Dear Editor,

We were surprised and dismayed to read the recommendations set out in this paper by such a well-respected body as the American Heart Association. Publication of this paper is likely to have a significant adverse impact on the incidence of infective endocarditis (IE) in the USA and possibly worldwide. Amongst patients “at risk” because of their structural heart disease, there will almost certainly be an increased frequency of this life-threatening condition as a result of antibiotic prophylaxis (ABP) being abandoned by dentists, physicians and surgeons carrying out invasive and interventional procedures which give rise to bacteraemia. Susceptible patients should not just include patients with the cardiac conditions listed in Table 3 but should include patients with non-rheumatic or rheumatic aortic or mitral valve disease (including mitral valve prolapse with mitral regurgitation), ventricular septal defect, primum atrial septal defect, hypertrophic obstructive cardiomyopathy, aortic root replacement, coarctation of the aorta and patent ductus arteriosus. IE continues to occur in such patients – particularly those with valvular heart disease, who have not received ABP although it is unusual to see IE in those receiving appropriate prophylactic antibiotics.

The pathogenesis of IE is well described in the paper and the case for protecting patients by ABP is well made. However, the accepted rationale for the use of ABP is then rejected for the above group of patients on the grounds that “IE is much more likely to result from frequent exposure to random bacteraemias associated with daily activities than from bacteraemia caused by a dental, GI tract or GU tract procedure”. This is neither logical, sensible nor based on any evidence whatsoever. Although we accept that IE does occur in patients without a history of having
undergone invasive procedures, are we as clinicians now to completely ignore the
temporal relationship between IE and bacteraemia-inducing procedures in patients
with structural heart disease, which has been (and continues to be) recognised for the
last 50 years or more? Are we also to ignore the noticeable fall in the numbers of
patients with IE following dental treatment that has occurred over the last 40 years or
more since ABP has been practised? The suggestion that “Prophylaxis may prevent an
exceedingly small number of cases of IE, if any, in individuals who undergo a dental,
GI tract, or GU tract procedure” is in our view incorrect and not based on any
evidence either. The statement that “the risk of antibiotic-associated adverse events
exceeds the benefit, if any, from prophylactic antibiotic therapy” is also neither borne
out in clinical practice nor based on any relevant evidence in the literature. Table 6 is
also disturbing in recommending that ABP should not be offered to patients with
valvular heart disease who have to undergo genitourinary or gastrointestinal
invasive/interventional procedures which are well documented as being associated
with bacteraemia and cases of IE. With regards to tattooing and body piercing, it
would have been more sensible to recommend that patients with “at-risk” cardiac
conditions should be advised against this form of “body art” or if they insist, that they
should be offered some form of ABP to protect them from staphylococcal bacteraemia
and subsequent IE which can be most destructive.

What we can be certain of is that when cases of IE occur in patients with
valvular heart disease having undergone unprotected dental or surgical treatment, the
patient is likely to become very sick. They may develop the destructive cardiac
complications such as valvular regurgitation and heart failure, intracardiac abscesses,
false aneurysms or fistulous communications between the cardiac chambers and/or
great vessels. Potentially just as devastating are the vasculitic and embolic
complications of IE including cerebral emboli leading to cerebral infarction and/or
haemorrhage, coronary artery emboli causing myocardial infarction, renal and splenic
infarction/abscess formation, glomerulonephritis and renal failure, superior
mesenteric artery emboli leading to bowel infarction, Osler’s nodes, peripheral emboli
and even digital gangrene, and mycotic aneurysms leading to the fatal complications
following arterial rupture such as subarachnoid or intracerebral haemorrhage. In order
to survive this serious condition, individuals will require prolonged in-hospital (and
usually intensive-care) treatment with high doses of intravenous antibiotics and
possibly cardiac or other surgery to deal with the complications of IE and patients will
usually require numerous in-patient investigations. The cost of such care and the long-lasting effects of the complications that may arise far outweigh the extremely small risks associated with ABP.

