoperative redosing of antibiotic prophylaxis reduces complications.

Kanayama et al² performed a retrospective comparative study to compare the rate of surgical site infections in lumbar spine surgeries for two different antibiotic prophylaxis protocols. A first-generation cephalosporin was administered unless the patient had a history of a significant allergy such as anaphylactic shock, systemic skin eruption or toxic liver dysfunction. The postoperative group patients received antibiotics for five to seven days after surgery. The no postoperative dose group patients received antibiotics only on the day of surgery; antibiotics were given 30 minutes before skin incision. An additional dose was administered every three hours to maintain therapeutic levels throughout surgery. The rate of surgical site infection was compared between the two prophylaxis groups. At a maximum of six months, a positive wound culture and/or typical infectious signs including a purulent exudate, surrounding erythema and wound fluctuance detected infections. Laboratory studies were also referenced, such as prolonged elevation in the C-reactive protein value. There were 1133 patients in the postoperative dose group and 464 patients in the no postoperative-dose group. The rate of instrumentation surgery was not statistically different between the postoperative-dose group (43%) and the no postoperative-dose group (39%). The overall rate of surgical site infection was 0.7%. The infection rate was 0.8% (9/1133) in the postoperative-dose group and 0.4% (2/464) in the no postoperative-dose group; the difference between the two was not significant. Regarding the organisms of surgical site infection, resistant strains of bacteria were cultured in five (83.3%) of six patients in the postoperative-dose group, whereas none was cultured in the single-dose group. The authors concluded there was no statistical difference was observed between protocols. The CDC protocol of preoperative dosing prevents development of resistant

strains while reducing the risk of surgical site infections. This study provides Level III therapeutic evidence that there was no significant difference between the postoperative and no postoperative dosing group protocols, ie this study suggests no advantage to giving extra antibiotic doses.

Klekamp et al³ performed a retrospective review to determine the risk factors associated with methicillin resistant staphylococcus aurea (MRSA) wound infection after spinal surgery. The study compared 35 patients with postoperative methicillin-resistant Staphylococcus aureas (MRSA) infection to 35 uninfected control patients in order to determine risk factors. Regarding antibiotic prophylaxis, 19% of patients in the MRSA group received vancomycin at the time of index surgery, while 46% of the control group patients did not. The authors found that lymphopenia, history of chronic infections; alcohol abuse, recent hospitalization and prolonged postoperative wound drainage were significant risk factors for MRSA infection. In critique of this study, the authors did not state which prophylaxis regimen was used if vancomycin was not administered; the reader is left to assume that it is cefazolin or a similar agent. There was an equivalent rate of instrumented cases in the infected and non-infected groups; however, conclusions regarding the efficacy of vancomycin prophylaxis based only on the presence of instrumented fusion are difficult to draw. The authors concluded that there is potential for resistance to develop with increased use of vancomycin. This study offers Level III prognostic evidence that if intravenous vancomycin prophylaxis is to be considered, it should be utilized in patients at risk for MRSA and not the general population.

Future Directions for Research

Large multicenter randomized controlled trials should be conducted to assess the efficacy of various protocols designed to decrease the complications resulting from antibiotic administration and emergence of antibiotic resistance bacterial strains. These should be tailored to specific patient populations (eg, obesity, diabetes, trauma, neuromuscular injury or disease, prolonged multilevel instrumented surgery) at increased risk for surgical site infections.

