

Infective Endocarditis Prevention: Update on 2007 Guidelines

Mary Jane Burton, MD, Stephen A. Geraci, MD

Department of Medicine, University of Mississippi Medical Center, Medical Service, G.V. (Sonny) Montgomery VA Medical Center, Jackson, Miss.

ABSTRACT

Antibiotic prophylaxis for preventing infective endocarditis is unproven. The recently issued American Heart Association guidelines for endocarditis prevention call for restricting the use of preprocedure antibiotics. We discuss how these revisions apply to clinical practice in patients undergoing elective medical and dental procedures.

© 2008 Elsevier Inc. All rights reserved. • *The American Journal of Medicine* (2008) 121, 484-486

KEYWORDS: Antibiotic prophylaxis; Bacterial/etiology; Bacterial/prevention and control; Endocarditis

Infective endocarditis is an uncommon disease with considerable morbidity and mortality. Uniformly fatal in the pre-antibiotic era, mortality rates have remained stable at approximately 25% of cases over the past 30 years despite improvements in health care.^{1,2} Given the grave outcome of this disease, prevention is desirable.

The American Heart Association (AHA) issued the first guidelines for prevention of infective endocarditis in 1955.³ The justification for these recommendations was largely based on expert opinion and case reports. Since that time, little evidence has accumulated to support this widely instituted practice.⁴ The global medical consensus is that few, if any, cases of infective endocarditis can be prevented by preprocedure antibiotics.^{5,6} This collective change in opinion influences the most recent version of the AHA guidelines for endocarditis prophylaxis.⁷ This article presents a practice-based summary of these recommendations.

BACKGROUND

The rarity and severity of infective endocarditis complicates the execution of randomized, controlled trials to clarify the role of antibiotics in preventing this disease. Animal studies suggest that preprocedure antibiotics can consistently prevent bacterial endocarditis; thus, prophylaxis seems appropriate for patients perceived to be at higher risk of devel-

oping this infection. Higher risk groups, including those with chronic rheumatic heart disease, congenital heart disease, and acquired valvular dysfunction, were identified by retrospective studies. Procedures requiring prophylaxis were selected from case reports and documentation of bacteremia with common endocarditis pathogens (*viridans streptococci* and *enterococci*). Administering antistreptococcal antibiotics in these circumstances has been widely accepted, but lacks scientific support. Retrospective studies indicate that the majority of unprotected procedures in at-risk individuals do not result in infective endocarditis.⁸ Additionally, failures of prophylaxis have been documented.⁹ Thus, prior recommendations lacked supporting science.

SUMMARY OF 2007 AHA GUIDELINES

Patient Selection

The previous version of the AHA guidelines for bacterial endocarditis prophylaxis recommended antibiotics for patients considered to have high and moderate *risk of acquiring* the disease.¹⁰ The 2007 guidelines, in contrast, restrict prophylaxis to those patients who have the highest *risk of an adverse outcome* should they contract infective endocarditis. These groups are limited to those with previous history of endocarditis, prosthetic valves, cardiac transplants with graft valvulopathy, and certain forms of congenital heart disease (Table 1). The rationale for this change stems from the absence of prospective evidence for benefit of prophylaxis in any group, while retrospective studies suggest that

Requests for reprints should be addressed to Mary Jane Burton, Medical Service, G.V. (Sonny) Montgomery VA Medical Center, 1500 E. Woodrow Wilson Drive (111), Jackson, MS 39216.

E-mail address: maryburton2@va.gov

the morbidity from endocarditis is greater in the listed populations than in others.⁷

The 2007 guidelines also limit the procedures for which prophylaxis is advised (Table 2). High-risk patients are recommended to receive antibiotics before dental procedures involving the gingiva, and operations that incise or biopsy the respiratory mucosa. Skin and soft tissue procedures involving infected sites also are reasonable situations for prophylaxis.

