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# Science Over Dogma

Dispelling myths about dental antibiotic prophylaxis for patients with total joint replacements

Some dentists, orthopedic surgeons and patients continue to believe that giving antibiotics prior to invasive dental procedures to people with prosthetic joints is better for patients and keeps practitioners out of court. We now know that these beliefs are false, and the opposite may even be true. Many myths surround this practice — a practice that has been called irresponsible and indefensible (1).

In dispelling these myths, it is important to acknowledge that infection of a prosthetic joint is not merely an undesirable complication — it is a disastrous event for patients, surgeons and the health-care system (2, 3). At the same time, of the greater than 100,000 hip and knee replacements reported in Canada in 2012-13 (4), only seven per cent required revision surgery and of those, less than 10 per cent were done because of prosthetic joint infections. While the concern about prosthetic joint infection is real and entirely rationale, the supposition that dental procedures cause these infections or that antibiotic prophylaxis prior to dental procedures will prevent them is steeped in mythology rather than science.

Prosthetic joint infection can be classified according to the onset of symptoms after implantation, as well as the route of infection: early (less than three months, acquired during or several days after surgery, caused by highly virulent organisms); delayed (three to 24 months, usually acquired during surgery, caused by less virulent organisms); or, late (greater than 24 months, mostly caused by hematogenous seeding from remote infections) (5).

Antibiotic prophylaxis for patients with total joint replacement has been a controversial topic in North America over the past 10 years. In the late 1970s, orthopedic surgeons and dentists began to recommend antibiotic prophylaxis for patients with prosthetic joints undergoing invasive dental procedures. This was based on several erroneous assumptions, most notably the notion that the pathogenesis of late prosthetic joint infections is the same as that of bacterial endocarditis (6), which is not the case.

**“The great tragedy of science: The slaying of a beautiful hypothesis by an ugly fact.”**

— Thomas Henry Huxley,  
English biologist (1825-1895)

Since the early 1990s, experts in Britain, Europe and Canada have not only discouraged the practice of antibiotic prophylaxis prior to invasive dental procedures, citing compelling evidence, but also cautioned about the consequences of antibiotic overuse, warnings we can no longer ignore, as we face the threat of a global antimicrobial resistance crisis (1, 7-12). What follows is a description of the prevalent myths surrounding this practice and the science that, hopefully, corrects these false beliefs.

### **Myth #1. Bacteremia from dental procedures causes late prosthetic joint infections**

In large part, this myth has arisen because clinicians assumed that if dental procedure-induced bacteremia could cause infective endocarditis in a very small subset of cardiac patients, then the same etiology might be responsible for late prosthetic joint infections. While nearly 50 per cent of cardiac valve infections are caused by the viridans group streptococci, part of the normal skin, oral, respiratory and gastrointestinal tract flora (13), 75 per cent of joint infections are caused by staphylococci (14), which are rarely found in the oral flora (15, 16) and less than five per cent are caused by streptococcus species (14), which can arise from multiple sites in the body.

It should be noted that the American Heart Association Science Advisory and Coordinating Committee approved a report in 2003 (17) that stated there is “no convincing evidence” that bacteria associated with dental procedures “cause infection of nonvalvular vascular devices at any time after implantation” and therefore does not

recommend antibiotic prophylaxis for these patients. Like prosthetic joint infection, infection of these devices is most commonly caused by staphylococci and other organisms not usually found in the oral cavity and occurs at the time of device implantation or as a result of wound or other active infections (17).

While much of the literature on bacteremia has focused on that induced by dental procedures, “everyday” bacteremia from chewing, tooth brushing and flossing is much more significant. This cumulative physiologic exposure has been estimated to be in the range of 5,370 minutes per month compared to, for example, a six-minute exposure from a dental extraction (18, 19). In a study of bacteremia associated with tooth brushing and dental extractions, Lockhart and colleagues concluded that tooth brushing may be a greater threat than extraction for people at risk for infective endocarditis (20). Other studies have shown that poor oral hygiene and periodontal inflammation contribute to bacteremia on a daily basis (21, 22).