Minimizing Complications References

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IV. Appendices

A. Levels of Evidence for Primary Research Questions¹

Types of Studies				
	Therapeutic Studies – Investigating the results of treatment	Prognostic Studies – Investigating the effect of a patient characteristic on the outcome of disease	Diagnostic Studies – Investigating a diagnostic test	Economic and Decision Analyses – Developing an economic or decision model
Level I	<ul style="list-style-type: none"> High quality randomized trial with statistically significant difference or no statistically significant difference but narrow confidence intervals Systematic review² of Level I RCTs (and study results were homogenous³) 	<ul style="list-style-type: none"> High quality prospective study⁴ (all patients were enrolled at the same point in their disease with $\geq 80\%$ follow-up of enrolled patients) Systematic review² of Level I studies 	<ul style="list-style-type: none"> Testing of previously developed diagnostic criteria on consecutive patients (with universally applied reference “gold” standard) Systematic review² of Level I studies 	<ul style="list-style-type: none"> Sensible costs and alternatives; values obtained from many studies; with multiway sensitivity analyses Systematic review² of Level I studies
Level II	<ul style="list-style-type: none"> Lesser quality RCT (eg, $< 80\%$ follow-up, no blinding, or improper randomization) Prospective⁴ comparative study⁵ Systematic review² of Level II studies or Level I studies with inconsistent results 	<ul style="list-style-type: none"> Retrospective⁶ study Untreated controls from an RCT Lesser quality prospective study (eg, patients enrolled at different points in their disease or $< 80\%$ follow-up) Systematic review² of Level II studies 	<ul style="list-style-type: none"> Development of diagnostic criteria on consecutive patients (with universally applied reference “gold” standard) Systematic review² of Level II studies 	<ul style="list-style-type: none"> Sensible costs and alternatives; values obtained from limited studies; with multiway sensitivity analyses Systematic review² of Level II studies
Level III	<ul style="list-style-type: none"> Case control study⁷ Retrospective⁶ comparative study⁵ Systematic review² of Level III studies 	Case control study ⁷	<ul style="list-style-type: none"> Study of non-consecutive patients; without consistently applied reference “gold” standard Systematic review² of Level III studies 	<ul style="list-style-type: none"> Analyses based on limited alternatives and costs; and poor estimates Systematic review² of Level III studies
Level IV	Case series ⁸	Case series	<ul style="list-style-type: none"> Case-control study Poor reference standard 	Analyses with no sensitivity analyses
Level V	Expert Opinion	Expert Opinion	Expert Opinion	Expert Opinion

1. A complete assessment of quality of individual studies requires critical appraisal of all aspects of the study design.
2. A combination of results from two or more prior studies.
3. Studies provided consistent results.
4. Study was started before the first patient enrolled.
5. Patients treated one way (eg, cemented hip arthroplasty) compared with a group of patients treated in another way (eg, uncemented hip arthroplasty) at the same institution.
6. The study was started after the first patient enrolled.
7. Patients identified for the study based on their outcome, called “cases” (eg, failed total arthroplasty) are compared to those who did not have outcome, called “controls” (eg, successful total hip arthroplasty).
8. Patients treated one way with no comparison group of patients treated in another way.

This clinical guideline should not be construed as including all proper methods of care or excluding or other acceptable methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific procedure or treatment is to be made by the physician and patient in light of all circumstances presented by the patient and the needs and resources particular to the locality or institution

B. Grades of Recommendation for Summaries or Reviews of Studies

A: Good evidence (Level I Studies with consistent finding) for or against recommending intervention.

B: Fair evidence (Level II or III Studies with consistent findings) for or against recommending intervention.

C: Poor quality evidence (Level IV or V Studies) for or against recommending intervention.

I: Insufficient or conflicting evidence not allowing a recommendation for or against intervention.

C. Linking Levels of Evidence to Grades of Recommendation

Grade of Recommendation	Standard Language	Levels of Evidence	
A	Recommended	Two or more consistent Level I studies	
B	Suggested	One Level I study with additional supporting Level II or III studies	Two or more consistent Level II or III studies
C	May be considered; is an option	One Level I, II or III study with supporting Level IV studies	Two or more consistent Level IV studies
I (Insufficient or Conflicting Evidence)	Insufficient evidence to make recommendation for or against	A single Level I, II, III or IV study without other supporting evidence	More than one study with inconsistent findings*
*Note that in the presence of multiple consistent studies, and a single outlying, inconsistent study, the Grade of Recommendation will be based on the level of consistent studies.			

D. Protocol for NASS Literature Searches

One of the most crucial elements of evidence analysis to support development of recommendations for appropriate clinical care or use of new technologies is the comprehensive literature search. Thorough assessment of the literature is the basis for the review of existing evidence, which will be instrumental to these activities. It is important that all searches conducted at NASS employ a solid search strategy, regardless of the source of the request. To this end, this protocol has been developed and NASS-wide implementation is recommended.

NASS research staff will work with the requesting parties and the NASS-contracted medical librarian to run a comprehensive search employing at a minimum the following search techniques:

1. A comprehensive search of the evidence will be conducted using the following clearly defined search parameters (as determined by the content experts). The following parameters are to be provided to research staff to facilitate this search.
 - Time frames for search
 - Foreign and/or English language
 - Order of results (chronological, by journal, etc.)
 - Key search terms and connectors, with or without MeSH terms to be employed
 - Age range
 - Answers to the following questions:
 - o Should duplicates be eliminated between searches?
 - o Should searches be separated by term or as one large package?
 - o Should human studies, animal studies or cadaver studies be included?