Routine bacterial endocarditis prophylaxis in gastrointestinal and genitourinary procedures is not recommended (no high grade data to support the practice), despite the colonization of these areas with *enterococci*, a common endocarditis pathogen. The guidelines state that when gastrointestinal or genitourinary procedures require antibiotics for reasons other than endocarditis prevention (eg, gastrostomy tube placement, transurethral prostatectomy), it is reasonable to include enterococcal coverage in high-risk individuals. Also, if gastrointestinal or genitourinary procedures are done in the setting of infection, antibiotic coverage targeted at known/suspected pathogens in these same high-risk patients is reasonable.

Antibiotic Regimens

Recommended antibiotic regimens before dental procedures are summarized in Table 3. Antibiotics should be given 30 to 60 minutes before starting the indicated procedure. If the drug is inadvertently omitted before the procedure, it may be administered up to 2 hours after the procedure with some protective benefit.

Regimens for respiratory procedures also are listed in Table 3, although a few caveats are worth noting. Amoxi-

illin does not target *Staphylococcus aureus*; when the procedure involves tissues infected or colonized with this organism, an anti-staphylococcal antibiotic may be given (no specific antibiotic choices are recommended). Both cefazolin and clindamycin target *S. aureus*; at the doses listed in

Table 3, either should provide adequate protection. Vancomycin should be limited to settings where infection with methicillin-resistant *Staphylococcus aureus* (MRSA) is known or highly suspected, or in patients who have penicillin or cephalosporin allergies. Previous guidelines recommended the intravenous vancomycin dose of 1 g in adults and 20 mg/kg in children.¹⁰ To avoid adverse reactions from vancomycin, the drug should be given over a 1- to 2-hour period ending 30 minutes before the planned procedure. *S. aureus* or MRSA coverage as listed above also is appropriate for procedures on infected skin and skin structures.

There are no formal recommendations about choice of antibiotic coverage for gastrointestinal or genitourinary procedures. When enterococcal coverage is desired, amoxicillin and ampicillin at the doses listed in Table 3 are reasonable choices. Vancomycin can be used in the setting of penicillin allergy. The paucity of data in this area complicates discussion about optimal antibiotic choices. In the setting of infections with antibiotic-resistant organisms, consultation with an infectious disease specialist is the most prudent course.

There are limited data on the risks of antibiotic use in endocarditis prophylaxis, but with little evidence of proven benefit, treatment risk warrants consideration. Fatal reactions from penicillin occur in only 0.001% of 100,000 courses.¹¹ There are no reports of fatal anaphylaxis from one-time doses of amoxicillin, but this remains a possibility, especially if prior exposure is suspected. *Clostridium difficile* colitis has been reported in the setting of dental pro-

CLINICAL SIGNIFICANCE

- Infective endocarditis prophylaxis should be reserved for those individuals who would suffer the greatest morbidity from acquiring infective endocarditis.
- Infective endocarditis prophylaxis should be limited to these individuals, and only in situations in which there is some suggestion of possible benefit.
- In some instances, the risk of adverse events from unnecessary antibiotics may outweigh the risk of infective endocarditis.

Table 1 Cardiac Conditions Recommended as Requiring Infective Endocarditis Prophylaxis

Previous episode of bacterial endocarditis
 Prosthetic cardiac valves
 Cardiac transplant patients with acquired graft valvular dysfunction
 Congenital Heart Disease* (CHD), limited to:
 Unrepaired cyanotic CHD
 Completely repaired CHD within the first 6 months after corrective surgery
 Repaired CHD with residual defects

Adapted from: Wilson W et al. Prevention of infective endocarditis. *Circulation*. 2007;116:1745.⁷

*Subspecialty consultation for endocarditis prophylaxis recommended by the authors.

Table 2 Summary of Procedures for which Routine Endocarditis Prophylaxis in Individuals with Greatest Risk of Adverse Outcome is Recommended

Dental procedures involving the gingiva or periapical region of the tooth
 Respiratory procedures with incision of the respiratory mucosa or drainage of infected tissue
 Procedures involving drainage of infected skin or skin structures
 No routine GI or GU procedures

Adapted from: Wilson W et al. Prevention of infective endocarditis. *Circulation*. 2007;116:1746.⁷

