

Prevention of Orthopaedic Implant Infection in Patients Undergoing Dental Procedures

Executive Summary on the AAOS/ADA Clinical Practice Guideline

Michael P. Rethman, DDS, MS, William Watters, III, MD, Elliot Abt, DDS, Paul A. Anderson, MD, Kevin Boyer, MPH, Karen C. Carroll, MD, FCAP, Richard Parker Evans, MD, Harry C. Futrell, DMD, Kevin Garvin, MD, Stephen O. Glenn, DDS, Michael J. Goldberg, MD, Nicholas B. Hanson, MPH, John Hellstein, DDS, MS, Angela Hewlett, MD, MS, David Kolessar, MD, Calin Moucha, MD, Richard J. O'Donnell, MD, Douglas R. Osmon, MD, John E. O'Toole, MD, Anthony Rinella, MD, Mark J. Steinberg, DDS, MD

BACKGROUND

Approximately 200,000 primary total hip arthroplasties and 400,000 primary total knee arthroplasties were performed in the United States in 2003, with a projected increase to 380,000 hip procedures and over 1,500,000 knee procedures in 2020. Orthopaedic implant infection rates range from 0.3% to 8.3% in the published literature included in this guideline.^[2-14] These infections can be caused by entry of organisms into the wound during surgery, hematogenous spread, recurrence of sepsis in a previously infected joint, or contiguous spread of infection from a local source.^[15] Orthopaedic implant infections can be catastrophic and life threatening.

It has long been debated that patients with orthopaedic implants, primarily total hip and knee replacements, are prone to implant infection from routine dental procedures via hematogenous seeding of the implant from dental-procedure-related bacteremia. This potential complex pathway has never been completely elucidated.

In order to assess the current state of evidence and provide guidance to clinicians, the American Academy of Orthopaedic Surgeons (AAOS) and the American Dental Association (ADA) conducted a systematic review of the literature. The review served as the foundation for new clinical practice guidelines on prevention of orthopaedic implant infection in patients undergoing dental procedures.

The following systematic review summarized herein considered literature published through July 2011 and demonstrates the best evidence in the relationship of orthopaedic implant infection in patients undergoing dental procedures. (The full review is available at www.aaos.org/guidelines) AAOS and ADA staff methodologists and the physician/dentist work group systematically reviewed the available literature and subsequently wrote the following recommendations based on a rigorous, standardized process commensurate with IOM standards.^[16, 17]

This guideline is an educational tool to guide clinicians through treatment decisions in an effort to improve the quality and effectiveness of care. This guideline should not be construed as including all proper methods of care or excluding methods of care reasonably directed to obtaining the same results. The decision regarding any specific procedure or treatment must be made in light of all circumstances presented by the patient, the needs and resources particular to the locality or institution, and the clinical judgment of the provider.

METHODS

To develop this guideline, the AAOS-ADA work group held an introductory meeting on November 20 and 21, 2010 to establish the scope of the guideline and the systematic review. At the introductory meeting the work group constructed preliminary recommendations which specified [what] should be done in [whom], [when], [where], and [how often or how long]. The preliminary recommendations functioned as research questions for the systematic review, not as final recommendations or conclusions. Upon completing the systematic review, the work group participated in a two-day recommendation meeting on October 15 and 16, 2011 at which time the final recommendations and rationales were edited, written, and voted on. The language and grade of each recommendation was directly influenced by the best available evidence. Economical and adverse outcomes were not formally considered in creating these recommendations per AAOS policy. This guideline was created with the best available evidence as it relates to antibiotic prophylaxis, dental procedures, and orthopaedic implant infections. Detailed information on the literature search, screening, and quality/applicability appraisal can be found in the full guideline (www.aaos.org/guidelines).

Forty-seven outside organizations were solicited to provide peer reviewers for this guideline. The draft was sent to seventeen review organizations who responded to the solicitation. The disposition of all non-editorial peer review comments was documented and accompanied this guideline through the public commentary and the AAOS/ADA guideline approval process.

RESULTS

The best available evidence published in studies that met the inclusion criteria was considered for this guideline. The following is a summary of this evidence. As illustrated in Figure 1, the quality of evidence that explains the proposed association between dental procedures and orthopaedic implant infection varies. Only one study that provided direct evidence of moderate strength (represented by the arching arrow in Figure 1) was identified by the literature search and considered for this guideline. The results of this study show that dental procedures are not risk factors for subsequent implant infection and furthermore that antibiotic prophylaxis does not reduce the risk of subsequent infection.^[18]

