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# Infective endocarditis and antibiotic prophylaxis – an update for South African dental practitioners

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Since the 1950's, the practice of prescribing antibiotics for the prophylaxis of endocarditis prior to invasive procedures has been widely accepted by the dental profession. The rationale for this is to reduce or eliminate the bacteraemia that may result from such procedures. The paradigm of this model is the prevention of bacterial endocarditis - a rare, but life-threatening disease. In developed countries, empiric guidelines for antibiotic prophylaxis for endocarditis, based primarily on pathophysiology and expert opinion, are put forward by committees of the American Heart Association (AHA), European Society of Cardiology (ESC) and British Society for Antimicrobial Chemotherapy (BSAC). These commonly-used guidelines, which are not in the first instance based on clinical evidence, have been periodically updated and we reviewed the latest recommendations of the AHA and BSAC in the SADJ in 2008.1 In that paper we referred to the lack of scientific evidence for linking infective endocarditis to dental procedures and the uncertainty regarding the effectiveness of prophylaxis - both these factors challenging the entire concept of antibiotic prophylaxis in dentistry.1 Subsequent to our review of 2008, important communications have appeared in the literature. In 2008, an updated version of the Cochrane review of 2004 on antibiotics for the prophylaxis of bacterial endocarditis in dentistry was published, as well as a guideline by the United Kingdom's National Institute for Health and Clinical Excellence (NICE).<sup>2,3</sup> Furthermore, a survey was conducted among dental practitioners in South Africa to determine their knowledge of the guidelines of the AHA and NICE.<sup>4</sup> Although this survey had a low response rate, it was clear that knowledge in the profession of the use of infective endocarditis prophylaxis and compliance with existing guidelines was generally poor.

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#### **ACRONYMS**

AHA:	American Heart Association
BSAC:	British Society for Antimicrobial Chemotherapy
ESC:	European Society of Cardiology
NICE:	National Institute for Health and Clinical Excellence

In the current update we attempt to clarify some of the prevailing confusion among South African dental professionals regarding when and for whom antibiotic prophylaxis is indicated.

#### **GUIDELINES**

The traditionally accepted guidelines of the BSAC and the AHA as modified in 2006 and 2007 respectively, are recommended for use by South African dental practitioners.<sup>5,6</sup> Their advantages and disadvantages, as well as the proposed antibiotic regimens of both these sets of guidelines have been discussed in some detail in our previous review.<sup>1</sup> As mentioned in that review, the main characteristics of both guidelines are a simplification, in terms of complexity and broadness, of the published pre-2006 and pre-2007 guidelines, resulting in a reduction in the indications for antibiotic prophylaxis. Only a few categories of high-risk patients who require antibiotic prophylaxis prior to dental procedures, are identified in the 2006 and 2007 guidelines. The dental procedures requiring prophylaxis are those involving manipulation of gingival tissue or the periapical region of teeth, or perforation of the oral mucosa. Of significance is that the updated Cochrane review of 2008 has not provided conclusive evidence about whether penicillin prophylaxis is effective against bacterial endocarditis in people at risk who are about to undergo an invasive dental procedure.<sup>2</sup> Evidence from that review is insufficient to support previously published guidelines, such as those of the BSAC and AHA. Additionally, it is of interest that the overall incidence of infective endocarditis has remained stable from 1950 to 2000, i.e. approximately 3.6 - 7.0 cases per 100 000 patient-years.7 This incidence has remained unchanged over half a century despite improvements in cardiac imaging techniques, which may have enhanced the detection of endocarditis.

In March 2008, the National Institute for Health and Clinical Excellence (NICE) in the United Kingdom published a controversial new guideline, which was a radical departure in that it recommends complete abolition of antibiotic prophy-

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References: 1. Euromonitor International. 2. Fine DH, Barnett ML, et al. Effect of an essential oil-containing antiseptic mouthrinse on plaque and salivary Streptococcus mutans levels. J Clin Periodontol 2000;27:157-161. 3. Santos T. Evidenced-based control of plaque and gingivitis. J Clin Periodontal 2003;30(Suppl 5):13-16.

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laxis for patients at risk of infective endocarditis undergoing dental and a wide range of other invasive procedures.<sup>3</sup> The rationale of the NICE guidelines is the absence of a consistent association between interventional procedures, dental or otherwise, and the development of endocarditis as well as the unproven effectiveness, the potential mortality of anaphylaxis and increased expense. NICE guidelines recommend that antibiotic cover should be offered to patients only if the procedure is at a site where there is already a suspected infection. Furthermore, the NICE guidelines do not recommend the use of chlorhexidine mouthrinses prior to dental procedures. Although the guidelines do recognise certain cardiac conditions which present a high risk for developing infective endocarditis, these are mainly listed to emphasise the need for good oral hygiene and awareness of infective endocarditis. Although the AHA and ESC for Cardiology modified their guidelines more or less simultaneously, both of these authoritative bodies still recommended administering antibiotic prophylaxis in certain high-risk groups.<sup>6,8</sup>

#### **CONTROVERSIES**

Theoretically, antibiotic prophylaxis in patients with cardiac risk factors should decrease the incidence of infective endocarditis; however, to date this principle has not been underpinned by sound scientific evidence. Several factors contribute to this failure of what appears to be a linear-logic approach. While it has been shown that invasive procedures, e.g. dental extractions, cause bacteraemias, other common daily activities, e.g. toothbrushing, interdental flossing and mastication, do so as well. The transient bacteraemias which may be caused by surgical dental procedures are several orders of magnitude higher than those resulting from common daily activities.<sup>9</sup> The latter, however, may cumulatively be several million times higher than those resulting from single invasive procedures (so-called cumulative bacteraemia).9 Additionally, it has been shown that only a small proportion, if any, of cases of infective endocarditis were causally linked to dental procedures.<sup>10,11</sup> Conflicting evidence has been reported regarding the reduction or prevention of bacteraemias by means of antibiotic prophylaxis.<sup>12</sup>