Table 3 Recommended Antibiotics for Dental and Respiratory Procedures

| Route | Regimen | Adults | Children |
|--------------------|---|----------------------------------|--------------------------------------|
| Oral | Amoxicillin* | 2 g | 50 mg/kg |
| IV/IM | Ampicillin or Cefazolin†‡ or ceftriaxone† | 2 g (IM/IV) 1 g (IM/IV) | 50 mg/kg (IM/IV) 50 mg/kg (IM/IV) |
| Penicillin allergy | | | |
| Oral | Cephalexin†‡ or Clindamycin† or Azithromycin, clarithromycin | 2 g 600 mg 500 mg | 50 mg/kg 20 mg/kg 15 mg/kg |
| IV/IM | Cefazolin†‡ or ceftriaxone† or Clindamycin | 1 g (IM/IV) 600 mg (IM/IV) | 50 mg/kg (IM/IV) 20 mg/kg (IM/IV) |

IM = intramuscular; IV = intravenous. Adapted from: Wilson W et al. Prevention of infective endocarditis. *Circulation*. 2007;116:1747.⁷

*Preferred drug in a patient with no contraindications.

†Cephalosporins should not be used in a patient with history of severe penicillin allergy.

‡Provide antimicrobial coverage for methicillin-sensitive *Staphylococcus aureus*.

phylaxis.¹² The impact of endocarditis prophylaxis on antibiotic resistance is unknown, but certainly of concern.

CONCLUSION

The role of preprocedure antibiotics for infective endocarditis prevention is unknown. The current AHA guidelines recommend far fewer settings where such practice should be considered. Patients and procedures for which prophylaxis is recommended have been limited. Clinicians have a responsibility to inform patients of the potential risks and

benefits of endocarditis prophylaxis. Guidelines should never replace clinical judgment; however, the risk of antibiotics in some situations may outweigh the risk of bacterial endocarditis.

References

1. Mylonakis E, Calderwood SB. Infective endocarditis in adults. *N Engl J Med*. 2001;345:1318-1330.
2. Tleyjeh IM, Steckelberg JM, Murad HS, et al. Temporal trends in infective endocarditis: a population based study in Olmsted County, Minnesota. *JAMA*. 2005;293:3022-3028.
3. Jones T, Baumgartner L, Bellows M, et al. Prevention of rheumatic fever and bacterial endocarditis through control of streptococcal infections. *Circulation*. 1955;11:317-320.
4. Oliver R, Roberts GJ, Hooper L. Penicillins for the prophylaxis of bacterial endocarditis in dentistry. *Cochrane Database Syst Rev*. 2004;(2):CD003813.
5. Duval X, Alla F, Hoen B, et al. Estimated risk of endocarditis in adults with predisposing cardiac conditions undergoing dental procedures with or without antibiotic prophylaxis. *Clin Infect Dis*. 2006;42:e102-e107.
6. Gould FK, Elliott TS, Foweraker J, et al. Guidelines for the prevention of endocarditis: report of the Working Party of the British Society for Antimicrobial Chemotherapy. *J Antimicrob Chemother*. 2006;57:1035-1042.
7. Wilson W, Taubert KA, Gewitz M, et al. Prevention of infective endocarditis: guidelines from the American Heart Association: a guideline from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. *Circulation*. 2007;116:1736-1754.
8. van der Meer JT, van Wijk W. Efficacy of antibiotic prophylaxis for prevention of native-valve endocarditis. *Lancet*. 1992;339:135-139.
9. Durack DT, Kaplan ET, Bisno AL. Apparent failures of endocarditis prophylaxis. Analysis of 52 cases submitted to a national registry. *JAMA*. 1983;250:2318-2322.
10. Dajani AS, Taubert KA, Wilson W, et al. Prevention of bacterial endocarditis. Recommendations by the American Heart Association. *Circulation*. 1997;96:358-366.
11. Idsoe O, Guthe T, Willcox RR, de Weck A. Nature and extent of penicillin side-reactions, with particular reference to fatalities from anaphylactic shock. *Bull World Health Organ*. 1968;38:159-188.
12. Bombassaro AM, Wetmore SJ, John MA. Clostridium difficile colitis following antibiotic prophylaxis for dental procedures. *J Can Dent Assoc*. 2001;67:20-22.