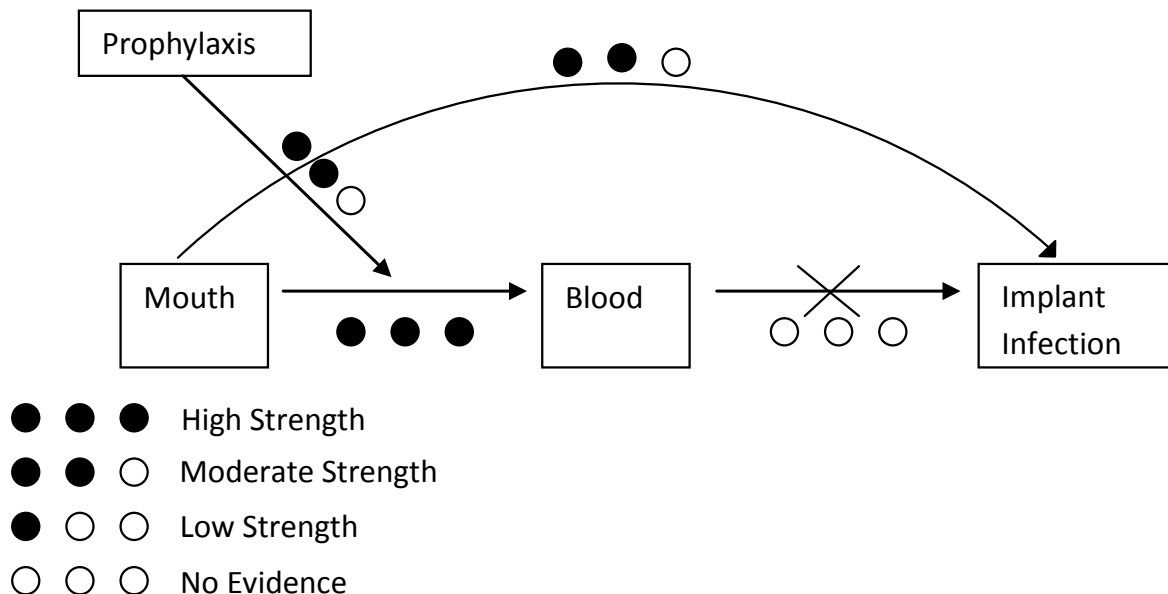


Figure 1. Overview of the Evidence

However, a multitude of indirect evidence was included in this guideline that investigates particular components of this complex mechanism. Multiple high strength studies link oral procedures to bacteremia, a surrogate measure of risk for orthopaedic implant infection. Some low strength studies investigate potential risk factors for these bacteremias. In addition, multiple moderate strength studies suggest that prophylaxis decreases the incidence of post dental procedure bacteremia. But no studies explain the microbiological relationship between bacteremia and orthopaedic implant infection.

Rates of bacteremia after dental procedures varied significantly by and within dental procedure group. Median incidence rates range from approximately 5% for chewing to upwards of 65% for simple tooth extraction and gingivectomy. (See Figure 2) As expected, the more invasive oral procedures produced the highest median incidence of bacteremia, but common daily habits such as flossing (interdental cleaners), tooth brushing, and even chewing resulted in bacteremia in some cases.

Instances of bacteremia following dental procedures may be modified by individual risk factors. While the strength of the evidence is low, several prognostic studies have addressed a multitude of patient characteristics as potential risk factors for developing bacteremia from dental procedures. These low strength studies report on oral health indicators and general patient characteristics such as age, gender, etc. The results, which are often contradictory, vary across and within procedure groups (see full guideline for details).^[19-41] No conclusions about risk factors could be drawn from these studies.

Bacteremia (Incidence)

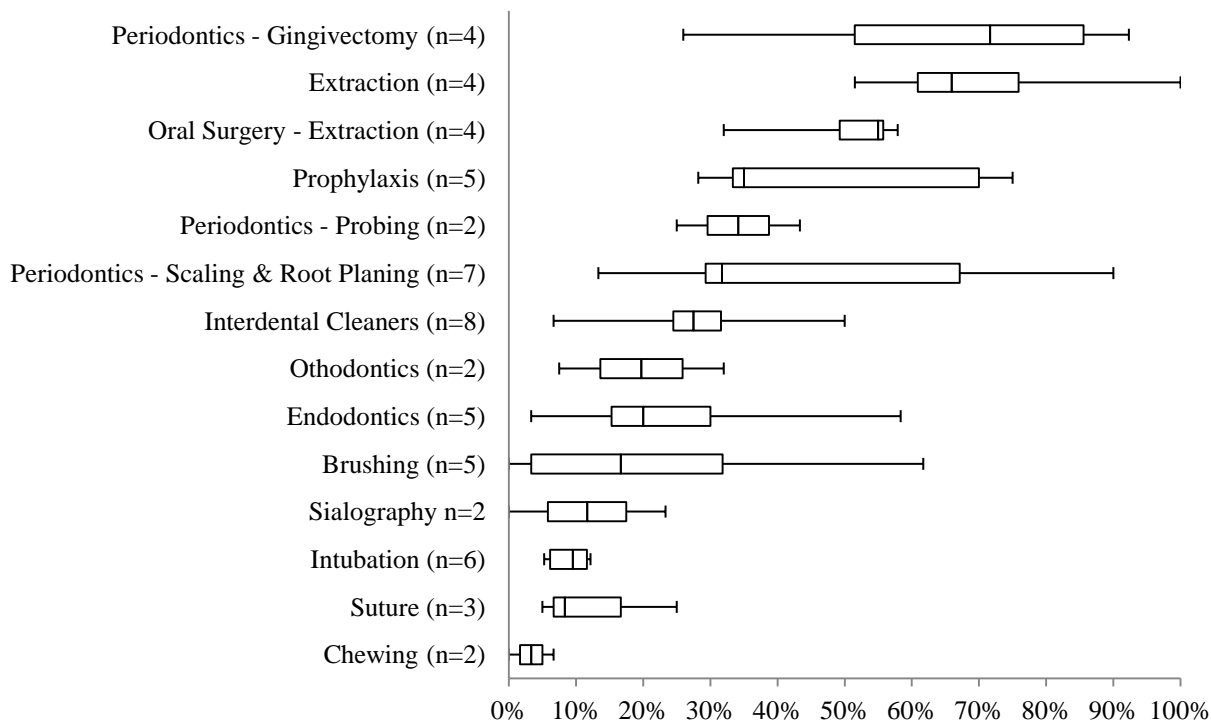


Figure 2. Incidence of Bacteremia by Procedure Group (Periodontics-Gingivectomy^[41-44], Extraction^[44-47], Oral Surgery-Extraction^[23, 29, 46, 48], Prophylaxis^[27, 28, 40, 49, 50], Periodontics-Probing^[31, 34], Periodontics-Scaling & Root Planing^[44, 45, 51-55], Interdental Cleaners^[21, 41, 56-61], Orthodontics^[62, 63], Endodontics^[44, 46, 64-66], Brushing^[28, 30, 67-69], Sialography^[70, 71], Intubation^[25, 72-76], Suture^[77-79], Chewing^[28, 80])

We recognize the diversity of opinion concerning the clinical importance of bacteremia as a surrogate outcome for orthopaedic implant infection, and understand the clinician’s concern and rationale for wanting to prevent bacteremia. Therefore, we conducted two independent network meta-analyses on the efficacy of antibiotic and topical antimicrobial prophylaxis for bacteremia post simple tooth extraction. Other studies exist that investigate different dental procedures, but the most robust data resides in tooth extraction studies. Several studies of moderate strength were included in these analyses. These studies investigated the effect of many different antibiotic drugs and topical antimicrobials. Twenty-one antibiotic studies^[32, 37, 45, 49, 67, 81-96], and thirteen topical oral antimicrobial studies^[35, 45, 97-107] were included in our network meta-analyses. The majority of the results from the individual studies and the overall effect of these prophylactic agents according to our analyses were favorable and clinically meaningful (Tables 1 and 2).

