

## Antibiotic prophylaxis for infective endocarditis

Despite advances in diagnosis and treatment, infective endocarditis remains a dangerous disease, particularly for people at risk because of a prosthetic valve, congenital heart disease, or a history of infective endocarditis, in whom morbidity and mortality approach 50%.<sup>1</sup> Antibiotic prophylaxis for such patients at the time of invasive procedures has been a tenet of cardiac and dental practice for half a century, although the evidence of benefit is limited. Few cases of infective endocarditis are now secondary to oral streptococci, and *Staphylococcus aureus* (frequently acquired as a result of nosocomial infection or misuse of intravenous drugs) is now the most common pathogen, with attendant higher mortality.<sup>2</sup>

Efficacy of antibiotic prophylaxis for infective endocarditis has never been shown in a randomised trial. However, the underlying rationale is based on a three-part theory: bacteraemia provokes infective endocarditis in patients with valve abnormalities; many patients undergoing invasive procedures have subsequent bacteraemia; and, in animal models, antibiotics before bacterial challenge significantly reduce the risk of the disorder. However, relevance of results from these models to human beings in vivo is questionable.

Furthermore, antibiotic prophylaxis is not an option for many in whom infective endocarditis arises without previously documented cardiac disease (47% in one recent French series).<sup>3</sup> The knowledge that certain cardiac disorders predispose to infective endocarditis and that certain procedures can lead to bacteraemia has led to antibiotic prophylaxis being recommended by international bodies of authority. Until now.

Daily oral activities (eg, tooth brushing, chewing) cause transient streptococcal bacteraemia, resulting in annual cumulative exposure thousands to millions times greater than that caused by tooth extraction.<sup>4</sup> Moreover, a direct link between routine dental procedures and infective endocarditis has never been proven, and the associated bacteraemia is two to four orders of magnitude below that needed to cause infective endocarditis in animals.<sup>5</sup> There is no evidence that the duration of bacteraemia of this magnitude is proportional to the risk of infective endocarditis, however illogical that might seem, and a Cochrane review concluded that no evidence supported the use of penicillin prophylaxis.<sup>6</sup>

Frequency, magnitude, and duration of bacteraemia for any procedure vary greatly between studies, so calculations are prone to a large degree of error. Moreover,

	French recommendations, 2002 <sup>22</sup>	British Society for Antimicrobial Chemotherapy, 2006 <sup>23</sup>	American Heart Association, 2007 <sup>24</sup>	National Institute for Health and Clinical Excellence, 2008 <sup>25</sup>
High-risk patients	Previous infective endocarditis. Cardiac-valve replacement. Prosthetic systemic or pulmonary shunt or conduit	Previous infective endocarditis. Cardiac-valve replacement. Prosthetic systemic or pulmonary shunt or conduit	Previous infective endocarditis. Prosthetic valve. Unrepaired or incompletely repaired cyanotic congenital heart disease. Congenital heart disease repaired with prosthetic material (for 6 months after the procedures). Valve disease in cardiac transplant recipients	Previous infective endocarditis. Acquired valvular heart disease with stenosis or regurgitation. Prosthetic valve. Structural congenital heart disease, including surgically corrected or palliated structural conditions, but excluding isolated atrial septal defect, fully repaired ventricular septal defect or fully repaired patent ductus arteriosus, and closure devices that are judged to be endothelialised. Hypertrophic cardiomyopathy
Low-risk patients	Other valve disease (including mitral-valve prolapse with mitral insufficiency or valve thickening). Non-cyanotic congenital heart disease (except atrial septal defect). Hypertrophic obstructive cardiomyopathy	..	..	..
Procedures requiring prophylaxis in high-risk patients	All invasive dental, respiratory, gastrointestinal, and genitourinary procedures	All invasive dental, respiratory, gastrointestinal, and genitourinary procedures	Dental procedures involving manipulation of gingival tissue, the periapical region of teeth, or perforation of the oral mucosa. Invasive procedures of the respiratory tract needing incision or biopsy of the respiratory mucosa	Gastrointestinal and genitourinary procedures at a site where there is suspected infection
Procedures requiring prophylaxis in low-risk patients	Optional, based on composite clinical assessment of the patient and procedural risk. Post-hoc prophylaxis can be given in the event of unanticipated procedural complexity	..	..	..

**Table: Summary of current international guidelines**

which parameter contributes most to the risk of infective endocarditis is still uncertain. Antibiotic prophylaxis before invasive procedures is, therefore, a token gesture, and general dental and skin hygiene are probably more important for prevention of infective endocarditis.

