

Caries and Company

SADJ August 2016, Vol 71 no 7 p294 - p297

WG Evans

In the continuing battle against Oral Disease, the endeavour to control dental caries and periodontal disease ranks paramount, correctly so, for these diseases are historically considered by WHO as the "most important global oral health burdens". Worldwide, caries affects nearly 100% of adults while periodontal disease ranks second in frequency only to the common cold. The focus during Oral Health Month will be on the motivation of the population to commit to the daily routines proven to have preventive influence on these afflictions. To this end the Association in conjunction with Colgate, sponsor of the Month, will arrange free oral examinations at the major malls throughout the country, together with the vital and yet simple instruction on oral health care. The question is put: caries and gum disease can be prevented, why not prevent?

But there is a wider dimension. The mouth is the portal to the body, it serves as the barbican, the outer defence to invasion. It is also a place of signals, for many systemic

diseases have manifestations in the oral cavity. A July 2016 paper (<http://emedicine.medscape.com/article/1081029-overview#showall>), detailed a rather awesome list of illnesses which have signs and symptoms appearing in the mouth. Gastrointestinal, Nutritional, Haematological, Connective tissue disorders, Pulmonary conditions, Neurologic diseases, Endocrine diseases, Drug induced conditions, let us not omit HIV, amyloidosis, Kaposi sarcoma.

And lurking in this array is the possibility that oral infections may be the cause of Infective endocarditis. The dilemma of the role and responsibility of the Oral Health Care Team in the prevention of this serious problem has been considered by a Working Party of the Association. Their Report forms an ineluctable part of the commitment of the Oral Health Month. It is reproduced here, with appreciation to those who spent time and effort in their deliberations on all the sometimes: conflicting evidence.

PREVENTION OF INFECTIVE ENDOCARDITIS BEFORE DENTAL PROCEDURES SA Heart Position Statement, endorsed by the South African Dental Association

Infective endocarditis (IE) is a rare but severe disease and occurs when circulating microorganisms colonize cardiac valves (both natural and prosthetic), the endocardium, or intracardiac devices.¹ Certain preexisting conditions render an individual more susceptible. Because of the serious associated morbidity and mortality, prevention of IE is an important clinical issue.

IE in South Africa (and other developing countries) is predominantly a disease of young patients with rheumatic heart disease (RHD) and carries a very poor prognosis. In contrast, IE in Europe / North America, (where guidelines and indications for antibiotic prophylaxis have been reduced) have a different spectrum of risk factors. These patients are older; suffer mainly with degenerative valve disease / mitral valve prolapse. IE may also occur as a result of invasive health care-associated procedures or in the setting of prosthetic valves and implantable cardiac devices.¹⁻³

The University of Stellenbosch conducted a three-year prospective epidemiological study of IE in the Western Cape. RHD was the major predisposing condition in 76.6% and 17% of the patients had prosthetic valves. Degenerative valve disease, intravenous drug use and HIV infection were not important risk factors. Outcome was extremely poor; six-month mortality was 35.6% (much higher reported international rates of 6 to 27%), while nearly half of the patients required subsequent valve replacement. Cardiac failure developed or worsened in just over 75%, which may in part be related to late referral and other inefficiencies in local health care services.³

RHD markedly elevates the risk of IE. In a review of cases in the northern territories of Australia, the relative-risk for IE was 58, in those with RHD.⁴ This association is well documented in the developing world,⁴⁻⁷ but is no longer seen in many higher income countries,^{4,8} where the prevalence of rheumatic fever has declined,^{4,9} and the use of intravenous recreational drugs is more common.^{4,10}

It is obvious that the first step in the prevention of IE in developing countries would be to reduce the pool of patients who are susceptible to this infection. This would require effective programs to prevent rheumatic fever (and recurrences) and, hence, RHD. Regrettably, this has not happened.²

The rationale for antibiotic prophylaxis is based on the assumption that bacteraemia subsequent to medical procedures may cause IE, particularly in those with predisposing cardiac disease; prophylactic antibiotics might prevent IE by minimizing bacteraemia, or by altering bacterial properties leading to reduced adherence to the endocardium.^{1,2,11} This concept led to the recommendation for antibiotic prophylaxis in a large number of patients with predisposing cardiac conditions who were undergoing a wide range of procedures.