Table 1. Number Needed to Treat (NNT) to Prevent Bacteremia Post Tooth Extraction

Treatment	NNT
Amoxicillin	1.8
Penicillin	2.5
Erythromycin	5.0
Clindamycin	3.0
Josamycin	14.0
Moxifloxacin	1.9
Cefaclor	9.3
IV Tetracycline	1.5
IV Cefuroxime	2.1
IM Teicoplanin	2.2
Topical Amoxicillin	4.0
Antiseptic Rinse	3.2
IM Pen. OR IV Erythro. OR Oral OR IV Amox.	3.7

Table 2. Number Needed to Treat (NNT) to Prevent Bacteremia Post Tooth Extraction

Treatment	NNT
Saline Rinse	70.0
Chlorhexidine Rinse	2.5
Povidone-Iodine Rinse	2.3
Chloramine T Rinse/Brush	2.5
Lugol's Solution Rinse	11.7
Hydrogen Peroxide Rinse	3.9
Sodium Perborate-Ascorbic Acid Rinse	2.5
Phenolated Rinse	2.8
Placebo Rinse	n/a
Operative Field Isolation	1.8
Isolation + Iodine Rinse	1.8
Isolation + Chlorhexidine Rinse	1.5

While there was no direct evidence to explain the proposed association between bacteremia and orthopaedic implant infection, we summarized the microbiological information pertaining to cases and rates of bacteremia and implant infection when available based on our included literature. According to orthopaedic implant cohort studies^[2-14] approximately 53% of organisms responsible for the infections were *Staphylococcus* species. The overall rate of infection was approximately 1.5%. Of the studies that distinguished early from late infections^[2, 5, 6, 9-12, 14] we were able to calculate rates of 0.4% and 0.9% respectively. According to orthopaedic implant infection case series^[18, 108-123] approximately 64% of the infections were *Staphylococcus* species. Of the studies that distinguished early from late infections, 36.7% were early and 63.3% were late^[18, 108-112, 114-119, 121]. Dental-related bacteremia varied greatly by procedure and study, as did the organism responsible for the bacteremia.^[21, 25, 27, 28, 31, 42, 45-47, 51, 53-57, 59-63, 65, 66, 69, 71, 73-79, 90, 92, 94, 124-140] No clear association between the organisms found in the prosthetic implant infections and bacteremia exists. However, the majority of the organisms found in implant infections are *Staphylococcus* and the majority of the organisms found as the cause of bacteremias are *Streptococcus*. (See full guideline for detailed information)

Considering all of the above information in accordance with AAOS clinical practice guideline protocol, the workgroup created the following recommendations:

Recommendation 1

The practitioner might consider discontinuing the practice of routinely prescribing prophylactic antibiotics for patients with hip and knee prosthetic joint implants undergoing dental procedures.

Grade of Recommendation: Limited

A **Limited** recommendation means the quality of the supporting evidence that exists is unconvincing, or that well-conducted studies show little clear advantage to one approach versus another.

Practitioners should be cautious in deciding whether to follow a recommendation classified as **Limited**, and should exercise judgment and be alert to emerging publications that report evidence. Patient preference should have a substantial influencing role.

Recommendation 2

We are unable to recommend for or against the use of topical oral antimicrobials in patients with prosthetic joint implants or other orthopaedic implants undergoing dental procedures.

Grade of Recommendation: Inconclusive

An **Inconclusive** recommendation means that there is a lack of compelling evidence resulting in an unclear balance between benefits and potential harm.

Practitioners should feel little constraint in deciding whether to follow a recommendation labeled as **Inconclusive** and should exercise judgment and be alert to future publications that clarify existing evidence for determining balance of benefits versus potential harm. Patient preference should have a substantial influencing role.

Recommendation 3

In the absence of reliable evidence linking poor oral health to prosthetic joint infection, it is the opinion of the work group that patients with prosthetic joint implants or other orthopaedic implants maintain appropriate oral hygiene.

Grade of Recommendation: Consensus

A **Consensus** recommendation means that expert opinion supports the guideline recommendation even though there is no available empirical evidence that meets the inclusion criteria.

Practitioners should be flexible in deciding whether to follow a recommendation classified as **Consensus**, although they may set boundaries on alternatives. Patient preference should have a substantial influencing role.

DISCUSSION

Direct support for Recommendation 1 comes from a single well-conducted case-control study. Case-control studies are appropriate to answer questions regarding risk factors or etiology. Study enrollment consisted of 339 patients with prosthetic hip or knee infections (cases) and 339 patients with hip or knee arthroplasties without infection (controls) hospitalized on an orthopaedic service during the same time period. The comparison between these groups was for differences in dental visits (exposure) in terms of high and low-risk dental procedures, with and without antibiotic prophylaxis. Results reported as odds ratios with 95% confidence interval, demonstrate no statistically significant differences between groups. Neither dental procedures nor antibiotic prophylaxis prior to dental procedures were associated with risk of prosthetic hip or knee infections. The authors performed a sample size calculation and withdrawals were low, minimizing attrition bias. The prospective nature of this study minimized recall bias. Additionally, blinding of the treatment group to those assessing outcomes limits detection bias.

Although this one study of direct evidence was of moderate strength, it did have limitations. The authors conducted covariate analysis on some subgroups of higher risk patients. The number of patients in these subgroups, however, was relatively small, and there is insufficient data to suggest that these patients are at higher risk of experiencing hematogenous infections.

