

A microscopic view of various bacteria, including several large, spherical cocci with a textured surface, and smaller, rod-shaped bacilli. The background is a soft, out-of-focus pink and purple hue.

The role of prophylactic antibiotics for preventing infective endocarditis in people undergoing dental or other minor procedures

Infective endocarditis is a relatively rare infection of the inner layer of the heart's valves and chambers. Approximately one-third of cases of endocarditis in New Zealand are caused by streptococci that are normal oral flora and are associated with plaque, dental caries, gingivitis and peri-odontitis. New Zealand guidelines for the prevention of infective endocarditis recommend good oral hygiene for people at higher risk because of a pre-disposing cardiac condition, and prophylactic oral antibiotics when undergoing specific dental procedures or tonsillectomy/adenoidectomy. The routine use of prophylactic antibiotics solely for endocarditis prevention for people who are not at high risk is not recommended. In this article we discuss the rationale for giving endocarditis prophylaxis, present the key points of the New Zealand 2008 Heart Foundation guidelines and provide an update on recent developments in this field.

The pathogenesis of infective endocarditis

Infective endocarditis is an infection of the inner layer of the heart's valves and chambers, which can damage cardiac structures and spread to other areas of the body.¹ The condition generally begins around an abnormal valve (e.g. degenerative, rheumatic, prosthetic or damaged from previous endocarditis) or where turbulent blood flow damages the cardiac endothelium.¹ An initial non-infected platelet-fibrin thrombus is colonised by microorganisms transiently circulating in the blood.¹ Deposition of more fibrin, platelet aggregation and microorganism proliferation then combine to form an infected outgrowth, referred to as a vegetation.¹ The infective process may cause damage to the valve and surrounding structures or infection and/or infarction in other areas of the body due to embolism of vegetation fragments.¹ Infective endocarditis is always fatal unless treated,² and even with appropriate treatment it is associated with a one-year mortality rate of nearly 40%.³

Are prophylactic antibiotics indicated to prevent endocarditis associated with dental procedures?

Approximately one-third of cases of infective endocarditis in New Zealand are caused by streptococci that occur normally in the oral cavity,⁴ and are associated with plaque, dental caries, gingivitis and peri-odontitis. Microorganisms generally need to enter the blood stream for infective endocarditis to develop.

Oral streptococci most often enter the blood stream due to routine activities such as teeth brushing, flossing or chewing, especially if the peri-odontium is unhealthy. This spontaneous bacteraemia is low-grade and brief but very frequent and is thought to cause most cases of oral streptococcal endocarditis.⁵

Streptococci also enter the blood stream during and after invasive dental procedures involving manipulation of gingival tissue or perforation of the oral mucosa, or gastrointestinal procedures such as oesophageal dilation.³ The magnitude and duration of procedure-associated bacteraemia are greater than with spontaneous bacteraemia and the hypothesis that this can lead to endocarditis has driven the use of antibiotic prophylaxis with dental procedures for decades. Although there are indirect data in animals and humans suggesting a likely benefit of prophylaxis, the data are somewhat contradictory and there is currently no high quality evidence that antibiotic prophylaxis is either effective or ineffective.⁶ However, in the absence of good data supporting one strategy or the other, New Zealand and most international guidelines continue to recommend antibiotic prophylaxis for selected dental and other procedures in high risk people.

What do the New Zealand guidelines recommend for prophylactic antibiotics?

The New Zealand guidelines for the prevention of infective endocarditis emphasise that all people who are at risk of developing this infection need to take particular care to remain free of dental disease.⁷ This is best achieved by regular visits to professionally trained dental staff and the appropriate use of toothbrushes, dental floss and other plaque-control products, e.g. antibacterial mouthwashes.⁷ New Zealand has a disproportionately high number of young Māori and Pacific peoples affected by rheumatic valvular heart disease as well as dental and periodontal disease.⁷ It is therefore of added importance that optimal oral health is maintained within Māori and Pacific communities.