Antibiotic prophylaxis has been accepted for decades, even though the efficacy has not been confirmed in a prospective randomized controlled trial. It is also unlikely that such a study will ever be conducted. Assumptions are based on non-uniform expert opinion, findings from animal

models, case reports and contradictory observational studies.^{1-3,11-20}

In the majority of those who suffer IE, no potential index procedure can be identified beforehand. The estimated risk of IE following dental procedures is very low.^{11,12} Prophylaxis may therefore avoid only a small number of IE cases, as shown by estimations of one case of IE per 150, 000 dental procedures (in intermediate risk patients) with prophylaxis and one per 46, 000 for procedures unprotected by antibiotics.¹²

Bacteria originating from the mouth account for a significant proportion of cases of IE. Transient bacteraemia occurs not only following dental (and other) procedures, but also after routine oral activities such as tooth brushing, flossing and chewing. The high incidence and cumulative effect of low-grade daily episodes, especially in those with poor oral hygiene, is a more important risk factor than sporadic bacteraemia occurring with a single invasive / dental procedure. Patients with underlying heart conditions that predispose to bacterial colonization are therefore exposed to a low but continual lifelong risk of developing IE. Eliminating gingivitis would reduce the incidence and degree of spontaneous bacteraemia and hence IE.^{1-3,11-20}

Oral health in South Africa is generally quite poor and addressing this at policy level will have more of an impact on IE prevalence than antibiotic prophylaxis.² A recent SA study concluded that inadequate attention is paid to the maintenance of oral hygiene in patients with severe rheumatic heart disease (RHD) requiring cardiac surgery.²¹

All Expert Committees on IE prevention agree that the maintenance of optimal oral hygiene (by regular professional dental care and the appropriate use of manual, powered, and ultrasonic toothbrushes; dental floss; and other plaque-removal devices) is the most effective intervention for the prevention of IE of oral origin.^{1-3,11-20}

It is recommended that patients with valvular heart disease be referred to a dentist / oral hygienist for ongoing treatment and advice. Patients and attending clinicians need to be educated in this regard. A medical history should be obtained from every patient before any dental treatment. A full oral examination, including dental radiography, should be performed. Further examinations at frequent and regular intervals will ensure maintenance of good oral hygiene, as well as early diagnosis and treatment of any oral infections. It is advisable to issue patients with a warning card to record their cardiac condition, drug therapy and suggested prophylactic measures to be taken before dental treatment.^{2,11,12}

Patients should be informed about their valve disease and the possible development of what constitutional symptoms might be associated with IE. They should be advised to seek prompt medical care in the event of suspicious symptoms such as fever that is more than transient.

SA Heart is an affiliated member of the European Society of Cardiology (ESC) and hence adopts the practice guidelines of the ESC as its own. In 2009, the "Guidelines on the Prevention, Diagnosis, and Treatment of Infective Endocarditis" was endorsed by the European Society of Clinical Microbiology and Infectious Diseases, and by the International Society of Chemotherapy for Infection and

Cancer.¹¹ The task force justified revision of their previous position with respect to prophylaxis of IE. The existing evidence did not support the extensive use of antibiotic prophylaxis recommended in previous guidelines. The intention was to avoid extensive, nonevidence-based use of antibiotics for all at-risk patients' under-going interventional procedures, but to limit prophylaxis to the highest-risk individuals. The indications for antibiotic prophylaxis for IE were therefore reduced in comparison with previous recommendations. The recently updated "2015 ESC Guidelines for the Management of Infective Endocarditis" maintains the same principles and recommendations.¹²

The ESC Guideline states that antibiotic prophylaxis should be limited to those with the highest risk of IE (Table 1), undergoing the highest risk dental procedure (Table 2). High-risk is defined as those with underlying cardiac conditions associated with the greatest risk of adverse outcome from IE, and not necessarily those with an increased lifetime risk of endocarditis.¹²

Table 1: Cardiac conditions at highest risk of IE for which prophylaxis is recommended, when a high-risk procedure is performed:

Patients with a prosthetic valve or prosthetic material used for cardiac repair have a higher risk of IE, greater mortality and develop more complications than those with native valve and an identical pathogen; this recommendation also applies to transcatheter-implanted prostheses.