Indirect evidence was also considered for Recommendation 1. There is high strength evidence that demonstrates the occurrence of bacteremia with dental procedures. Historically, there has been a suggestion that bacteremias can cause hematogenous seeding of total joint implants, both in the early postoperative period and for many years following implantation. Two years post joint replacement was previously considered the critical period for prophylaxis. In addition, bacteremias may occur during normal daily activities such as chewing and tooth brushing. It is likely that these daily activities induce many more bacteremias than dental-procedure-associated bacteremias. While evidence supports a strong association between certain dental procedures and bacteremia, there is no evidence to demonstrate a direct link between dental-procedure-associated bacteremia and infection of prosthetic joints or other orthopaedic implants. Multiple studies of moderate and high strength evidence suggest that antibiotic prophylaxis decreases the risk of dental-procedure-associated bacteremias. However, dental-procedure-associated bacteremia is a surrogate outcome for prosthetic joint infection. There is no evidence that these bacteremias are related to prosthetic joint infections. Surrogate outcomes may or may not relate to a clinically relevant patient outcome. A positive surrogate outcome (e.g. reduced bacteremias) however, could mask a negative patient-centered outcome (e.g. implant infection).

Recommendation 1 is limited to patients with hip and knee prostheses because the single study of direct evidence included only patients with these types of orthopaedic implants. There is no direct evidence that met our inclusion criteria for patients with other types of orthopaedic implants.

Evidence for Recommendation 2 is sparse. There was no direct evidence to support or refute the use of prophylaxis (topical antimicrobials) before dental procedures. The same indirect evidence discussed above relating to dental procedures and bacteremia was considered for Recommendation 2. There is conflicting evidence regarding the effect of antimicrobial mouth rinse on the incidence of bacteremia post dental procedures. One high strength study reports no difference in the incidence of bacteremia following antimicrobial mouth rinsing in patients undergoing dental extractions. Conversely, numerous studies suggest that topical antimicrobial prophylaxis decreases the incidence of dental-procedure-associated bacteremia. However, there is no evidence that application of antimicrobial mouth rinses before dental procedures prevents infection of prosthetic joints or other orthopaedic implants. Due to the lack of direct evidence, contradictory nature of the indirect evidence pertaining to topical oral antimicrobials, and continued concern with surrogate outcomes, Recommendation 2 is inconclusive. The work group is unable to recommend for or against the use of topical oral antimicrobials.

Recommendation 3 is an opinion statement due to the lack of evidence relating oral hygiene measures to prosthetic joint or other orthopaedic implant infections. Oral hygiene measures are low cost, provide potential benefit, are consistent with current practice, and are in accordance with good oral health. There is evidence of the relationship of oral microflora to bacteremia. This bacteremia may be associated with poor oral hygiene. This implies that improvement of oral hygiene (or maintenance of good oral hygiene) may be beneficial in reducing bacteremia.

These recommendations are not intended to stand alone. Treatment decisions should be made in light of all circumstances presented by the patient. Treatments and procedures applicable to the individual patient rely on mutual communication between patient, physician, dentist and other healthcare practitioners in accordance with evidence based medicine applicability.

1. Kurtz, S., et al., *Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030*. J Bone Joint Surg Am, 2007. **89**(4): p. 780-785.
2. Ainscow, D.A. and R.A. Denham, *The risk of haematogenous infection in total joint replacements*. J Bone Joint Surg Br., 1984. **66**(4): p. 580-582.
3. Choong, P.F., et al., *Risk factors associated with acute hip prosthetic joint infections and outcome of treatment with a rifampinbased regimen*. Acta Orthop., 2007. **78**(6): p. 755-765.
4. Goodman, S.B., et al., *Revision total hip arthroplasty in juvenile chronic arthritis: 17 revisions in 11 patients followed for 4-12 years*. Acta Orthop, 2006. **77**(2): p. 242-250.
5. Hamilton, H. and J. Jamieson, *Deep infection in total hip arthroplasty*. Can J Surg, 2008. **51**(2): p. 111-117.
6. Klenerman, L., D. Seal, and K. Sullens, *Combined prophylactic effect of ultraclean air and cefuroxime for reducing infection in prosthetic surgery*. Acta Orthop Belg., 1991. **57**(1): p. 19-24.
7. Mont, M.A., et al., *Clinical experience with a proximally porous-coated second-generation cementless total hip prosthesis: minimum 5-year follow-up*. J Arthroplasty, 1999. **14**(8): p. 930-939.
8. Petrie, R.S., et al., *Metal-backed patellar component failure in total knee arthroplasty: a possible risk for late infection*. Am J Orthop (Belle.Mead NJ), 1998. **27**(3): p. 172-176.
9. Sancheti, K.H., et al., *The INDUS knee prosthesis - Prospective multicentric trial of a posteriorly stabilized high-flex design: 2 years follow-up*. Indian J Orthop, 2009. **43**(4): p. 367-374.
10. Smith, J.A., H.K. Dunn, and B.J. Manaster, *Cementless femoral revision arthroplasty. 2- to 5-year results with a modular titanium alloy stem*. J Arthroplasty, 1997. **12**(2): p. 194-201.
11. Soutanis, K., et al., *Late infection in patients with scoliosis treated with spinal instrumentation*. Clin Orthop.Relat Res., 2003(411): p. 116-123.
12. Uckay, I., et al., *Low incidence of haematogenous seeding to total hip and knee prostheses in patients with remote infections*. J Infect., 2009. **59**(5): p. 337-345.