Roberts (19) devised a Cumulative Exposure Index to describe dental bacteremic challenges. The index includes the intensity of bacteremia (colony forming units or CFUs/ml), duration of bacteremia, frequency of bacteremia-inducing events and the percentage prevalence of bacteremia related to the dento-gingival manipulative procedure. Using this measure, it was demonstrated that procedures most often regarded as requiring antibiotic prophylaxis do not carry the greatest risk of cumulative bacteremia. In fact, procedures with no visible bleeding, such as tooth brushing, polishing and rubber dam placement were associated with bacteremia: the risk of bacteremia was 390 times greater for polishing than for single tooth extraction, 154,219 times greater for tooth brushing and more than two million times greater for rubber dam placement. In addition, significant bacteremia was shown in the first 10 seconds of extractions, when there was no discernible bleeding. These data suggest that there may be microscopic damage to blood vessels as a result of intermittent positive and negative pressures associated with tooth movement and lend substantial support to the importance of physiologic bacteremia.

Given that prosthetic joint infection occurs in less than one per cent of all total joint replacements, and considering the microbiology of those infections, as well as the role of daily physiologic bacteremia, the suggestion that dental procedure-induced bacteremia plays a meaningful role in prosthetic joint infection is not supported by the evidence.

## **Myth #2. Antibiotics prophylaxis is effective at preventing late prosthetic joint infection**

Even if dental procedure-induced bacteremia was a culprit in late prosthetic joint infection, the belief that antibiotics are completely effective in dealing with bacteremia is unfounded. In a study of bacteremia associated with tooth brushing, extraction with amoxicillin prophylaxis and extraction without amoxicillin (20), the placebo group had the highest prevalence of bacteremia (79 per cent), yet the prevalence in the extraction-amoxicillin group was still substantial at 56 per cent. The duration of bacteremia was similar in all three groups. Additional studies have also found that, although amoxicillin reduces the prevalence of bacteremia, it does not eliminate it (23, 24), while other studies have found no reduction in prevalence at all (25, 26).

A review of the evidence base for the efficacy of antibiotic prophylaxis for prevention of prosthetic joint infection by Lockhart et al. (27) found scant evidence to support this practice and classified the overall evidence as Class III: “evidence or general agreement that the procedure or treatment is not useful or effective, and in some cases may be harmful.” And in a rigorous prospective case-control study to assess the association of dental procedures — with or without antibiotic prophylaxis — and prosthetic joint infection, Berbari et al. (28) found no increased risk of prosthetic joint infection after dental procedures and no risk reduction when antibiotic prophylaxis was used.

## **Myth #3. The potential benefit of antibiotic prophylaxis outweighs the risk because antibiotics are safe and cost-effective**

Although dental treatment is not a meaningful risk factor for prosthetic joint infection and antibiotics are not 100 per cent effective in preventing or mitigating bacteremia, some believe that it is better to be “safe than sorry.” This myth is based on the perception that antibiotics are safe, especially when given as a peri-operative or one pre-operative dose.

Antibiotics are responsible for one out of every five visits to emergency departments for adverse drug reactions in the United States (29). Mild allergic reactions rank second and anaphylaxis 11th as the most common medical emergencies seen in dental offices (30). Analysis of prescribing data and adverse events over a 10-year period in England showed an adverse drug reaction rate for single-dose amoxicillin prophylaxis was zero fatal reactions/million prescriptions and 22.6 non-fatal reactions/million prescriptions. For clindamycin prophylaxis, it was 13 fatal and 149 non-fatal reactions/million prescriptions. Most clindamycin-adverse drug reactions were *Clostridium difficile* infections (31).