People with high risk cardiac conditions

In New Zealand, people with any of the following are clinically considered to be at high risk of developing infective endocarditis:⁷

- A prosthetic heart valve, either biological or mechanical
- Rheumatic valvular heart disease
- Previous endocarditis
- Unrepaired cyanotic congenital heart disease or a repair procedure within the last six months
- Cardiac shunts or conduits for palliation

It is estimated that a person with a prosthetic heart valve has a risk of developing infective endocarditis that is 50 times higher than a person in the general population; this risk is highest in the 6 – 12 months following valve replacement.³ For an unknown reason, infective endocarditis occurs twice as often in males as females, although females are more likely to have a worse prognosis.⁵

A New Zealand study of 336 patients (266 with definite infective endocarditis and 70 with probable endocarditis) found that almost one-third of all patients had prosthetic valve endocarditis, 10% had a previous episode of endocarditis and 4% had underlying rheumatic heart disease. Traditionally rheumatic heart disease has been considered a major risk factor for infective endocarditis and this result was less than might have been expected given the high incidence of rheumatic fever among Māori and Pacific communities.⁴

High risk dental procedures

Prophylactic antibiotics are recommended in New Zealand for people at high risk of developing infective endocarditis who are undergoing dental procedures involving manipulation of either gingival tissue or tooth root region or perforation of the oral mucosa, or tonsillectomy/adenoidectomy.⁷

People at high-risk who are undergoing the following routine dental procedures do NOT require prophylactic antibiotics:⁷

- Routine dental anaesthetic injections through non-infected tissue
- Dental x-rays
- Placement of removable prosthodontic or orthodontic appliances
- Adjustment of orthodontic appliances
- Placement of orthodontic brackets
- Losing deciduous teeth
- Treatment of bleeding due to trauma to the lips or oral mucosa

Prophylactic antibiotics are also not recommended in people at high risk of developing infective endocarditis who are undergoing non-dental invasive procedures (other than tonsillectomy/adenoidectomy) unless they require surgery at an anatomical location where there is already established infection, e.g. respiratory or gastrointestinal infection.

Choosing the prophylactic antibiotic regimen

Amoxicillin is the first-line prophylactic antibiotic for people undergoing invasive dental procedures who are at high risk of developing endocarditis.⁷ Clindamycin or clarithromycin are possible alternatives for people in whom amoxicillin treatment is inappropriate or potentially ineffective (Table 1).⁷ To ensure that levels in the blood are maximal at the time of procedure, the antibiotic should be given in the following timeframes:⁷

- Orally, one hour before the procedure
- Intramuscularly (IM), 30 minutes before the procedure
- Intravenously (IV), immediately before the procedure

If the patient inadvertently does not receive an antibiotic prior to the dental procedure, it may be administered up to two hours later, although the effectiveness of the prophylaxis may be reduced.⁷

People requiring surgery at sites where there is established infection

In addition to when invasive dental procedures are performed, people who are at high risk of developing infective endocarditis also require prophylactic antibiotics if they undergo surgery at an anatomical site that is actively infected; if major surgery is planned, a prophylactic antibiotic is likely to be administered anyway. The choice of antibiotic for these patients is dependent on the site of the infected tissue. For example:⁷

- Upper respiratory tract infections – amoxicillin is preferred with clindamycin or clarithromycin as alternatives
- Gastrointestinal, hepatobiliary, genitourinary, obstetric or gynaecological infections – amoxicillin is preferred with vancomycin as an alternative
- Skin or musculoskeletal infections – flucloxacillin is preferred. A cephalosporin, e.g. cefazolin, is an alternative for patients with a mild penicillin allergy, e.g. simple rash, and clindamycin for patients with a severe penicillin allergy, e.g. anaphylaxis, or if methicillin-resistant *Staphylococcus aureus* (MRSA) is suspected or present.

Table 1: Antibiotic regimens for the prophylaxis of infective endocarditis for high risk people undergoing invasive dental procedures⁷

	Adults	Children
First-line	Amoxicillin 2 g, single dose, orally, IV or IM	Amoxicillin 50 mg/kg (maximum 2 g), single dose, orally, IV or IM
Alternatives for patients who:	Clindamycin, 600 mg, single dose, orally, IV or IM;	Clindamycin, 15 mg/kg (maximum 600 mg), single dose, orally, IV or IM;
1. Have a penicillin allergy	or	or
2. Are taking long-term penicillin, e.g. for rheumatic fever prevention	Clarithromycin* 500 mg, single dose, orally.	Clarithromycin* 15 mg/kg (maximum 500 mg), single dose, orally.
3. Have taken a penicillin or cephalosporin in the previous month		

* Clarithromycin has a number of potentially serious interactions with other medicines – see NZF for details

Have changes in prescribing affected the incidence of endocarditis?