Patients with previous IE have a greater risk for new IE, higher mortality and develop more complications than patients with a first episode of IE.

Patients with congenital heart disease (CHD):

- a. Any type of cyanotic CHD.
- b. Any type of CHD repaired with prosthetic material, whether placed surgically or by percutaneous technique, up to 6-months after the procedure or lifelong if residual shunt or valvular regurgitation remains.

Prophylaxis was not recommended for any other form of native valve disease, with a small but increased life-time risk of IE; including the most commonly identified conditions, bicuspid aortic valve, mitral valve prolapse, and calcific aortic stenosis.^{11,12}

Although the American Heart Association / American College of Cardiology recommend prophylaxis in cardiac transplant recipients who develop cardiac valvulopathy,¹⁸ this is not supported by strong evidence and is not recommended by the ESC Task Force.¹²

It is the opinion of SA Heart that recently published guidelines cannot be automatically applied in developing countries where RHD is common and oral hygiene is poor. We concede that the evidence in favour of prophylaxis is not robust; however patients with RHD (undergoing dental procedures) represent a higher risk for IE (and poor outcome) and should receive antibiotic prophylaxis prior to the dental procedures listed below (Table 2). This recommendation is made, given our prevailing circumstances and the absence of evidence of significant harm for a potentially effective intervention, for the prescribing of oral amoxicillin. Antibiotic prophylaxis should be prescribed after stressing the role of good oral health and informing patients of the ESC guidelines, and why the approach differs in South Africa.

Guidelines from other countries with populations with similar high RHD prevalence, have also kept RHD on the

list of conditions for prophylaxis. The Infective Endocarditis Prophylaxis Expert Group has recommended that indigenous Australian patients with RHD are a special population at high risk for IE (and for adverse outcomes) and should receive antibiotic prophylaxis.²² An Australian survey has however since reported that RHD associated IE was not confined to indigenous Australians, with 42% being non-indigenous.⁴ It was therefore recommended that the indications for prophylaxis prior to procedures which cause bacteremia, should be broadened to include all with RHD,⁴ as do the New Zealand guidelines.²³ In India, there are no recommendations issued by any local professional organization, and hence the decision is left to the discretion of the individual physician /dentist. RHD is the major cause of valvular heart disease in Brazil, where the oral health of the general population is extremely poor and has not improved over decades. The Brazilian Society of Cardiology and the Inter-American Society of Cardiology therefore recommend prophylaxis for all patients with valvular or CHD (that represents a risk for IE), before dental interventional procedures.²⁴

HIV infection is not associated with an increased risk of IE. A significant number of patients with IE may be coincidentally HIV infected, given the high prevalence of both HIV and RHD in Africa.²⁵ In a South African prospective observational study that examined the risk factors for IE, only one of their cohort of 92 patients was HIV seropositive. The main risk factors included RHD, in addition to prosthetic valves, CHD, and a previous history of IE.³ Antibiotic prophylaxis in the setting of HIV is therefore indicated only in those with high-risk cardiac lesions / factors (Table 1), undergoing the procedures outlined in Table 2.

Table 2: Recommendations for prophylaxis of IE in the highest risk patients, according to the type of dental procedure:

Antibiotic prophylaxis should only be considered for procedures requiring manipulation of the gingival or peri-apical region of the teeth or perforation of the oral mucosa, where bleeding is anticipated. In such situations, this may include intra-ligamental local anaesthetic infiltration and placement of orthodontic bands.

Antibiotic prophylaxis is not recommended for local anaesthetic injections in noninfected tissue, treatment of superficial caries, removal of sutures, dental X-rays, placement of removable prosthodontics or orthodontic appliances or braces or following shedding of deciduous teeth or trauma to the lips or oral mucosa.