This search will encompass, at minimum, a search of PubMed, EMBASE, Cochrane and Web of Science. Additional databases may be searched depending upon the topic.

2. Search results with abstracts will be compiled by the medical librarian in Endnote software. The medical librarian typically responds to requests and completes the searches within two to five business days. Results will be forwarded to the research staff, who will share it with the appropriate NASS staff member or requesting party(ies). (Research staff has access to EndNote software and will maintain a database of search results for future use/documentation.)
3. NASS staff shares the search results with an appropriate content expert (NASS Committee member or other) to assess relevance of articles and identify appropriate articles to review.
4. NASS research staff will work with Galter library to obtain requested full-text articles for review.
5. NASS members reviewing full-text articles should also review the references at the end of each article to identify additional articles which should be reviewed, but may have been missed in the search.

Following this protocol will help ensure that NASS recommendations are (1) based on a thorough review of relevant literature; (2) are truly based on a uniform, comprehensive search strategy; and (3) represent the current best research evidence available. Research staff will maintain a search history in EndNote for future use or reference.

E. Comparing the Prevalence of Rare Events

Nikolai Bogduk, MD

When events, such as infections, are uncommon or rare, comparing their prevalence in two separate populations requires large sample sizes in order to achieve statistical significance.

If the prevalence in one sample is p_1 , and the prevalence in a second sample is p_2 , and the sample size is n , the two prevalences are significantly different statistically if the 95% confidence intervals of the two prevalences do not overlap. Algebraically, this condition is determined by the equation:

$$p_1 + 1.96\sqrt{\frac{p_1(1-p_1)}{n}} < p_2 - 1.96\sqrt{\frac{p_2(1-p_2)}{n}}$$

For this condition to apply, when p_1 and p_2 are small, as applies in the case of postoperative infection rates, n needs to be large.

For example, if:

$$p_1 = 2\%$$

$$p_2 = 6\%$$

n needs to be larger than 343, effectively 350 in round numbers.

$$0.02 + 1.96\sqrt{\frac{0.02(0.98)}{n}} = 0.06 - 1.96\sqrt{\frac{0.06(0.94)}{n}}$$

$$0.02 + 1.96\sqrt{\frac{0.0196}{n}} = 0.06 - 1.96\sqrt{\frac{0.0564}{n}}$$

$$1.96\sqrt{\frac{0.0196}{n}} + 1.96\sqrt{\frac{0.0564}{n}} = 0.06 - 0.02$$

$$\sqrt{\frac{0.0196}{n}} + \sqrt{\frac{0.0564}{n}} = 0.04/1.96$$

$$\sqrt{\frac{0.0196}{n}} + \sqrt{\frac{0.0564}{n}} = 0.0204$$

$$\sqrt{0.0196} + \sqrt{0.0564} = 0.0204 \sqrt{n}$$

$$0.0196 + 0.0564 + 2\sqrt{(0.0196)(0.0564)} = (0.0204)^2 n$$

$$0.0196 + 0.0564 + 0.0665 = 0.000416 n$$

$$0.0196 + 0.0564 + 0.0665 = 0.000416 n$$

$$0.1425 = 0.000416 n$$

$$0.1425 / 0.000416 = n$$

$$n = 342.5$$

Such a number is prohibitively large for a study to undertake with the express purpose of showing a statistically significant difference in infection rates of this order of magnitude. It would require deliberately exposing $0.06 \times 343 = 21$ patients to infection and its risk of complications.