13. Wagner, M. and H. Wagner, *Medium-term results of a modern metal-on-metal system in total hip replacement*. Clin Orthop Relat Res., 2000(379): p. 123-133.
14. Wimmer, C., M. Nogler, and B. Frischhut, *Influence of antibiotics on infection in spinal surgery: a prospective study of 110 patients*. J Spinal Disord., 1998. **11**(6): p. 498-500.
15. Della Valle, C.J., J.D. Zuckerman, and P.E. Di Cesare, *Periprosthetic Sepsis*. Clinical Orthopaedics and Related Research, 2004(420): p. 26-31.
16. Institute of Medicine, *Clinical Practice Guidelines We Can Trust*, 2011, National Academies Press: Washington, D.C.
17. Institute of Medicine, *Finding What Works in Health Care: Standards for Systematic Reviews* 2011, Washington, D.C.: National Academies Press.
18. Berbari, E.F., et al., *Dental procedures as risk factors for prosthetic hip or knee infection: a hospital-based prospective case-control study*. Clin Infect. Dis., 2010. **50**(1): p. 8-16.
19. Barbosa, M., et al., *General anesthesia increases the risk of bacteremia following dental extractions*. Oral Surg Oral Med. Oral Pathol. Oral Radiol. Endod., 2010. **110**(6): p. 706-712.
20. Ashare, A., et al., *Chronic liver disease impairs bacterial clearance in a human model of induced bacteremia*. Clin Transl. Sci., 2009. **2**(3): p. 199-205.
21. Crasta, K., et al., *Bacteraemia due to dental flossing*. J Clin Periodontol., 2009. **36**(4): p. 323-332.
22. Lockhart, P.B., et al., *Poor oral hygiene as a risk factor for infective endocarditis-related bacteremia*. J Am. Dent. Assoc., 2009. **140**(10): p. 1238-1244.
23. Enabulele, O.I., H.S.A. Aluyi, and O. Omokao, *Incidence of bacteraemia following teeth extraction at the dental clinic of the University of Benin Teaching Hospital, Benin city, Nigeria*. African Journal of Biotechnology, 2008. **7**(10): p. 1390-1393.
24. Tomas, I., et al., *Prevalence of bacteraemia following third molar surgery*. Oral Diseases, 2008. **14**(1): p. 89-94.
25. Valdes, C., et al., *The incidence of bacteraemia associated with tracheal intubation*. Anaesthesia, 2008. **63**(6): p. 588-592.
26. Brennan, M.T., et al., *The impact of oral disease and nonsurgical treatment on bacteremia in children*. J Am. Dent. Assoc., 2007. **138**(1): p. 80-85.
27. Cherry, M., et al., *Effect of rinsing with povidone-iodine on bacteraemia due to scaling: a randomized-controlled trial*. J Clin Periodontol., 2007. **34**(2): p. 148-155.
28. Forner, L., et al., *Incidence of bacteremia after chewing, tooth brushing and scaling in individuals with periodontal inflammation*. J Clin Periodontol., 2006. **33**(6): p. 401-407.
29. Takai, S., et al., *Incidence and bacteriology of bacteremia associated with various oral and maxillofacial surgical procedures*. Oral Surg Oral Med. Oral Pathol. Oral Radiol. Endod., 2005. **99**(3): p. 292-298.
30. Bhanji, S., et al., *Transient bacteremia induced by toothbrushing a comparison of the Sonicare toothbrush with a conventional toothbrush*. Pediatric Dentistry, 2002. **24**(4): p. 295-299.
31. Daly, C.G., et al., *Bacteremia due to periodontal probing: a clinical and microbiological investigation*. J Periodontol., 2001. **72**(2): p. 210-214.
32. Wahlmann, U., et al., *Clinical and microbiological efficacy of single dose cefuroxime prophylaxis for dental surgical procedures*. Int. J. Antimicrob. Agents, 1999. **12**(3): p. 253-256.
33. Roberts, G.J., et al., *Bacteremia of dental origin and antimicrobial sensitivity following oral surgical procedures in children*. Pediatric Dentistry, 1998. **20**(1): p. 28-36.
34. Daly, C., et al., *Bacteraemia caused by periodontal probing*. Aust. Dent. J., 1997. **42**(2): p. 77-80.
35. Lockhart, P.B., *An analysis of bacteremias during dental extractions. A double-blind, placebo-controlled study of chlorhexidine*. Archives of Internal Medicine, 1996. **156**(5): p. 513-520.
36. Okabe, K., K. Nakagawa, and E. Yamamoto, *Factors affecting the occurrence of bacteremia associated with tooth extraction*. Int. J. Oral Maxillofac. Surg., 1995. **24**(3): p. 239-242.
37. Coulter, W.A., et al., *Bacteremia in children following dental extraction*. J Dent. Res., 1990. **69**(10): p. 1691-1695.
38. Trivedi, D.N., *Bacteraemia due to operative procedure*. J Indian Dent. Assoc., 1984. **56**(12): p. 447-452.
39. Silver, J.G., A.W. Martin, and B.C. McBride, *Experimental transient bacteraemias in human subjects with varying degrees of plaque accumulation and gingival inflammation*. J Clin Periodontol., 1977. **4**(2): p. 92-99.