While the most common allergen in dental offices is latex and anaphylaxis is a rare event, dentists should not be complacent about the unintended consequences of antibiotic use, especially as it pertains to *Clostridium difficile* infections. Antibiotic therapy is a key factor in the pathogenesis of this potentially serious infection. Disruption of the microflora of the colon allows *C. difficile* to proliferate, causing infections that range from mild diarrhea and abdominal pain to severe diarrhea, dehydration, pseudomembranous colitis, renal failure, sepsis and death. The onset of *Clostridium difficile* infection is usually within 49 days of starting antibiotics and although nearly all classes of antibiotics have been implicated, the greatest risk is attributed to clindamycin, third generation cephalosporins and penicillins (32). Profound alterations in intestinal flora occur after a single dose of antibiotics (33, 34). Longer durations of antibiotic therapy confer a greater risk for *Clostridium difficile* infections, but even single doses used for prophylaxis increase a patient's risk (32, 35-37).

Studies that have modelled data on risk of infection, health outcomes and costs have shown that the significant cost of antibiotic prophylaxis to prevent prosthetic joint infection outweighs the benefits from a financial perspective (38, 39) and that for every one such infection that was prevented (*if* oral flora caused the infection and *if* antibiotic prophylaxis was highly effective), 37 to 80 patients would experience an adverse event from antibiotic prophylaxis (40).

The costs to individual patients, the community and society from antibiotic resistance are reaching crisis proportions. Each time an antibiotic is used, a patient is put at increased risk of developing a subsequent antibiotic-resistant infection. This risk may be life threatening in immunosuppressed patients, who, ironically, are the very group of patients requiring especially judicious antibiotic exposure and protection.

#### **Myth #4. Exceptions should be made for "high-risk" immunocompromised patients**

Using antibiotics appropriately in "immunocompromised dental patients" is the next major stewardship challenge in dentistry. Proponents of antibiotic prophylaxis for patients with total joint replacement are eager to ensure that "high-risk" patients are identified, largely based on patient medical co-morbidities. This notion, like many of the ideas about dental antibiotic prophylaxis for patients with total joint replacement, appears to come from an erroneous comparison to guidelines for prevention of infective endocarditis, where in fact high-risk patients have been identified — but based only on the underlying cardiac condition (13), not on any medical co-morbidities, resulting in a very few patients requiring coverage. The American Heart Association, in

its reports and guidelines on infective endocarditis (13) and nonvalvular cardiovascular device-related infections (17) acknowledges that co-morbid factors such as older age, diabetes, immunosuppressive conditions or therapy and dialysis often co-exist with and may complicate infective endocarditis and independently increase the risk of adverse outcomes, including morbidity and mortality, but *do not* increase risk for development of the initial infection. The American Heart Association states explicitly:

"Patients who are severely immunocompromised as a result of underlying disease or immunosuppressive treatment have increased risk of infection. However, immunosuppression is not an independent risk factor for nonvalvular device infections. Immunocompromised hosts who have a nonvalvular cardiovascular device should receive primary and secondary antibiotic prophylaxis as advocated for immunocompetent hosts" (17).

Preserving antibiotics for when they are really needed in all patients is vital — as is protecting patients from the morbidity and mortality of antimicrobial-resistant infections such as methicillin-resistant *Staphylococcus aureus* (MRSA) and *C. difficile*. Guidelines that suggest giving antibiotic prophylaxis to immunosuppressed patients to prevent prosthetic joint infection are not supported by the current evidence, and it is these patients in particular who are at greatest risk for antibiotic-resistant infections (41-46). As with cardiovascular devices (17), immunosuppression is not an independent risk factor for prosthetic joint infection: if antibiotic prophylaxis is not recommended for patients with prosthetic joints because dental procedures are not associated with prosthetic joint infection, then using prophylaxis in patients who are most susceptible to antibiotic resistance and adverse reactions is irresponsible (14).

#### **Myth #5. Better "safe than sorry" from a medical-legal perspective**

Although antibiotic prophylaxis for patients with total joint replacement is not advisable, the myth persists that giving antibiotics is the prudent thing to do on the basis of legal considerations. There are two possible scenarios that may arise in a medical-legal context.

The first is that the patient claims to have developed a prosthetic joint infection from a dental procedure. Less than one per cent of hip and knee replacements done in Canada in 2012-13 (4) developed infections requiring revision surgery. Less than five per cent of prosthetic joint infections are caused by streptococci species (14), which are part of the normal flora of multiple body sites including the oral cavity. If microbial genetic testing could ascertain that the causative bacteria is identical to


organisms found in the oral cavity of that patient and not found at other sites (there are no reports in the literature of this), it would still not be possible to determine if that infection occurred before, during or after the dental procedure, as a result of the procedure, or as a result of daily activities.