The use of dental implants raises concerns with regard to potential risk due to foreign material at the interface between the buccal cavity and blood. Very few data are available. The opinion of the ESC Task Force is that there is no evidence to contraindicate implants in all patients at risk. The indication should be discussed on a case-by-case basis. The patient should be informed of the uncertainties and the need for close follow-up.¹²

Table 3: Recommended antibiotic prophylaxis regimens:

Situation	Antibiotic	Single dose 60 minutes before procedure – p.o or i.v.	
		Adults	Children
No allergy to penicillin / ampicillin	Amoxicillin/ ampicillin	2g	50mg/kg PO
Allergy to penicillin / ampicillin	Clindamycin	600mg	20mg/kg
Alternatively cephalexin 2g i.v. for adults or 50mg/kg i.v. for children; cefazolin or ceftriaxone 1g i.v. for adults or 50mg/kg i.v. for children.			
Cephalosporins should not be used in those with a history of anaphylaxis, angio-oedema or urticaria after penicillin or ampicillin due to cross-sensitivity.			

Antibiotic prophylaxis should only be considered for patients at highest-risk described in Table 1 (in addition to those with RHD) undergoing any of the at-risk procedures (Table 2), and is not recommended in other situations. Oral *streptococci* are the main targets for prophylaxis. A single dose of antibiotic should be given before the procedure. There is no proven value to administering a follow-up dose six hours later. Table 3 summarizes the main regimens of antibiotic prophylaxis recommended before dental procedures. Fluoroquinolones and glycopeptides are not recommended due to their unclear efficacy and the potential induction of resistance.¹²

Antibiotic administration carries a small risk of anaphylaxis, which may become more significant in the event of widespread use, however the risk of lethal anaphylaxis is extremely low when using oral amoxicillin. In fact no fatal case has been reported (over at least a 35-year period) after oral administration for IE prophylaxis.^{11,12, 26, 27}

Curative antibiotics must be prescribed for any focus of bacterial infection.¹² Periodontal and endodontic infections are mainly due to gram-negative bacteria. Merely covering these with amoxicillin will not be effective, and broader therapy is required. The choice of antibiotics should be determined and administered as instructed by local practice. The ESC also strongly recommends that potential sources of dental sepsis (which may pose a risk for post-operative sepsis and IE) should be eliminated at least two weeks before implantation of a prosthetic valve, other intracardiac or intravascular foreign material, unless the procedure is urgent.¹²

In addition to antibiotic prophylaxis of IE, pre-procedural antiseptic mouth rinses (chlorhexidine or povidone-iodine) may reduce the incidence or magnitude of bacteremia occurring during invasive dental procedures. The results of studies of “oral degerming” have however been variable, and there is no conclusive evidence for this approach.^{1,28} The ESC protocol makes no reference to the use of antiseptic prophylaxis before at-risk dental manipulation.^{11,12} Further research is required to determine the effectiveness of preprocedural mouth rinsing and to investigate new antiseptic protocols.²⁸

Other national / association guidelines on IE prophylaxis have been revised. The American Heart Association (AHA) guidelines,¹⁸ as well as those of the working party of the British Society for Antimicrobial Chemotherapy (BSAC) are similar to the ESC recommendations.¹⁹

In 2008 the National Institute of Health and Clinical Excellence (NICE) radically recommended complete cessation of antibiotic prophylaxis, in any patient with valvular heart disease, whatever the risk.²⁰ It was concluded that in the absence of prospective, randomized trials, there is a lack of

proof for antibiotic prophylaxis, which is cost-ineffective. As a result, the United Kingdom is now the only place that does not recommend antibiotic prophylaxis for high-risk individuals; and has been a particular cause for concern amongst many dental practitioners. In addition Dayer *et al*, have recently reported a substantial fall in the prescribing of antibiotic prophylaxis in the five-years following the NICE recommendations, as well as a highly significant increase

in the incidence of IE. There were 419 more cases of IE per year, than would have been expected from projection of the pre-NICE trends.²⁹ These findings require cautious interpretation with respect to confounding factors, and in particular to an increase in healthcare-associated IE. Microbiological details were also not reported. It is therefore not clear whether the increased incidence of IE was due to bacteria covered by antibiotic prophylaxis or not.¹² After further review of the effectiveness of prophylaxis against IE, NICE (www.nice.uk.org) has since found no need to change their existing guidance. They concluded that the longstanding increase in the incidence of IE is not well understood, and may be due to other factors.²⁰