F. Comparison of 2007 Guideline Recommendations to Current Guideline Recommendations

Research Question	2007 Recommendations	Current Recommendations
A. EFFICACY		
For patients undergoing spine surgery, does antibiotic prophylaxis result in decreased infection rates compared to patients who do not receive prophylaxis?	<p>Patients undergoing spine surgery should receive preoperative prophylactic antibiotics.</p> <p>Grade of Recommendation: B</p>	<p>Preoperative prophylactic antibiotics are suggested to decrease infection rates in patients undergoing spine surgery.</p> <p>Grade of Recommendation: B</p> <hr/> <p>For a typical, uncomplicated lumbar laminotomy and discectomy, a single preoperative dose of antibiotics is suggested to decrease the risk of infection and/or discitis.</p> <p>Grade of Recommendation: B</p>
For patients undergoing spine surgery <i>without</i> spinal implants, does antibiotic prophylaxis result in decreased infection rates as compared to patients who do not receive prophylaxis?	<p>Prophylactic antibiotics are recommended to decrease the rate of spinal infections following uninstrumented lumbar spinal surgery.</p> <p>Grade of Recommendation: B</p>	<p>Prophylactic antibiotics are suggested to decrease the rate of spinal infections following uninstrumented lumbar spinal surgery.</p> <p>Grade of Recommendation: B</p>
For patients undergoing spine surgery <i>with</i> spinal implants, does antibiotic prophylaxis result in decreased infection rates as compared to patients who do not receive prophylaxis?	<p>Prophylactic antibiotics are recommended to decrease the rate of infections following instrumented spine fusion.</p> <p>Grade of Recommendation: C</p>	<p>Prophylactic antibiotics may be considered to decrease the rate of infections following instrumented spine fusion.</p> <p>Grade of Recommendation: C</p>
What rate of surgical site infections can be expected with the use of antibiotic prophylaxis, considering both patients with and patients without medical comorbidities?	Not Addressed	<p>CONSENSUS STATEMENT: Despite appropriate prophylaxis, the rate of surgical site infections in spine surgery is 0.7% - 10%. The expected rate for patients without comorbidities ranges from 0.7 – 4.3% and for patients with comorbidities ranges from 2.0 - 10%. Current best practice with antibiotic protocols has failed to eliminate (reach an infection rate of 0.0%) surgical site infections.</p> <hr/> <p>Despite appropriate prophylaxis, diabetes carries an increased infection rate compared with non-diabetic patients.</p> <p>Level of Evidence: III</p>

Research Question	2007 Recommendations	Current Recommendations
		<p>There is insufficient evidence to make a statement regarding the impact of obesity on the rate of surgical site infection in prophylaxed patients.</p> <p>Level of Evidence: I (Insufficient)</p>
B. PROTOCOL		
<p>For patients receiving antibiotic prophylaxis prior to spine surgery, what are the recommended drugs, their dosages and time of administration resulting in decreased postoperative infection rates?</p>	<p>Patients undergoing spine surgery should receive preoperative prophylactic antibiotics to decrease infection rates. The superiority of one agent or schedule over any other has not been clearly demonstrated.</p> <p>Grade of Recommendation: B</p>	<p>Preoperative antibiotic prophylaxis is suggested to decrease infection rates in patients undergoing spine surgery.</p> <p>In typical, uncomplicated spinal procedures, the superiority of one agent, dose or route of administration over any other has not been clearly demonstrated. When determining the appropriate drug choice, the patient's risk factors, allergies, length and complexity of the procedure and issues of antibiotic resistance should be considered.</p> <p>Grade of Recommendation: B</p> <hr/> <p>In typical, uncomplicated spinal procedures, a single dose of preoperative prophylactic antibiotics with intraoperative redosing as needed is suggested.</p> <p>Grade of Recommendation: B</p> <hr/> <p>CONSENSUS STATEMENT: In patients with comorbidities or for those undergoing complicated spine surgery, alternative prophylactic regimens including redosing, gram-negative coverage or the addition of intrawound application of vancomycin or gentamicin, are suggested to decrease the incidence of surgical site infections when compared to standard prophylaxis regimens.</p>
<p>For patients receiving antibiotic prophylaxis prior to spine surgery <i>without</i> spinal implants, what are the recommended drugs, their dosages and time of administration resulting in</p>	<p>Review of the current literature does not allow recommendation of one specific antibiotic protocol or dosing regimen over another in the prevention of postoperative infections following uninstrumented spinal surgery.</p>	<p>Preoperative antibiotic prophylaxis is suggested to decrease infection rates in patients undergoing spine surgery without spinal implants. In these typical, uncomplicated spinal procedures, the superiority of one agent, dose or route of administration over any other has not been</p>