The second scenario might arise if a patient has developed an adverse reaction to an antibiotic given for prophylaxis despite the advice of the Consensus Statement developed by the Canadian Orthopedic Association, the Association of Medical Microbiology and Infectious Disease Canada and the Canadian Dental Association (47). The statement was drafted by experts from the three associations, vetted by their members and approved by their Boards in 2016. While such a statement has no legal authority, the Canadian statement is based on scientific evidence and reasoning, rather than emotional and political perspectives.

In the second scenario, the nature and timing of the antibiotic in relation to the adverse event would be known with a great deal of certainty. Of particular concern to dentists should be the development of *Clostridium difficile* infection in patients, a very dire sequela of antibiotic use, the incidence of which is alarmingly on the rise in community, as well as hospital, settings. *Clostridium difficile* infection is increasingly reported after single or peri-operative doses of antibiotics, with profound morbidity (36, 37).

If a dentist decides to prescribe antibiotics for a patient with a hip or knee replacement, despite the lack of evidence of benefit and the known evidence of harm, discussion regarding the risk/benefit ratio of antibiotics must be part of the informed consent process. If a patient insists upon antibiotic prophylaxis or pressure is brought to bear by another practitioner, it is the dentist who has the ultimate responsibility for care and whose actions may not be defensible.

## Conclusion

For many years, dentists and orthopedic surgeons believed that antibiotic prophylaxis for patients with total joint replacement was appropriate, based on the devastating nature of infections of prosthetic joints, the difficulty of and morbidity associated with revision surgery and a compelling theory — the theory that the etiology and pathophysiology of infective endocarditis and prosthetic joint infections were similar, if not the same. This is not the case: the facts do not support this hypothesis. In short, misuse of antibiotics is harmful to individual patients and to society, and dentists have a role to play in protecting patients from harm and preserving antibiotics for when they are needed. 

## REFERENCES

1. Morris AM, Howie S. Recommendations for antibiotics in patients with joint prosthesis are irresponsible and indefensible. *J Can Dent Assoc.* 2009;75:513-5.
2. Bozic KJ, Ries MD. The impact of infection after total hip arthroplasty on hospital and surgeon resource utilization. *J Bone Joint Surg Am.* 2005;87:1746-51.
3. Cahill JL, Shadbolt B, Scarvell JM, Smith PN. Quality of life after infection in total joint replacement. *J Orthop Surg.* 2008;16:58-65.
4. Canadian Institute for Health Information. Hip and Knee Replacements in Canada: Canadian Joint Replacement Registry 2014 Annual Report. Ottawa, ON: CIHI; 2015. Available at: <https://secure.cihi.ca/estore/productFamily.htm?locale=en&pf=PFC2945&lang=en>. Accessed September 21, 2017.
5. Zimmerli W, Trampuz A, Ochsner PE. Prosthetic-joint infections. *N Engl J Med.* 2004;351:1645-54.
6. Lattimer GL, Keblish PA, Dickson TB, Jr., et al. Hematogenous infection in total joint replacement. Recommendations for prophylactic antibiotics. *JAMA.* 1979;242:2213-4.
7. Simmons NA, Ball AP, Cawson RA, et al. Case against antibiotic prophylaxis for dental treatment of patients with joint prostheses. *Lancet.* 1992;339:301.
8. Wahl MJ. Myths of dental-induced prosthetic joint infections. *Clin Infect Dis.* 1995;20:1420-5.
9. Sandhu SS, Lowry JC, Morton ME, Reuben SF. Antibiotic prophylaxis, dental treatment and arthroplasty: time to explode a myth. *J Bone Joint Surg (Br).* 1997;79:521-2.
10. Oswald TF, Gould FK. Dental treatment and prosthetic joints: antibiotics are not the answer! *J BJJ.* 2008;90:825-6.
11. Ellervall E, Vinge E, Rohlin M, Knutsson K. Antibiotic prophylaxis in oral healthcare — the agreement between Swedish recommendations and evidence. *Br Dent J.* 2010;208:E5; discussion 114-5.
12. Sendi P, Uckay I, Suva D, et al. Antibiotic Prophylaxis During Dental Procedures in Patients with Prosthetic Joints. *Journal of Bone and Joint Infection.* 2016;1:42-9.
13. Wilson W, Taubert KA, Gewitz M, et al. Prevention of infective endocarditis: guidelines from the American Heart Association: a guideline from the American Heart Association Rheumatic Fever, Endocarditis and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. *Journal of the American Dental Association.* 138:739-45.