The argument that ABP for such “at-risk” cardiac patients prior to dental or surgical treatment is likely to be responsible for the development of antibiotic resistance among microorganisms is not supported by any evidence in the literature and is not a good enough reason to abandon ABP for these cases.

In the UK, a survey of consultant cardiologists and cardiac surgeons has revealed that 95% of these professionals believe that ABP should be given to patients with valvular heart disease e.g. aortic stenosis, mitral valve prolapse with mitral regurgitation, or other cardiac structural abnormalities that are now excluded from the new AHA guidelines. We wonder whether the conclusions of this American Heart Association Committee have the same degree of support from the majority of cardiologists and cardiac surgeons in the USA?

The Committee quote that they “sought to construct the present recommendations such that they would be in the best interest of patients….” When a 29 year old primary school teacher suddenly develops aphasia and a right hemiplegia following embolisation of a large vegetation from her prolapsing mitral valve 6 weeks after having undergone dental treatment without ABP, the devastating consequences of not doing everything in our power to try and prevent IE are suddenly all too real and difficult to defend. Her career is ended abruptly, her sporting activities become impossible and much of her social and family life is severely affected forever by her disability. It will soon be all too apparent that the Committee’s recommendations were not in anyone’s best interest and certainly not the patient’s.

As clinicians, with our patients’ care and best interests at heart, we would advocate categorisation of patients with cardiac conditions into “at-risk” and “not-at-risk” groups, but would insist that those with the conditions that we describe above should be in the “at-risk” group and receive ABP prior to dental or surgical treatment. We would also favour concentrating our efforts on deciding which procedures give rise to significant enough bacteraemia to warrant protection for these “at-risk” cases by ABP rather than abandoning a strategy that is based on a sound knowledge of the pathology and careful clinical observations over many years of practice by cardiologists, cardiac surgeons and dentists.
Yours truly,

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July 6, 2007

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UNITED KINGDOM

Dear Doctor Ramsdale:

We would like to thank you and your colleagues for your letter dated May 10, 2007, regarding the recently published American Heart Association (AHA) guidelines for prevention of infective endocarditis (IE). We certainly value your opinion, but we respectfully disagree with some of the assertions stated in the letter. We would like to provide background information regarding the current guidelines and to respond to specific issues raised in your letter.

Publication of the revised AHA guidelines on prevention of IE was a culmination of more than three years of sustained effort and review with input from 33 authorities on IE representing eight different countries. The document underwent extensive external review by other authorities and internal review by leadership and experts within the AHA.

This extensive process was necessary because the Writing Committee recognized that the current document offered recommendations that differed substantially from those contained in the previous nine AHA documents on the prevention of IE published from 1955-1997. The Committee recognized that substantive changes and recommendations would likely violate longstanding expectations and practice patterns by patients and healthcare providers. Further, these new recommendations might cause concern among patients who previously received antibiotic prophylaxis to prevent IE before dental or other procedures and are now advised that such prophylaxis is unnecessary. Finally, the Committee steadfastly believed that the interest of the patient was of foremost importance throughout this entire process. Accordingly, we were compelled to thoroughly review published data about the prevention of IE and to ensure to the extent possible that changes in recommendations were based on published data and would not place patients at increased risk.

The major assertions in your letter were:

- Antibiotic prophylaxis with dental or other procedures prevents IE.
- There has been a decrease in the number of cases of IE in the past 40 years as a result of antibiotic prophylaxis for dental procedures.
- It is unusual for patients to develop IE who have received antibiotic prophylaxis for a bacteremia producing procedure.
- There is a documented temporal relationship between IE and bacteremia producing procedures.
- IE is more likely to result from a bacteremia producing dental or other procedure than from bacteremia that occurs in association with routine daily activity.
- GI and GU tract procedures are well documented as causes of IE.
- The risk of antibiotic associated adverse events or development of microbial resistance from the use of prophylactic antibiotics is not established.
- The number of cases of IE will increase as the result of our recommendations.
We conducted MEDLINE database searches from 1950-2006 for English language publications on endocarditis and related topics. We also searched other databases using the same or similar search terms. Despite this extensive search, we were unable to identify convincing published data to support the major assertions in your letter listed above. In addition to the current AHA guidelines referenced in your letter, we refer you to a recent publication by Lockhart, et al, JADA 138:458, 2007. If you and the coauthors can provide published references to support your assertions, the Writing Committee and the AHA welcome the opportunity to review them.