Research Question	2007 Recommendations	Current Recommendations
decreased postoperative infections rates?	<i>Level of Evidence: II</i>	<p>clearly demonstrated. When determining the appropriate drug choice, the patient's risk factors, allergies, length and complexity of the procedure and issues of antibiotic resistance should be considered.</p> <p>Grade of Recommendation: B</p> <hr/> <p>In typical, uncomplicated open spine surgery without spinal implants, a single dose of preoperative prophylactic antibiotics with intraoperative redosing as needed is suggested.</p> <p>Grade of Recommendation: B</p>
For patients receiving antibiotic prophylaxis prior to spine surgery with spinal implants, what are the recommended drugs, their dosages and time of administration resulting in decreased postoperative infections rates?	<p>A systematic review of the literature did not reveal any high quality comparative studies addressing this specific question. The evidence reviewed does indicate that certain subpopulations are prone to polymicrobial infections. These populations include, but may not be limited to, patients with neuromuscular scoliosis, myelodysplasia and traumatic complete spinal cord injury. Other potential subgroups may exist, but have not yet been identified in the literature.</p> <hr/> <p>In patients with risk factors for polymicrobial infection, it is recommended that appropriate broad spectrum antibiotics be considered when instrumented fusion is performed.</p> <p>Grade of Recommendation: C</p>	<p>Preoperative antibiotic prophylaxis is suggested to decrease infection rates in patients undergoing spine surgery with spinal implants. In these complex spinal procedures, the superiority of one agent, dose or route of administration over any other has not been clearly demonstrated. When determining the appropriate drug choice, the patient's risk factors, allergies, length and complexity of the procedure and issues of antibiotic resistance should be considered.</p> <p>Grade of Recommendation: B</p> <hr/> <p>CONSENSUS STATEMENT: In patients with risk factors for polymicrobial infection, appropriate broad-spectrum antibiotics are suggested to decrease the risk of infection when instrumented fusion is performed.</p>
What is a reasonable algorithmic approach for antibiotic selection for a given patient?	Not Addressed	<p>CONSENSUS STATEMENT: Simple uncomplicated spine surgery (without instrumentation or comorbidities) => one single preoperative dose of antibiotic of choice with intraoperative redosing as needed</p> <p>CONSENSUS STATEMENT: Instrumented spine surgery, prolonged procedures,</p>

Research Question	2007 Recommendations	Current Recommendations
		comorbidities (eg, diabetes, neuromuscular disease, cord injury or general spine trauma) => one single preoperative dose of antibiotic of choice + consideration of additional gram-negative coverage and/or the application of intrawound vancomycin or gentamicin
C. REDOSING		
For patients receiving antibiotic prophylaxis prior to spine surgery, what are the intraoperative redosing recommendations for the recommended drugs (including dosages and time of administration) resulting in decreased postoperative infection rates?	Dosing regimens do not appear to affect infection rates. Although no study has shown any significant advantage to intraoperative redosing compared with a single dose, specific clinical situations may dictate additional doses (eg, length of surgery, comorbidities). <i>Level of Evidence: IV</i>	CONSENSUS STATEMENT: Intraoperative redosing within 3-4 hours may be considered to maintain therapeutic antibiotic levels throughout the procedure. The superiority of one drug has not been demonstrated in the literature. When determining the appropriate drug choice, the patient's risk factors, allergies, length and complexity of the procedure and issues of antibiotic resistance should be considered.
D. DISCONTINUATION		
For patients receiving antibiotic prophylaxis prior to spine surgery, does discontinuation of prophylaxis at 24 hours result in decreased or increased postoperative infection rates as compared to longer periods of administration?	A comprehensive review of the spine literature did not yield evidence to address the question related to the effect on postoperative infection rates of discontinuation of prophylaxis at 24 hours compared with longer periods of administration.	For typical, uncomplicated cases, a single dose of preoperative prophylactic antibiotics with intraoperative redosing as needed is suggested to decrease the risk of surgical site infection. Grade of Recommendation: B Prolonged postoperative regimens may be considered in complex situations (i.e., trauma, cord injury, neuromuscular disease, diabetes, or other comorbidities). Comorbidities and complex situations reviewed in the literature include obesity, diabetes, neurologic deficits, incontinence, preoperative serum glucose level of >125 mg/dL or a postoperative serum glucose level of >200 mg/dL, trauma, prolonged multilevel instrumented surgery, and other comorbidities. Grade of Recommendation: C
E. WOUND DRAINS		
For patients receiving antibiotic prophylaxis prior to spine surgery and who receive placement of	A comprehensive review of the literature did not yield evidence to address the question related to the effect on postoperative	A comprehensive review of the literature did not yield evidence to address the question related to the effect on postoperative