The only efficacy studies of prophylaxis have been case-control analyses. A 2-year study of 275 patients in the Netherlands showed that most cases of infective endocarditis are not attributable to invasive procedures, but to random bacteraemia.<sup>7</sup> The authors concluded that even if antibiotic prophylaxis was 100% effective, then it would only prevent a few cases each year. For example, if dental treatment was responsible for 1% of infective endocarditis due to oral streptococci, the overall risk in the general population would be one in 14 million dental procedures, rising to one in 95 000 in higher risk groups. Similarly, dental procedures in France were not associated with increased risk of infective endocarditis.<sup>8</sup> Although dental scaling was independently associated with infective endocarditis due to oral streptococci, the protective efficacy of antibiotic prophylaxis was not significant. A third case-control study in 54 US hospitals found that dental treatment in the preceding 3 months was no more likely to have taken place in people with infective endocarditis than in controls.<sup>9</sup>

Although negative, the results of these studies do not show that antibiotic prophylaxis for infective endocarditis is ineffective. However, the risk of infective endocarditis from a dental procedure without antibiotic prophylaxis has been estimated at one in 46 000, falling to one in 150 000 with prior antibiotic treatment.<sup>10</sup> The authors reasonably conclude that "a huge number of prophylaxis doses would be necessary to prevent a very low number of cases". There has been no randomised controlled trial, which would be a massive undertaking requiring huge numbers of patients to provide adequate statistical power. The heterogeneity of underlying cardiac disorders and invasive procedures would make stratification very difficult, and the completion of such a trial is unlikely.

With the high number needed to treat, the use of antibiotics is by no means risk-free. Although prophylactic regimens suggest only single-dose administration, from which non-fatal side-effects are usually minor, there is a risk of fatal anaphylaxis, which affects 15–25 people per million.<sup>11</sup> Although less likely with single doses, antibiotic resistance is also a concern.

The paucity of evidence and changing clinical profile of infective endocarditis has led several organisations to update their guidelines significantly in recent years (table). Innovative French guidelines<sup>12</sup> published in 2002 challenged accepted practice by emphasising the importance of general oral hygiene, and suggesting restriction of prophylaxis to people with the highest ratio of benefit to individual and collective risk.

The British Society for Antimicrobial Chemotherapy<sup>13</sup> 2006 guidelines acknowledged that many clinicians are reluctant to withhold antibiotic prophylaxis despite the lack of evidence. Instead, they recommended prophylaxis only for those at high-risk and for whom infective endocarditis would result in high mortality.

American Heart Association (AHA) 2007 guidelines<sup>14</sup> suggested prophylaxis only for patients with high-risk cardiac disorders, indicating that antibiotic prophylaxis is no longer recommended for patients with native valve disease or for any gastrointestinal or genitourinary procedures.

Even more controversially, guidelines published in March, 2008, by the National Institute for Health and Clinical Excellence (NICE) suggest an end to antibiotic prophylaxis altogether.<sup>15</sup> Although NICE identifies patients at increased risk of infective endocarditis, it no longer advocates prophylaxis for dental or respiratory procedures and only for gastrointestinal and genitourinary procedures where there is suspected pre-existing infection. NICE recognises the need for patients to receive clear and consistent information and for a detailed explanation of the significant change in practice.

These recommendations have encountered mixed reactions—many dental workers, confused by increasingly complicated and ambiguous guidelines, have praised them as "a victory for science and common sense".<sup>16</sup> However, many cardiologists believe that new guidelines are a dangerous departure from established practice. Although such resistance could reflect concern about the possibility of litigation, adherence to recognised guidelines provides substantial legal protection.<sup>17</sup>

Despite the absence of evidence (and in conflict with NICE), neither the AHA nor the British Society for Antimicrobial Chemotherapy recommended the withdrawal of antibiotic prophylaxis for the highest risk patients. In doing so, the AHA acknowledged that "in patients with underlying cardiac conditions associated with the highest risk of adverse outcome from [infective

endocarditis], prophylaxis for dental procedures may be reasonable, even though its effectiveness is unknown".<sup>14</sup>

Additional prophylactic measures for infective endocarditis include education of at-risk patients about the need for meticulous dental and skin hygiene and avoidance of unnecessary invasive procedures (eg, intravenous cannulae, urinary catheters). Strict adherence to institutional hygiene is crucial—a third of cases of prosthetic valve or *S aureus* infective endocarditis are nosocomial in origin and mortality in this setting exceeds 30%.<sup>18,19</sup> Early diagnosis is assisted by a high index of suspicion for the possibility of infective endocarditis and avoidance of antibiotic treatment without blood cultures in the event of unexplained febrile illness affecting high-risk patients.

Practices for prophylaxis of infective endocarditis seem set to change. New guidelines aim to provide simple, unambiguous protocols for everyone involved in the care of those few patients at risk of the disease. Consensus on their implementation is needed to avoid confusion in the minds of health professionals and, most importantly, patients.

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## Public-health crisis after the election violence in Kenya

When the centre cannot hold, things fall apart

*Chinua Achebe, Nigerian novelist and poet,  
from his 1958 book, Things fall apart*

After the disputed Presidential poll outcome of the Dec 27, 2007, elections, violence erupted in various parts of Kenya and led to deaths, injuries, massive displacements of people, and increased insecurity. Anger over the election outcome quickly translated into civil unrest over economic inequalities, land grievances, and

ethnic animosity. Simultaneously, property was destroyed on an unprecedented scale, and transport, health services and research, and public services were disrupted.<sup>1</sup> At least 1000 people might have died (from mortuary counts) and more than half a million have been displaced from their homes.<sup>2</sup> Because many bodies were buried without compliance with legal procedures (eg, admission to a mortuary) or disposed of unconventionally (eg, mass burial or into pit latrines), these numbers might have been grossly underestimated.<sup>3</sup>