We were unable to find convincing published evidence that demonstrated a conclusive link between dental procedures and IE or that antibiotic prophylaxis for bacteremia producing procedures prevents IE. The Committee recognizes that dental or other procedures may cause transient bacteremia and that patients with predisposing cardiac conditions would be a potential risk of acquisition of IE as a result of this bacteremia. However, the absolute risk of IE from a dental procedure is estimated to range from 1 per 1.1 million procedures in patients with mitral valve prolapse to 1 per 95,000 dental procedures in patients with a history of previous IE (1, 2). Based on these estimates, even if antibiotic prophylaxis for a dental procedure were 100% effective, the number of cases of IE that could be prevented is exceedingly small.

Published retrospective studies which suggest that antibiotic prophylaxis may be effective to prevent IE often contain a small sample size of patients with IE or provide insufficient clinical data or methodology. The evidence linking bacteremia associated with a dental procedure with IE is largely circumstantial as outlined in detail on page 8 of our manuscript. There are numerous poorly documented case reports that implicate dental procedures associated with the development of IE, but these reports are far from evidence of a direct causal relationship. It is not possible to determine with certainty whether the bacteremia that caused IE originated from a dental procedure or from a randomly occurring bacteremia as a result of routine daily activities during the same time period. Many case reports and reviews have included cases with a remote preceding dental procedure often three to six months before the diagnosis of IE.

We could not identify a prospective controlled study that demonstrated that antibiotic prophylaxis with a dental, gastrointestinal (GI), or genitourinary (GU) tract procedure prevents IE. van der Meer, et al (3) reported that dental procedures caused only a small fraction of cases of IE, and prophylaxis would prevent only a small number of cases even if 100% effective. In a case-control study (4), these authors reported that five of 20 cases of IE occurred despite receiving prophylactic antibiotics for a dental procedure. These data are in agreement with an AHA registry of cases of IE that occurred despite receiving antibiotic prophylaxis for a dental procedure.(5) These and other studies concluded that antibiotic prophylaxis for a dental procedure is not effective to prevent endocarditis. These studies are in agreement with a case-control study published by Strom, et al (6) and a recently published study in France by Duval, et al (7).

We are unaware of published data which demonstrate a decreased number of cases of IE during the past 40 years as a result of antibiotic prophylaxis for dental or other procedures. We would be very interested if you could provide such publications.

Case reports of IE temporally associated with a GI or GU tract procedure are anecdotal with either a single or a very small number of cases reported (8). There are no published data that we are aware of that demonstrate a conclusive link between procedures of the GI or GU tract and the development of IE (9) nor are there studies which show that antibiotic prophylaxis prevents IE in these cases.
The risk of the development of microbial resistance associated with prophylactic antibiotic use is an extensively well documented global problem. The potential adverse events of antibiotic use are equally well known. Both of these issues are extensively referenced in our document.

In summary, we certainly agree that there are a number of underlying cardiac conditions which predispose to a lifetime risk of the acquisition of IE. We cannot exclude that antibiotic prophylaxis may prevent an exceedingly small number of cases of IE associated with a dental procedure. However, the available literature does not provide scientifically credible evidence that the administration of antibiotic prophylaxis outweighs its risks. We are confident in the thoroughness and rigor of our analysis of the published data, the process, and impartiality of peer review and the rationale for the recommendations made in the current AHA guidelines. We hope our revised guideline will stimulate prospective studies on IE prophylaxis.

Sincerely,

(signatures on original letter)

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