40. De Leo, A.A., et al., *The incidence of bacteremia following oral prophylaxis on pediatric patients*. Oral Surg Oral Med.Oral Pathol., 1974. **37**(1): p. 36-45.
41. Lineberger, L.T. and T.J. De Marco, *Evaluation of transient bacteremia following routine periodontal procedures*. J Periodontol., 1973. **44**(12): p. 757-762.
42. Rogosa, M., et al., *Blood sampling and cultural studies in the detection of postoperative bacteremias*. J Am.Dent.Assoc., 1960. **60**: p. 171-180.
43. Wada, K., M. Tomizawa, and I. Sasaki, *Study on bacteriemia in patients with pyorrhea alveolaris caused by surgical operations*. J Nihon Univ Sch Dent., 1968. **10**(2): p. 52-57.
44. Bender, I.B., et al., *Dental procedures in patients with rheumatic heart disease*. Oral Surg Oral Med.Oral Pathol., 1963. **16**: p. 466-473.
45. Casolari, C., et al., *Incidence of oral bacteremia and antimicrobial prophylaxis*. J Chemother., 1989. **1**(4 Suppl): p. 968-971.
46. Heimdahl, A., et al., *Detection and quantitation by lysis-filtration of bacteremia after different oral surgical procedures*. J Clin Microbiol., 1990. **28**(10): p. 2205-2209.
47. Khairat, O., *The non-aerobes of post-extraction bacteremia*. J Dent.Res., 1966. **45**(4): p. 1191-1197.
48. Josefsson, K., et al., *Effect of phenoxymethylpenicillin and erythromycin prophylaxis on anaerobic bacteraemia after oral surgery*. J Antimicrob.Chemother., 1985. **16**(2): p. 243-251.
49. Hall, G., et al., *Prophylactic administration of penicillins for endocarditis does not reduce the incidence of postextraction bacteremia*. Clin Infect.Dis., 1993. **17**(2): p. 188-194.
50. Forner, L., et al., *Increased plasma levels of IL-6 in bacteremic periodontitis patients after scaling*. J Clin Periodontol., 2006. **33**(10): p. 724-729.
51. Morozumi, T., et al., *Effects of irrigation with an antiseptic and oral administration of azithromycin on bacteremia caused by scaling and root planing*. J Periodontol., 2010. **81**(11): p. 1555-1563.
52. Lofthus, J.E., et al., *Bacteremia following subgingival irrigation and scaling and root planing*. J Periodontol., 1991. **62**(10): p. 602-607.
53. Waki, M.Y., et al., *Effects of subgingival irrigation on bacteremia following scaling and root planing*. J Periodontol., 1990. **61**(7): p. 405-411.
54. Lafaurie, G.I., et al., *Periodontopathic microorganisms in peripheric blood after scaling and root planing*. J Clin Periodontol., 2007. **34**(10): p. 873-879.
55. Lucartorto, F.M., C.K. Franker, and J. Maza, *Postscaling bacteremia in HIV-associated gingivitis and periodontitis*. Oral Surg Oral Med.Oral Pathol., 1992. **73**(5): p. 550-554.
56. Ramadan, A.E., S.A. Zaki, and Z.M. Nour, *A study of transient bacteremia following the use of dental floss silk and interdental stimulators*. Egypt.Dent.J, 1975. **21**(4): p. 19-28.
57. Berger, S.A., et al., *Bacteremia after the use of an oral irrigation device. A controlled study in subjects with normal-appearing gingiva: comparison with use of toothbrush*. Annals of Internal Medicine, 1974. **80**(4): p. 510-511.
58. *Oral irrigation and bacteremia*. J N.C Dent.Soc., 1972. **55**(2): p. 23-24.
59. Romans, A.R. and G.R. App, *Bacteremia, a result from oral irrigation in subjects with gingivitis*. J Periodontol., 1971. **42**(12): p. 757-760.
60. Felix, J.E., S. Rosen, and G.R. App, *Detection of bacteremia after the use of an oral irrigation device in subjects with periodontitis*. J Periodontol., 1971. **42**(12): p. 785-787.
61. Wank, H.A., et al., *A quantitative measurement of bacteremia and its relationship to plaque control*. J Periodontol., 1976. **47**(12): p. 683-686.
62. Gurel, H.G., F.A. Basciftci, and U. Arslan, *Transient bacteremia after removal of a bonded maxillary expansion appliance*. Am.J Orthod.Dentofacial Orthop., 2009. **135**(2): p. 190-193.
63. Erverdi, N., et al., *Investigation of bacteremia after orthodontic banding*. Am.J Orthod.Dentofacial Orthop., 1999. **116**(6): p. 687-690.
64. Savarrio, L., et al., *Detection of bacteraemias during non-surgical root canal treatment*. J Dent., 2005. **33**(4): p. 293-303.
65. Baumgartner, J.C., J.P. Hegggers, and J.W. Harrison, *The incidence of bacteremias related to endodontic procedures. I. Nonsurgical endodontics*. J Endod., 1976. **2**(5): p. 135-140.

66. Baumgartner, J.C., J.P. Hegggers, and J.W. Harrison, *Incidence of bacteremias related to endodontic procedures. II. Surgical endodontics.* J Endod., 1977. **3**(10): p. 399-402.
67. Lockhart, P.B., et al., *Bacteremia associated with toothbrushing and dental extraction.* Circulation, 2008. **117**(24): p. 3118-3125.
68. Sconyers, J.R., D.D. Albers, and R. Kelly, *Relationship of bacteremia to toothbrushing in clinically healthy patients.* General Dentistry, 1979. **27**(3): p. 51-52.
69. Sconyers, J.R., J.J. Crawford, and J.D. Moriarty, *Relationship of bacteremia to toothbrushing in patients with periodontitis.* J Am.Dent.Assoc., 1973. **87**(3): p. 616-622.
70. Nixon, P.P., et al., *Does sialography require antibiotic prophylaxis?* Br.J Radiol., 2009. **82**(981): p. 732-734.
71. Lamey, P.J., et al., *Bacteraemia consequential to sialography.* Br.Dent.J, 1985. **158**(6): p. 218-220.
72. Ali, M.T., et al., *The occurrence of bacteraemia associated with the use of oral and nasopharyngeal airways.* Anaesthesia, 1992. **47**(2): p. 153-155.
73. Dinner, M., M. Tjeuw, and J.F. Artusio, Jr., *Bacteremia as a complication of nasotracheal intubation.* Anesthesia and Analgesia, 1987. **66**(5): p. 460-462.
74. Berry, F.A., Jr., W.L. Blankenbaker, and C.G. Ball, *Comparison of bacteremia occurring with nasotracheal and orotracheal intubation.* Anesthesia and Analgesia, 1973. **52**(6): p. 873-876.
75. Oncag, O., et al., *Investigation of bacteremia following nasotracheal intubation.* Paediatric Anaesthesia, 2005. **15**(3): p. 194-198.
76. Hansen, C.P., et al., *Bacteraemia following orotracheal intubation and oesophageal balloon dilatation.* Thorax, 1989. **44**(8): p. 684-685.
77. King, R.C., J.J. Crawford, and E.W. Small, *Bacteremia following intraoral suture removal.* Oral Surg Oral Med.Oral Pathol., 1988. **65**(1): p. 23-28.
78. Wampole, H.S., A.L. Allen, and A. Gross, *The incidence of transient bacteremia during periodontal dressing change.* J Periodontol., 1978. **49**(9): p. 462-464.
79. Brown, A.R., et al., *Bacteremia and intraoral suture removal: can an antimicrobial rinse help?* J Am.Dent.Assoc., 1998. **129**(10): p. 1455-1461.
80. Murphy, A.M., et al., *Chewing fails to induce oral bacteraemia in patients with periodontal disease.* J Clin Periodontol., 2006. **33**(10): p. 730-736.
81. Lockhart, P.B., et al., *Impact of amoxicillin prophylaxis on the incidence, nature, and duration of bacteremia in children after intubation and dental procedures.* Circulation, 2004. **109**(23): p. 2878-2884.
82. Aitken, C., et al., *Comparative efficacy of oral doses of clindamycin and erythromycin in the prevention of bacteraemia.* Br.Dent.J, 1995. **178**(11): p. 418-422.
83. Cannell, H., et al., *Failure of two macrolide antibiotics to prevent post-extraction bacteraemia.* Br.Dent.J, 1991. **171**(6): p. 170-173.
84. Diz, D.P., et al., *Comparative efficacies of amoxicillin, clindamycin, and moxifloxacin in prevention of bacteremia following dental extractions.* Antimicrobial Agents and Chemotherapy, 2006. **50**(9): p. 2996-3002.
85. Hall, G., A. Heimdahl, and C.E. Nord, *Effects of prophylactic administration of cefaclor on transient bacteremia after dental extraction.* Eur.J Clin Microbiol.Infect.Dis., 1996. **15**(8): p. 646-649.
86. Hall, G., C.E. Nord, and A. Heimdahl, *Elimination of bacteraemia after dental extraction: comparison of erythromycin and clindamycin for prophylaxis of infective endocarditis.* J Antimicrob.Chemother., 1996. **37**(4): p. 783-795.
87. Head, T.W., et al., *A comparative study of the effectiveness of metronidazole and penicillin V in eliminating anaerobes from postextraction bacteremias.* Oral Surg Oral Med.Oral Pathol., 1984. **58**(2): p. 152-155.
88. Jokinen, M.A., *Bacteremia following dental extraction and its prophylaxis.* Suomen Hammaslaakariseuran Toimituksia, 1970. **66**(3): p. 69-100.
89. Khairat, O., *An effective antibiotic cover for the prevention of endocarditis following dental and other post-operative bacteraemias.* J Clin Pathol., 1966. **19**(6): p. 561-566.
90. Maskell, J.P., et al., *Teicoplanin as a prophylactic antibiotic for dental bacteraemia.* J Antimicrob.Chemother., 1986. **17**(5): p. 651-659.
91. Roberts, G.J., P. Radford, and R. Holt, *Prophylaxis of dental bacteraemia with oral amoxycillin in children.* Br.Dent.J, 1987. **162**(5): p. 179-182.