Research Question	2007 Recommendations	Current Recommendations
<p>wound drains at wound closure, does discontinuation of prophylaxis at 24 hours result in decreased or increased postoperative infection rates as compared to discontinuation of antibiotics at time of drain removal?</p>	<p>infection rates of the duration of prophylaxis in the presence of a wound drain.</p> <p>The use of drains is not recommended as a means to reduce infection rates following single level surgical procedures.</p> <p>Grade of Recommendation: I (Insufficient Evidence)</p>	<p>infection rates of the duration of prophylaxis in the presence of a wound drain.</p> <p>There is insufficient evidence to make a recommendation for or against the early discontinuation of antibiotic prophylaxis in patients with wound drains.</p> <p>Grade of Recommendation: I (Insufficient Evidence)</p> <hr/> <p>The use of drains is not recommended as a means to reduce infection rates following single level surgical procedures.</p> <p>Grade of Recommendation: I (Insufficient Evidence)</p>
F. BODY HABITUS		
<p>For patients receiving antibiotic prophylaxis prior to spine surgery, should the recommended protocol differ based upon body habitus (eg, body mass index)?</p>	<p>Obese patients are at higher risk for postoperative infection, when given a standardized dose of antibiotic prophylaxis. In spite of this conclusion, the literature search did not yield sufficient evidence to recommend any specific modifications to antibiotic protocols for this specific population.</p> <p><i>Level of Evidence: III</i></p>	<p>Obese patients are at higher risk for postoperative infection, when given a standardized dose of antibiotic prophylaxis. In spite of this conclusion, there is insufficient evidence to make a recommendation for or against recommending a different protocol for patients based upon body habitus.</p> <p>Grade of Recommendation: I (Insufficient Evidence)</p>
G. COMORBIDITIES		
<p>For patients receiving antibiotic prophylaxis prior to spine surgery, do comorbidities (other than obesity) such as diabetes, smoking, nutritional depletion and immunodeficiencies alter the recommendations for antibiotic prophylaxis?</p>	<p>Based on the literature reviewed to address this question, information was only available on patients with diabetes, older age or instrumentation. While this information suggests that these three groups are at higher risk for postoperative infection when given a standardized dose of antibiotic prophylaxis, the literature search did not yield sufficient evidence to recommend any specific modifications to antibiotic protocols for this specific population.</p> <p><i>Level of Evidence: III</i></p>	<p>CONSENSUS STATEMENT: In patients with comorbidities or for those undergoing complicated spine surgery, alternative prophylactic regimens are suggested to decrease the incidence of surgical site infections when compared to standard prophylaxis regimens.</p> <hr/> <p>There is insufficient evidence to make a recommendation for or against the specific alternative regimens that are efficacious. However, promising alternative regimens that have been studied include redosing, gram-</p>

Research Question	2007 Recommendations	Current Recommendations
		<p>negative coverage and the addition of intrawound application of vancomycin or gentamicin.</p> <p>Grade of Recommendation: I (Insufficient Evidence)</p>
<p>For patients with a history of MRSA infection, does prophylaxis with vancomycin reduce infections with MRSA compared to other antimicrobial agents?</p>	Not Addressed	<p>Although no literature was available to address this specific question about patients with a history of MRSA, the search did identify studies that addressed prophylaxis to reduce infections with MRSA.</p> <p>There is insufficient evidence to make a recommendation for or against the prophylactic use of vancomycin compared with other antimicrobial agents to reduce infections with MRSA.</p> <p>Grade of Recommendation: I (Insufficient Evidence)</p>
H. COMPLICATIONS		
<p>What are the incidence and severity of complications/adverse events resulting from the use of prophylactic antibiotics?</p>	Not Addressed	<p>CONSENSUS STATEMENT: Reported isolated complications related to prophylactic antibiotics include flushing, hypotension, rashes, intramembranous colitis and, most seriously, Stevens-Johnson Syndrome.</p>
<p>What strategies can be implemented to minimize complications/adverse events resulting from the use of prophylactic antibiotics in spine surgery?</p>	Not Addressed	<p>CONSENSUS STATEMENT: In typical, uncomplicated spinal procedures, a single dose of preoperative prophylactic antibiotics with intraoperative redosing as needed is suggested to reduce the risk of complications/adverse events.</p> <p>Reported isolated complications/adverse events related to prophylactic antibiotics are discussed in the previous section and include: flushing, hypotension, rashes, intramembranous colitis and, most seriously, Stevens-Johnson Syndrome.</p>

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