Editorial: Diagnostic Criteria for Identifying Cases of Endocarditis—Revisiting the Duke Criteria Two Years Later

It has been over a century since Osler delivered his famous Gulstonian Lecture series on "malignant endocarditis." Since then, scientific investigators have delineated a large body of information concerning the pathophysiology and pathogenesis of infective endocarditis (IE) as well as the molecular mechanisms involved in its induction and propagation. However, it is interesting to note that physicians still struggle when they must clinically identify cases of IE in an accurate, reproducible manner. The four cardinal Oslerian manifestations of IE that remain the crux of the diagnosis are the presence of persistent bacteremia or fungemia, the presence of active valvulitis, the occurrence of large-vessel embolic events, and the presence of immunologic vascular phenomena [1].

See the article by Hoen et al. on pages 298–302.

Patients who fulfill all four of these criteria present few diagnostic dilemmas to the clinician. However, in the past two decades, notable shifts in the microbiology of IE (i.e., from a predominantly streptococcal etiology to an ever-increasing staphylococcal etiology), the mean age of patients with IE (now ~55 years), and the underlying cardiac conditions predisposing to IE (e.g., injection drug abuse and use of cardiac prostheses) have resulted in a substantially lower proportion of cases characterized by classic Oslerian manifestations [2].

Because of these shifts, von Reyn and co-workers [3] introduced the Beth Israel criteria for the strict case definition of IE in 1981; these criteria represented a major advance in the diagnosis of this disease. The critical need for an accurate schema for diagnosing IE has become abundantly clear, since the long-term prognosis in bona fide cases of IE is often complex despite microbiological cure of the infection. An initial episode of IE becomes a high life-long risk for subsequent episodes of the infection, and such patients require antimicrobial prophylaxis for all bacteremia-inducing medical procedures. Moreover, more than one-half of patients with left-sided involvement who survive 15 years after an episode of IE require a cardiac prosthesis because of progressive valvular insufficiency.

Despite the intrinsic merits of the Beth Israel criteria for diagnosing IE, they suffered from "bad timing"; they were formulated in an era when the use of echocardiography for defining valvular vegetations was in its early stage and before the importance of injection drug use as a key predisposing factor in IE had been fully recognized. Two years ago, Durack and colleagues [4] modified the Beth Israel criteria and published a new diagnostic schema (the Duke criteria) for the clinical diagnosis of IE, incorporating echocardiographic findings and injection drug use into the clinical parameters.

Since promulgation of these criteria, six major studies have compared the Duke criteria with the Beth Israel criteria [4–10] (table 1). Of note, these studies have included the following elements: both retrospective and prospective analysis of patient populations; patients who were predominantly injection drug users as well as those who were non-drug-users; children and adults; patients treated in private hospitals, universities, and public hospitals; and patient populations from Europe, North America, and South America.

The data from these studies have been remarkably similar, yielding the following conclusions: (1) the Duke criteria are more sensitive than the Beth Israel criteria for clinically diagnosing IE in patients who are leveraged toward this disease (i.e., when entry criteria are "rule out IE"): among patients who do not undergo open heart surgery, use of the Duke criteria yields a clinical diagnosis of IE in ~60% of cases, whereas use of the Beth Israel criteria yields a diagnosis of "probable IE" in ~40%; (2) it is clear from these studies that the Duke criteria are particularly useful in clinically diagnosing IE in the setting of *Staphylococcus aureus* bacteremia, right-sided valvulitis, and negative blood cultures; (3) the improved sensitivity of the Duke criteria is closely linked to the use of modern transthoracic and transesophageal echocardiography; and (4) in "gold standard" cases of IE (those in which the diagnosis has been confirmed surgically), the Duke criteria remain more sensitive than the Beth Israel criteria—no cases are rejected on the basis of the Duke criteria.

Table 1. Comparison between the Duke criteria and the Beth Israel criteria for the clinical diagnosis of infective endocarditis.

Category, criteria	No. (%) of patients with indicated diagnosis			
	Clinically definite	Probable	Possible	Rejected
Surgery (n = 112)*				
Beth Israel	...	54 (48)	35 (31)	23 (21)
Duke	93 (83)	...	19 (17)	0
No surgery (n = 861)				
Beth Israel	...	323 (38)	295 (34)	243 (28)
Duke	540 (63)	...	263 (30)	58 (7)

NOTE. Data are from [10]. Ellipses indicate diagnosis not included in schema.

* Evaluated clinically for infective endocarditis as if surgery had not been performed.

Received 24 April 1996.

Reprints or correspondence: Dr. Arnold S. Bayer, Division of Infectious Diseases, Department of Medicine, B1 RB2, 2nd Floor, Harbor UCLA Medical Center, 1000 West Carson Street, Torrance, California 90509.