92. Shanson, D.C., et al., *Comparison of intravenous teicoplanin with intramuscular amoxycillin for the prophylaxis of streptococcal bacteraemia in dental patients.* J Antimicrob.Chemother., 1987. **20**(1): p. 85-93.
93. Shanson, D.C., et al., *Erythromycin stearate, 1.5 g, for the oral prophylaxis of streptococcal bacteraemia in patients undergoing dental extraction: efficacy and tolerance.* J Antimicrob.Chemother., 1985. **15**(1): p. 83-90.
94. Shanson, D.C., P. Cannon, and M. Wilks, *Amoxycillin compared with penicillin V for the prophylaxis of dental bacteraemia.* J Antimicrob.Chemother., 1978. **4**(5): p. 431-436.
95. Vergis, E.N., et al., *Topical antibiotic prophylaxis for bacteremia after dental extractions.* Oral Surg Oral Med.Oral Pathol.Oral Radiol.Endod., 2001. **91**(2): p. 162-165.
96. DeVries, J., L.E. Francis, and D. Lang, *Control of post-extraction bacteraemias in the penicillin-hypersensitive patient.* J Can Dent.Assoc.(Tor.), 1972. **38**(2): p. 63-66.
97. Jokinen, M.A., *Prevention of postextraction bacteremia by local prophylaxis.* Int.J Oral Surg, 1978. **7**(5): p. 450-452.
98. MacFarlane, T.W., M.M. Ferguson, and C.J. Mulgrew, *Post-extraction bacteraemia: role of antiseptics and antibiotics.* Br.Dent.J, 1984. **156**(5): p. 179-181.
99. Rahn, R., et al., *Preventing post-treatment bacteremia: comparing topical povidone-iodine and chlorhexidine.* J Am.Dent.Assoc., 1995. **126**(8): p. 1145-1149.
100. Scopp, I.W. and L.D. Orvieto, *Gingival degerming by povidone-iodine irrigation: bacteremia reduction in extraction procedures.* J Am.Dent.Assoc., 1971. **83**(6): p. 1294-1296.
101. Sweet, J.B., et al., *Nitroblue tetrazolium and Limulus assays for bacteremia after dental extraction: effect of topical antiseptics.* J Am.Dent.Assoc., 1978. **96**(2): p. 276-281.
102. Tomas, C.I., et al., *Effect of a chlorhexidine mouthwash on the risk of postextraction bacteremia.* Infection Control and Hospital Epidemiology, 2007. **28**(5): p. 577-582.
103. Cutcher, J.L., et al., *Control of bacteremia associated with extraction of teeth. II.* Oral Surg Oral Med.Oral Pathol., 1971. **31**(5): p. 602-605.
104. Francis, L.E., J. DeVries, and D. Lang, *An oral antiseptic for the control of post-extraction bacteraemia.* J Can Dent.Assoc.(Tor.), 1973. **39**(1): p. 55-57.
105. Jones, J.C., et al., *Control of bacteremia associated with extraction of teeth.* Oral Surg Oral Med.Oral Pathol., 1970. **30**(4): p. 454-459.
106. Nasif, A.S., *The incidence of post-extraction bacteremia after irrigation of the gingival sulcus with hydrogen peroxide solution.* Egypt.Dent.J, 1977. **23**(3): p. 51-55.
107. Yamalik, M.K., S. Yucetas, and U. Abbasoglu, *Effects of various antiseptics on bacteremia following tooth extraction.* J Nihon Univ Sch Dent., 1992. **34**(1): p. 28-33.
108. Chiu, F.Y. and C.M. Chen, *Surgical debridement and parenteral antibiotics in infected revision total knee arthroplasty.* Clin Orthop.Relat Res., 2007. **461**: p. 130-135.
109. Cordero-Ampuero, J., J. Esteban, and E. Garcia-Cimbrelo, *Oral antibiotics are effective for highly resistant hip arthroplasty infections.* Clin Orthop.Relat Res., 2009. **467**(9): p. 2335-2342.
110. Cordero-Ampuero, J., et al., *Low relapse with oral antibiotics and two-stage exchange for late arthroplasty infections in 40 patients after 2-9 years.* Acta Orthop., 2007. **78**(4): p. 511-519.
111. Crockarell, J.R., et al., *Treatment of infection with debridement and retention of the components following hip arthroplasty.* J Bone Joint Surg Am., 1998. **80**(9): p. 1306-1313.
112. Fink, B., et al., *The value of synovial biopsy, joint aspiration and C-reactive protein in the diagnosis of late periprosthetic infection of total knee replacements.* J Bone Joint Surg Br., 2008. **90**(7): p. 874-878.
113. Hoad-Reddick, D.A., et al., *Is there a role for extended antibiotic therapy in a two-stage revision of the infected knee arthroplasty?* J Bone Joint Surg Br., 2005. **87**(2): p. 171-174.
114. Insall, J.N., F.M. Thompson, and B.D. Brause, *Two-stage reimplantation for the salvage of infected total knee arthroplasty.* J Bone Joint Surg Am., 1983. **65**(8): p. 1087-1098.
115. Jerosch, J. and M. Schneppenheim, *Management of infected shoulder replacement.* Arch.Orthop Trauma Surg, 2003. **123**(5): p. 209-214.
116. Mont, M.A., et al., *Multiple irrigation, debridement, and retention of components in infected total knee arthroplasty.* J Arthroplasty, 1997. **12**(4): p. 426-433.