The routine use of prophylactic antibiotics for infective endocarditis prevention began in the 1950s. In 2007, there was a change in thinking when the American Heart Foundation (AHA) produced guidance recommending that antibiotics should be limited to patients who had the highest lifetime risk of infective endocarditis and specifically only prior to invasive dental procedures.⁸ The National Heart Foundation of New Zealand produced similar guidelines in 2008,⁷ as did the European Society of Cardiology in 2009.⁵

The principle reason for the reduction in antibiotic use was that the risk of a person developing infective endocarditis following a dental procedure is very low, even for those with a high lifetime risk. For example, it is estimated that the likelihood of a person with a previous episode of infective endocarditis having a repeat occurrence following a dental procedure is 1 in 95 000 procedures.⁸ It has also been estimated that the sum of spontaneous bacteraemia from twice daily tooth brushing for one year is over 150,000 times that of one dental extraction procedure.⁹ Based on these estimates it was argued that the use of prophylactic antibiotics for people other than those at the highest lifetime risk of infective endocarditis would prevent very few cases of infective endocarditis. In addition, widespread use of antibiotics would result in an increased number of adverse reactions as well as contributing to the growing problem of antimicrobial resistance.³

NICE guidelines recommend against prophylactic antibiotics for any patients

In 2008, the United Kingdom National Institute for Health and Care Excellence (NICE) went one step further than other groups and recommended that antibiotics should no longer be prescribed solely for the prevention of infective endocarditis, regardless of the patient's risk.¹⁰ The NICE recommendation was based on clinical evidence as well as cost-effectiveness, but was also strongly influenced by the possibility that the use of antibiotics for infective endocarditis prevention may result in a net loss of life due to adverse effects associated with antibiotic use.¹⁰

Have the NICE guidelines gone too far?

A study two years after the introduction of the 2008 NICE guidelines failed to detect a significant increase in the incidence of infective endocarditis in England compared with before the guidelines, however, there was some concern that a clinically significant difference would not be detected within this time frame.^{11,12} A further study by the same authors

in 2015 examined the number of antibiotic prescriptions dispensed for the prevention of infective endocarditis and the incidence of infective endocarditis in England from 2000 to 2013. It was found that the number of prescriptions fell sharply after the 2008 NICE guidelines were released and that there has subsequently been an increase in the incidence of infective endocarditis in both high and lower risk people.¹² Unfortunately, the authors do not say whether these extra cases of endocarditis were caused by oral streptococci or related to dental procedures. The finding that the incidence of infective endocarditis increased in people considered low risk, i.e. who would not have been prescribed antibiotics anyway, suggests that reduced antibiotic prescribing may not be the reason for the observed increase in morbidity. For example, it may be possible that improvements in the diagnosis of infective endocarditis or an increase in invasive staphylococcal disease has resulted in an increasing incidence across the entire population. Although a causal relationship has not been established between a reduction in prophylactic antibiotic prescribing and an increase in the incidence of infective endocarditis in England, this finding has prompted NICE to review its 2008 guideline;¹³ the outcome of this review is still to be announced.

The study from England was not the first to examine the relationship between antibiotic prescribing and rates of infective endocarditis. Four studies conducted in America following the introduction of the modified 2007 AHA guidelines (which recommended prophylaxis for less people and for fewer invasive procedures) also did not detect an increase in the incidence of infective endocarditis, including streptococcal infections.^{14–17} However, the cohort size of several of the American studies was relatively small compared to the English study and one study was conducted only nine months after the AHA guidelines were introduced.¹⁶ Another study demonstrated no increase in oral streptococcal endocarditis in France in the six years following a guideline change in 2002 to reduced antibiotic prophylaxis.¹⁸

Keep calm and carry on

Over 60 years of published data still do not provide evidence on which to make strong recommendations for antibiotic prophylaxis against endocarditis at the time of dental procedures. The 2008 New Zealand guidelines represent a conservative consensus of local expert opinions and seven years after they were written there does not seem to be a good reason to change these recommendations.

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