The risk assessment suggests that it would be safer to recommend antibiotic prophylaxis, while waiting for a randomized controlled trial. It is likely that cumulative regular small bacteraemias from daily activities pose a significant threat to patients at risk of IE; this does not mean that occasional large bacteraemias from invasive dental procedures do not. Our aim should be to minimize all causes of bacteraemia in susceptible individuals.³⁰ The evidence suggests that antibiotic prophylaxis may prevent a number of cases of IE,^{30,31} and at least for those without a history of penicillin allergy, oral amoxicillin prophylaxis is safe, with a low likelihood of anaphylaxis.^{26,27,30}

SA Heart recommends antibiotic prophylaxis to individuals with the greatest risk of an adverse outcome with IE (outlined in Table 1, in addition to those with RHD, undergoing the procedures described in Table 2). We again emphasize the maintenance of optimal oral health, which is likely to play the most important role in protecting those at risk of IE, in addition to the education of patients in this regard. There should be close cooperation between the dental practitioner / physician / pediatrician / cardiologist / cardiac surgeon as to who should receive prophylaxis or not.

References

- Durack DT. Prophylaxis of Infective Endocarditis. In Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases. 2015. 8th edition. Bennett JE, Dolin R, Blaser MJ editors; 1057.
- Maharaj B, Parrish A. Prevention of infective endocarditis in developing countries. *Cardiovasc J Afr.* 2012; 23; 303.
- Koegelenberg CFN, Doubell AF, Orth H *et al.* Infective endocarditis in the Western Cape Province of South Africa: a three-year prospective study. *QJM.* 2003; 96; 217.
- Baskerville CA, Hanrahan BB, Burke AJ *et al.* Infective endocarditis and rheumatic heart disease in the north of Australia. *Heart Lung Circ.* 2012; 21; 36.
- Choudhury R, Grover A, Varma J, *et al.* Active Infective endocarditis observed in an Indian hospital 1981–1991. *Am J Cardiol.* 1992; 70; 1453.
- Garg N, Kandpal B, Tewari S *et al.* Characteristics of infective endocarditis in a developing country-clinical profile and outcome in 192 Indian patients, 1992–2001. *Int J Cardiol.* 2005; 98; 253.
- Jalal S, Khan KA, Alai MS, *et al.* Clinical spectrum of infective endocarditis: 15 years experience. *Indian Heart J.* 1998; 50; 516.
- Tleyjeh IM, Steckelberg JM, Murad HS *et al.* Temporal trends in infective endocarditis: a population-based study in Olmsted County, Minnesota. *JAMA.* 2005; 293; 3022.
- Quinn RW. Comprehensive review of morbidity and mortality trends for rheumatic fever, streptococcal disease, and scarlet fever: the decline of rheumatic fever. *Rev Infect Dis.* 1989; 11; 928.
- Heiro M, Helenius H, Makila S, *et al.* Infective endocarditis in a Finnish teaching hospital: a study on 326 episodes treated during 1980–2004. *Heart.* 2006; 92; 1457.
- Habib G, Hoen B, Tornos P *et al.* ESC Committee for Practice Guidelines. Guidelines on the Prevention, Diagnosis, and Treatment of Infective Endocarditis (new version 2009): the Task Force on the Prevention, Diagnosis, and Treatment of Infective Endocarditis of the European Society of Cardiology (ESC). *Eur Heart J.* 2009; 30; 2369.
- Habib B, Lancellotti P, Antunes MJ *et al.* 2015 ESC Guidelines for the Management of Infective Endocarditis. The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). 2015; <http://dx.doi.org/10.1093/eurheartj/ehv319> ehv319. Published online: 29 August 2015