117. Munoz-Mahamud, E., et al., *Comparison of a low-pressure and a high-pressure pulsatile lavage during debridement for orthopaedic implant infection*. Arch.Orthop Trauma Surg, 2011.
118. Rao, N., et al., *Long-term suppression of infection in total joint arthroplasty*. Clin Orthop.Relat Res., 2003(414): p. 55-60.
119. Rodriguez, D., et al., *Acute Hematogenous Prosthetic Joint Infection: Prospective Evaluation of Medical and Surgical Management*. Clin Microbiol.Infect., 2009.
120. Soriano, A., et al., *Efficacy and tolerability of prolonged linezolid therapy in the treatment of orthopedic implant infections*. Eur.J Clin Microbiol.Infect.Dis., 2007. **26**(5): p. 353-356.
121. Waldman, B.J., et al., *Infected total knee arthroplasty treated by arthroscopic irrigation and debridement*. J Arthroplasty, 2000. **15**(4): p. 430-436.
122. Windsor, R.E., et al., *Two-stage reimplantation for the salvage of total knee arthroplasty complicated by infection. Further follow-up and refinement of indications*. J Bone Joint Surg Am., 1990. **72**(2): p. 272-278.
123. Wroblewski, B.M., *One-stage revision of infected cemented total hip arthroplasty*. Clin Orthop.Relat Res., 1986(211): p. 103-107.
124. Lucas, V. and G.J. Roberts, *Odontogenic bacteremia following tooth cleaning procedures in children*. Pediatric Dentistry, 2000. **22**(2): p. 96-100.
125. Silver, J.G., A.W. Martin, and B.C. McBride, *Experimental transient bacteraemias in human subjects with clinically healthy gingivae*. J Clin Periodontol., 1979. **6**(1): p. 33-36.
126. Marzoni, F.A. and D.R. Kelly, *Bacteremia following cleft palate repair--a prospective study*. Ann.Plast.Surg, 1983. **10**(6): p. 473-474.
127. Pineiro, A., et al., *Bacteraemia following dental implants' placement*. Clin Oral Implants Res., 2010. **21**(9): p. 913-918.
128. Winslow, M.B. and S.D. Kobernick, *Bacteremia after prophylaxis*. J Am.Dent.Assoc., 1960. **61**: p. 69-72.
129. Debelian, G.J., I. Olsen, and L. Tronstad, *Bacteremia in conjunction with endodontic therapy*. Endodontics and Dental Traumatology, 1995. **11**(3): p. 142-149.
130. Rahn, R., et al., *The effect of topical Povidone-Iodine and Chlorhexidine on the incidence of bacteremia following dental treatment procedures*. Hygiene + Medizin, 1994. **19**(3): p. 128-131.
131. Flood, T.R., et al., *Bacteraemia following incision and drainage of dento-alveolar abscesses*. Br.Dent.J, 1990. **169**(2): p. 51-53.
132. Martin, W.J. and A. Schirger, *PREVENTION OF BACTEREMIA AFTER ORAL SURGERY*. Minnesota Medicine, 1964. **47**: p. 1519-1523.
133. Burden, D.J., et al., *The prevalence of bacteraemia on removal of fixed orthodontic appliances*. Eur.J Orthod., 2004. **26**(4): p. 443-447.
134. Conner, H.D., et al., *Bacteremias following periodontal scaling in patients with healthy appearing gingiva*. J Periodontol., 1967. **38**(6): p. 466-472.
135. Gutverg, M., *Studies on bacteremia following oral surgery: Some prophylactic approaches to bacteremia and the results of tissue examination of excised gingiva*. J Periodontol., 1962. **33**: p. 105.
136. Kinane, D.F., et al., *Bacteraemia following periodontal procedures*. J Clin Periodontol., 2005. **32**(7): p. 708-713.
137. Giglio, J.A., et al., *Suture removal-induced bacteremia: a possible endocarditis risk*. J Am.Dent.Assoc., 1992. **123**(8): p. 65-70.
138. Soliman, N.A., Y.A. el-Batawy, and A.K. Abdallah, *Bacteriologic study of the systemic disturbances accompanying primary teething*. Egypt.Dent.J, 1977. **23**(2): p. 111-113.
139. Crawford, J.J., et al., *Bacteremia after tooth extractions studied with the aid of prereduced anaerobically sterilized culture media*. Appl Microbiol., 1974. **27**(5): p. 927-932.
140. Peterson, L.J. and R. Peacock, *The incidence of bacteremia in pediatric patients following tooth extraction*. Circulation, 1976. **53**(4): p. 676-679.