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## Review

# Infective endocarditis - An update for dental surgeons



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### ABSTRACT

Infective endocarditis (IE) is associated with significant morbidity and mortality. The prevention of infective endocarditis, for many years, has involved the identification of at risk patients undergoing medical or dental procedures and the use of pre-procedural antibiotic prophylaxis. However, evidence regarding the effectiveness of such measures is lacking while evidence is mounting for the adverse effects of inappropriate antibiotic use. International guidelines for antibiotic prophylaxis were amended, radically in some cases to reflect this. Subsequent epidemiological observations of IE have shown mixed results, strengthening calls for well conducted randomised control trials, now that there is genuine clinical equipoise among clinicians about this question.

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## Introduction

Infective endocarditis (IE), is a rare but serious condition which currently still carries a mortality of up to 25% [1]. A yearly incidence of 3–10 per 1000,000 people has been

reported [2]. Clinical features of IE are non-specific and include high fever (which may be absent in the elderly or immunocompromised), loss of weight, lethargy, shortness of breath, new or changing heart murmurs and possibly skin manifestations. Major complications include sepsis, stroke

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and heart failure from valvular dysfunction. Treatment is with prolonged intravenous antibiotics with a significant proportion requiring valvular surgery. Long term complications include the increased risk of re-infection, mechanical complications requiring repeated procedures and possibly life-long anticoagulation with its own attendant complications if prosthetic heart valve replacement is needed [2,3].

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### Risk factors

Traditional risk factors for the development of IE include the presence of a prosthetic heart valve, structural or congenital heart disease, intravenous drug use (IDU) and a recent history of an invasive medical or dental procedure. Of note, up to 50% of IE cases may develop in patients without a previously known cardiac valvular lesion [3].

The most common microorganisms identified as pathogens in IE include streptococci (including oral streptococci – viridans group streptococci [VGS]), staphylococci and enterococci species. *Staphylococcus aureus* IE and prosthetic valve IE are both associated with poorer outcomes. Indeed, a mortality of 40% or more among patients with prosthetic-valve infective endocarditis due to *Staphylococcus aureus* has been reported [3]. The mortality from IE due to VGS involving native valves is much lower and is estimated at 5% compared to up to 20% when prosthetic valves are involved [4]. The epidemiology of IE cases has shifted, in high-income countries, from underlying rheumatic heart disease with IE caused by VGS to underlying degenerative valvular disease, prosthetic valves or indwelling cardiac devices such as cardiac pacemakers and implantable cardio-defibrillators and infections caused by Staphylococci – both *S.aureus* and coagulase negative Staphylococci [1,5]. In recent years *Enterococcus faecalis* IE has also increased especially in the elderly, some of whom have had concomitant colorectal neoplasms detected; an association between the two has been suggested although robust data are lacking [6].

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### Infective endocarditis in Singapore

Data on IE cases locally have recently been published from the two tertiary hospitals in Singapore [7,8]. For instance, at the National University Hospital (NUH), 233 patients were diagnosed with IE over a 11 year period (2001 to 2011). The mean age of patients was 50 years with a slight male predominance. The commonest organism implicated was *Staphylococcus* species in 65% of cases, the remainder were due to streptococci (other than VGS). The in-hospital mortality was high at 23%. A high proportion (40–45%) of patients had underlying chronic kidney disease and diabetes mellitus, with a only a relatively small number having a known pre-existing cardiac condition such as congenital heart disease (9.1%) or a prosthetic valve (13%) [7]. Similar patient characteristics were reported from a study at National Heart Centre, Singapore General Hospital by Pang et al. in a review of 191 patients [8].

IE in children in Singapore is uncommon. In a 7-year period (May 1997 to April 2004), at KK Women's and Children

Hospital [9], 27 children were diagnosed with IE. The mean age of the affected children was 8 years. Most of the children had a pre-existing congenital heart condition (either cyanotic or acyanotic). Only one child had a history of rheumatic valvular disease. The most common causative agent was VGS followed by *Staphylococcus aureus*. Forty percent of patients had a medical/surgical or dental procedure performed 2 to 6 months prior to the diagnosis of IE. The majority of these patients were given antibiotic prophylaxis perioperatively for their respective procedures. Of note, there was one affected child who had a dental procedure performed without antibiotic cover. These children also suffered significant adverse effects with 25.9% having a major embolic complication (transient ischaemic attack, cerebrovascular accident, pulmonary embolism) and two recorded fatalities in the study cohort.

A small but significant cohort of patients affected by IE in Singapore are the injecting drug users/abusers. Affected individuals are normally males in the younger age group (third decade), where right sided *S. aureus* IE predominates, and who traditionally have poorer outcomes, a mortality of 45% recorded in one such cohort of buprenorphine (Subutex) abusers in NUH during the period 2005-6 [10].

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### Infective endocarditis and antimicrobial prophylaxis

Due to the substantial morbidity and mortality associated with the development of IE, the reported “significant” role of “oral streptococci” (VGS) bacteraemia, presumably after dental procedures, in IE development, expert committees and professional societies have made several recommendations for antimicrobial prophylaxis for the prevention of bacterial endocarditis secondary to dental procedures since 1955 [4]. All these guidelines have been expert based rather than evidence-based as the efficacy of preprocedural antibiotics for prevention of IE has never been proven in a double-blinded randomised control trial. A 2013 Cochrane Database systematic review of antibiotic prophylaxis of IE in dentistry [11], concluded that there is no evidence to determine whether antibiotic prophylaxis before dental procedures is effective or ineffective. A recent publication by Cahill TJ et. al., 2017 [12] is the most extensive systematic review and meta-analysis of all studies available from 1960 to 2016 on antibiotic prophylaxis for infective endocarditis. The reviewers found limited evidence for benefit or harm and could not come to any definite conclusion on the effectiveness of antibiotic prophylaxis.

Additionally, in recent years, questions were raised on the relative importance of infrequent dental procedures causing IE compared with the cumulative impact of recurrent bacteraemia associated with daily activities such as toothbrushing, flossing, mastication, which, curiously, normally cause no harm. Further, doubt was cast on case reports linking IE to dental procedures as in many of these reports, IE developed many months after the procedure and were not caused by oral streptococci. To this end, it was felt that the maintenance of optimal oral health was more important to reduce the incidence of bacteraemia (and IE) from daily activities

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