It is contentious whether antibiotic prophylaxis is cost-effective for at-risk patients.<sup>12</sup> Strains of antibiotic-resistant organisms may emerge and antibiotic-related side-effects do occur, but these phenomena are both rare following high, single-dose antibiotic administration on an infrequent basis, such as during prophylaxis. While minor unwanted effects may occur during prophylactic antibiotic usage, no cases of anaphylaxis have been reported to the AHA during the 50 years that they have recommended using a penicillin for the prophylaxis of infective endocarditis.<sup>13</sup> The AHA believes that it is safe to administer a single dose of a broad-spectrum penicillin, e.g. amoxicillin or ampicillin, to persons who do not have a history of hypersensitivity to a penicillin, such as anaphylaxis, urticaria or angioedema. While the NICE committee quotes the potential of fatal anaphylaxis to penicillins as one of the reasons for their stance, reports of oral amoxicillin causing this condition have never been reported in the world literature.14

#### DISCUSSION

Publication of the NICE guidelines in the UK in 2008 has challenged the standard of care for prevention of infective endocarditis. That these guidelines have been accepted by many practitioners in the UK is evidenced by a 78.6% reduction in antibiotic prophylaxis.<sup>15</sup> NICE is unique in recommending

#### Table1: Cardiac conditions requiring antibiotic prophylaxis for highrisk dental procedures included in international guidelines, but excluded by NICE<sup>15</sup> (adapted from reference<sup>14</sup>)

- Replacement valves or prosthetic material used for cardiac valve repair
- Previous episodes of infective endocarditis
- Congenital heart disease
  - Unrepaired cyanotic congenital heart disease including palliative shunts and conduits
  - Completely repaired using prosthetic material or device during the first 6 months after the procedure (surgical or percutaneous)
  - Repaired with residual defect at the site or adjacent to the site of a prosthetic patch or device
- Cardiac transplantation with valvular regurgitation due to a structurally abnormal valve\*

#### \*Included in the AHA guideline, but excluded in the ESC guideline

no antibiotic prophylaxis for cardiac patients undergoing dental or non-dental procedures, except for manipulations at an infected site.<sup>14</sup> While most national or international guidelines from the USA, Europe and Australia have pared down their indications, they still recommend prophylaxis for certain dental procedures in high-risk cardiac patients (Table 1).<sup>14</sup> Even though the NICE committee correctly stated that, in the absence of prospective, randomised trials, the clinical effectiveness of antibiotic prophylaxis remains unproven, some clinical and animal studies reviewed by the AHA and BSAC have suggested that there are benefits.<sup>5,6,14</sup> It has been estimated that a randomised, placebo-controlled trial to demonstrate the effectiveness of antibiotic prophylaxis for infective endocarditis would require the participation of 60 000 individuals, making such a study unlikely to transpire.<sup>16</sup>

#### THE SOUTH AFRICAN CONTEXT

A variety of arguments have been advanced that the guidelines emanating from the USA and Europe cannot be extrapolated to the local situation, namely: (i) the high prevalence of rheumatic heart disease predisposes to IE; (ii) HIV might predispose to infective endocarditis; and (iii) the local microbiological profile of infective endocarditis differs.<sup>17</sup>

The theory of cumulative bacteraemia takes rheumatic heart disease into account. However, there is no evidence that it poses a significantly higher risk for development of infective endocarditis than other, accepted risk factors, or that the severity and consequences of the disease are far worse than those seen with other risk factors. Therefore, it should not be seen as an exception. The evidence that HIV predisposes to infective endocarditis is scant.

Although the data are scarce, the most common pathogenic organisms in a South African setting are oral streptococci, and the antibiotic choice should therefore be no different to that of the international guidelines.<sup>18</sup> This is an issue unrelated to the threshold/indications for prophylaxis.

The opinion of the authors, as evidenced in our previous review, is that in the absence of any data to the contrary, the guidelines as set forth by the AHA, ESC and BSAC are appropriate and apply also in the South African context. It is clear that the risk of developing infective endocarditis following dental procedures is low. There is little scientific evidence that prophylactic administration of antibiotics prior to dental procedures would lower the risk of developing the disease and it should be kept in mind that the above guidelines are not infallible. However, in the absence of hard evidence on prophylactic efficacy and being mindful of the potential legal consequences, we recommend adherence to the AHA, ESC and BSAC guidelines in high-risk cardiac patients (Table I) who are undergoing manipulation of dento-gingival tissue, procedures involving the periapical region of teeth and endodontics. Of further importance is that dental treatment plans be drawn up and executed in such a manner that patients are not unnecessarily exposed to prophylactic antibiotics – this might include concurrent execution of procedures. Where that is not possible, the AHA and BSAC respectively recommend intervals of at least 10 and 14 days. Otherwise, amoxicillin may be alternated with clindamycin and, in patients being treated with these two antibiotics for other infections, azithromycin or clarithromycin may be substituted.

Patients should be well-informed by their dental practitioner, with the option of obtaining written consent for the administration/omission of prophylaxis being very reasonable. They should be advised to report any adverse effects following prophylaxis to their practitioner via a direct line of communication.

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