14. Lamagni T. Epidemiology and burden of prosthetic joint infections. *Journal of Antimicrobial Chemotherapy*. 2014 Sep 1;69(suppl\_1):i5-10.
15. Paster BJ, Boches SK, Galvin JL, et al. Bacterial diversity in human subgingival plaque. *J Bacteriol*. 2001;183:3770-83.
16. Kazor CE, Mitchell PM, Lee AM, et al. Diversity of bacterial populations on the tongue dorsa of patients with halitosis and healthy patients. *J Clin Microbiol*. 2003;Feb 1;41(2):558-63.
17. Baddour LM, Bettmann MA, Bolger AF, et al. Non-valvular cardiovascular device-related infections. *Circulation*. 2003 Oct 21;108(16):2015-31.
18. Guntheroth WG. How important are dental procedures as a cause of infective endocarditis? *Am J Cardiol*. 1984 Oct 1;54(7):797-801.
19. Roberts GJ. Dentists are innocent! "Everyday" bacteremia is the real culprit: A review and assessment of the evidence that dental surgical procedures are a principal cause of bacterial endocarditis in children. *Pediatr Cardiol*. 1999 ;20:317-25.
20. Lockhart PB, Brennan MT, Sasser HC, et al. Bacteremia associated with toothbrushing and dental extraction. *Circulation*. 2008;117:3118-25.
21. Forner L, Larsen T, Kilian M, Holmstrup P. Incidence of bacteremia after chewing, tooth brushing and scaling in individuals with periodontal inflammation. *J Clin Periodontol*. 2006;33:401-7.
22. Lockhart PB, Brennan MT, Thornhill M, et al. Poor oral hygiene as a risk factor for infective endocarditis-related bacteremia. *J Am Dent Assoc*. 2009;140:1238-44.
23. Lockhart PB, Brennan MT, Kent ML, et al. Impact of amoxicillin prophylaxis on the incidence, nature, and duration of bacteremia in children after intubation and dental procedures. *Circulation*. 2004 Jun 15;109(23):2878-84.
24. Roberts GJ, Radford P, Holt R. Prophylaxis of dental bacteraemia with oral amoxycillin in children. *Br Dent J*. 1987 Mar;162(5):179-82.
25. Hall G, Heimdahl A, Nord CE. Bacteremia after oral surgery and antibiotic prophylaxis for endocarditis. *Clin Infect Dis*. 1999 Jul 1;29:1-8;quiz 9-10.
26. Hall G, Hedstrom SA, Heimdahl A, Nord CE. Prophylactic administration of penicillins for endocarditis does not reduce the incidence of postextraction bacteremia. *Clin Infect Dis*. 1993 Aug 1:188-94.
27. Lockhart PB, Loven B, Brennan MT, Fox PC. The evidence base for the efficacy of antibiotic prophylaxis in dental practice. *J Am Dent Assoc* 2007 Apr 30;138:458-74;quiz 534-5, 437.
28. Berbari EF, Osmon DR, Carr A, et al. Dental procedures as risk factors for prosthetic hip or knee infection: a hospital-based prospective case-control study. *Clin Infect Dis*. 2010 Jan 1;50:8-16.
29. Shehab N, Patel PR, Srinivasan A, Budnitz DS. Emergency department visits for antibiotic-associated adverse events. *Clin Infect Dis*. 2008 Sep 15;47:735-43.
30. Malamed SF. Handbook of Medical Emergencies in the Dental Office. 7th ed. St. Louis: CV Mosby; 2015.
31. Thornhill MH, Dayer MJ, Prendergast B, et al. Incidence and nature of adverse reactions to antibiotics used as endocarditis prophylaxis. *J Antimicrob Chemother*. 2015 Apr 29;70:2382-8.
32. Owens Jr RC, Donskey CJ, Gaynes RP, et al. Antimicrobial-associated risk factors for *Clostridium difficile* infection. *Clin Infect Dis*. 2008 Jan 15;46 Suppl 1:S19-31.
33. Buffie CG, Jarchum I, Equinda M, et al. Profound alterations of intestinal microbiota following a single dose of clindamycin results in sustained susceptibility to *Clostridium difficile*-induced colitis. *Infect Immun*. 2012;80:62-73.
34. Privitera G, Scarpellini P, Ortisi G, et al. Prospective study of *Clostridium difficile* intestinal colonization and disease following single-dose antibiotic prophylaxis in surgery. *Antimicrob Agents and Chemother*. 1991 Jan 1;35:208-10.
35. Rangel SJ, Fung M, Graham DA, et al. Recent trends in the use of antibiotic prophylaxis in pediatric surgery. *Journal of Pediatric Surgery*. 2011 Feb 28;46:366-71.
36. Hansen D, Pollan LD, Fernando H. Fulminant *Clostridium difficile* colitis: a complication of perioperative antibiotic prophylaxis. *J Oral Maxillofac Surg*. 2013 Nov 30;71:1880-5.
37. Bombassaro AM, Wetmore SJ, John MA. *Clostridium difficile* colitis following antibiotic prophylaxis for dental procedures. *Journal Canadian Dental Association*. 2001 Jan;67:20-24.
38. Lockhart PB, Blizzard J, Maslow AL, et al. Drug cost implications for antibiotic prophylaxis for dental procedures. *Oral surg, oral med, oral pathol and oral radiol*. 2013 Mar 31;115:345-53.
39. Skaar DD, Park T, Swiontkowski MF, Kuntz KM. Cost-effectiveness of antibiotic prophylaxis for dental patients with prosthetic joints: Comparisons of antibiotic regimens for patients with total hip arthroplasty. *J Am Dent Assoc*. 2015 Nov 30;146:830-9.
40. Young H, Hirsh J, Hammerberg EM, Price CS. Dental disease and periprosthetic joint infection. *J Bone Joint Surg Am*. 2014;96:162-8.