- Andrade J, Stadnick E, Mohamed A. Infective endocarditis prophylaxis: An update for clinical practice. *BC Medical Journal.* 2008; 50; 451.
- Parrish A, Maharaj B. Prevention of infective endocarditis in developing countries – justifiable caution? *S Afr Med J* 2012; 102; 652.
- Bobhate P, Pinto RJ. Summary of the new guidelines for prevention of Infective Endocarditis: Implications for the developing countries. *Ann Pediatr Card.* 2008;1; 56.
- Nishimura, Otto CM, Bonow RO *et al.* 2014 AHA/ACC Valvular Heart Disease Guideline. *JACC.* 2014; 63; e57.
- Shanson D. New British and American guidelines for the antibiotic prophylaxis of infective endocarditis: do the changes make sense? A critical review. *Curr Opin Infect Dis.* 2008; 21; 191.
- Nishimura RA, Carabello BA, Faxon DP, *et al.* ACC/AHA 2008 Guideline update on valvular heart disease: focused update on infective endocarditis. A report of the American College of Cardiology/ American Heart Association Task Force on Practice Guidelines. *Circulation.* 2008; 118; 887.
- Gould FK, Elliott TS, Foweraker J. Guidelines for the prevention of endocarditis: report of the Working Party of the British Society for Antimicrobial Chemotherapy. *J Antimicrob Chemother.* 2006; 1035.
- NICE Short Clinical Guidelines Technical Team. Prophylaxis against infective endocarditis: antimicrobial prophylaxis against infective endocarditis in adults and children undergoing interventional procedures. National Institute for Health and Clinical Excellence Clinical Guideline 64. 2008. Published online <http://www.nice.org.uk/CG064>.
- Maharaj B, Vayej AC. Oral health of patients with severe rheumatic heart disease. *Cardiovasc J Afr.* 2012; 23; 336.
- Moulds RFW, Jeyasingham MS, for the Infective Endocarditis Prophylaxis Expert Group, Therapeutic Guidelines Ltd. Antibiotic prophylaxis against infective endocarditis: time to rethink. *Med J Australia.* 2008; 189; 301.
- National Heart Foundation of New Zealand Advisory Group. New Zealand guideline for prevention of infective endocarditis associated with dental and other medical interventions. Auckland: National Heart Foundation of New Zealand; 2008. Published online <http://www.heartfoundation.org.nz>
- Fernandes JRC, Max Grinberg M. Prophylaxis of Infective Endocarditis: A different Brazilian reality? *Arq Bras Cardiol.* 2013; 101; e37.
- Ntsekhe M, Hakim J. Impact of Human Immunodeficiency Virus infection on cardiovascular disease in Africa. *Circulation.* 2005; 112; 3602.
- Thornhill MH, Dayer MJ, Prendergast B *et al.* Incidence and nature of adverse reactions to antibiotics used as endocarditis prophylaxis. *J Antimicrob Chemother.* 2015; 70; 2382.
- Lee P, Shanson D. Results of a UK survey of fatal anaphylaxis after oral amoxicillin. *J Antimicrob Chemother.* 2007; 60; 117.
- Tomás I, Álvarez-Fernández M. History of antimicrobial prophylaxis protocols for infective endocarditis secondary to dental procedures. In: *Recent Advances in Infective Endocarditis.* 2013. Kerrigan SW editor; 53. Published online <http://dx.doi.org/10.5772/56118>.
- Dayer MJ, Jones S, Prendergast B, Baddour LM, Lockhart PB, Thornhill MH. Incidence of infective endocarditis in England, 2000 – 13: a secular trend, interrupted time-series analysis. *Lancet.* 2015; 385; 1219.
- Thornhill MH, Lockhart PB, Prendergast B *et al.* NICE and antibiotic prophylaxis to prevent endocarditis. *British Dental Journal.* 2015; 218; 619.
- Van der Bijl (jr) P, van der Bijl P. Infective endocarditis and antibiotic prophylaxis – an update for South African dental practitioners SADJ. 2014; 69; 118.