41. Binion DG. Strategies for management of Clostridium difficile infection in immunosuppressed patients. *Gastroenterology & hepatology*. 2011 Nov;7:750-2.
42. Shakov R, Salazar RS, Kagunye SK, et al. Diabetes mellitus as a risk factor for recurrence of Clostridium difficile infection in the acute care hospital setting. *Am J Infect Control*. 2011 Apr 30;39:194-8.
43. Collini PJ, Kuijper E, Dockrell DH. Clostridium difficile infection in patients with HIV/AIDS. *Curr HIV/AIDS Reports* 2013 Sep 1;10:273-82.
44. Dubberke ER, Riddle DJ. Clostridium difficile in solid organ transplant recipients. *Am J Transplant*. 2009 Dec 1;9 Suppl 4:S35-40.
45. Haines CF, Moore RD, Bartlett JG, et al. Clostridium difficile in a HIV-infected cohort: incidence, risk factors, and clinical outcomes. *AIDS (London, England)* 2013 Nov 13;27(17).
46. Imlay H, Kaul D, Rao K. Risk factors for Clostridium difficile infection in HIV-infected patients. *SAGE Open Med*. 2016 Dec 14;4:2050312116684295.
47. Canadian Orthopedic Association, Canadian Dental Association, Canada AoMMaID. Consensus Statement: Dental Patients with Total Joint Replacement. 2016. Available at: [https://www.cda-adc.ca/en/about/position\\_statements/jointreplacement/](https://www.cda-adc.ca/en/about/position_statements/jointreplacement/) (Accessed September 21, 2017).



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