Clinical Infectious Diseases 1996; 23:303–4

1058–4838/96/2302–0014$02.00

In the preceding article, Hoen et al. [11] have attempted to further define the utility of the Duke criteria by analyzing the specificity of this schema in patients with acute fever or fevers of unknown origin who underwent echocardiography and had at least two samples of blood for culture obtained before antibiotic therapy was administered. For 100 such patients, IE was rejected on the basis of the Duke criteria by virtue of either a firm alternate diagnosis or resolution of the febrile syndrome with little or no (≤4 days) antibiotic therapy. In reapplying the Duke criteria to these 100 cases in which IE was ruled out, only one patient was reclassified as having "clinically definite" IE on the strength of one major criterion (new regurgitant heart murmur) and three minor criteria, yielding a specificity rate of 99%. In a recent similar study, Dodds et al. [12] examined the negative predictive value of the Duke criteria by performing long-term follow-up (>3 months) of 52 patients in whom the diagnosis of IE was rejected by the Duke schema. This study confirmed a negative predictive value of ~98% for the Duke criteria.

Despite the impressive data from these two studies, each had several limitations that should be pointed out. In the study by Hoen et al. [11], most of the patients studied had a low pretest likelihood of having IE. For example, only ~25% of their patients had known underlying valvular heart disease, and only ~10% of the patients had echocardiographic abnormalities defined. Moreover, the retrospective nature of this study precluded uniform assessment of these patients for all the classic vascular phenomena (e.g., Roth's spots) and immunologic phenomena (e.g., serum positive for rheumatoid factor) associated with IE or a detailed serological work-up for blood culture–negative IE (e.g., Q fever or bartonella infection). Finally, only two of their patients had cultures of blood positive for pathogens: one culture was positive for *Escherichia coli* (an uncommon cause of IE), and the other was positive for *Streptococcus pneumoniae.*

Thus, it is apparent that the findings of Hoen et al. need to be confirmed in additional specificity studies that include febrile patients with a higher pretest likelihood of having IE, including those with staphylococcal bacteremia, those with peripheral emboli, or those with significant heart murmurs or known underlying valvular heart disease.

In summary, it is clear from multiple studies that the Duke criteria are substantially more sensitive than are the Beth Israel criteria in terms of both clinically diagnosing IE as well as in rejecting few patients with bona fide IE, as confirmed by open heart surgery. There are several additional issues that remain to be resolved concerning the Duke criteria. First, it will be important to apply the Duke criteria to two additional patient populations at risk for IE: febrile elderly patients and febrile prosthetic valve recipients, in whom the clinical and echocardiographic definition of IE may be much more problematic than it is in the general population. Two institutions, Duke University (Durham, NC) and Massachusetts General Hospital (Boston), are currently examining the utility of the Duke criteria for febrile prosthetic valve recipients (D. Sexton and S. Calderwood, personal communication); the publication of their findings is anxiously awaited.

Second, in subsequent prospective evaluations of the Duke criteria, it will be important to provide a "diagnostic floor" for the group of patients labeled as "possible" IE; specific parameters are needed for these patients, who do not fit into either the "clinically-definite" or the "rejected" groups. Assignment of a minimal set of qualifying parameters (e.g., at least one major criterion or at least two minor criteria) to the "possible" IE group should both reduce the size of this group and amplify the size of the "rejected" group. Such a modification of the Duke criteria would enable clinicians to focus on providing treatment to patients at highest risk of having IE and, potentially, to circumvent unneeded hospitalizations and excessive use of antibiotics. It will be interesting to revisit the evolving story of this new diagnostic schema for IE in 2 years hence.

Arnold S. Bayer
UCLA School of Medicine, Harbor-UCLA Medical Center, Torrance, California

References

1. von Reyn CF, Arbeit RD. Case definitions for infective endocarditis. Am J Med **1994**;96:220–2.
2. Bush LM, Johnson CC. Clinical syndrome and diagnosis. In: Kaye D, ed. Infective endocarditis. New York: Raven Press, **1992**:99–116.
3. von Reyn CF, Levy BS, Arbeit RD, Friedland G, Crumpacker CS. Infective endocarditis: an analysis based on strict case definitions. Ann Intern Med **1981**;94:505–18.
4. Durack DT, Lukes AS, Bright DK. New criteria for diagnosis of infective endocarditis: utilization of specific echocardiographic findings. Duke Endocarditis Service. Am J Med **1994**;96:200–9.
5. Bayer AS, Ward JI, Ginzton LE, Shapiro SM. Evaluation of new clinical criteria for the diagnosis of infective endocarditis. Am J Med **1994**;96:211–9.
6. Hoen B, Selton-Suty C, Danchin N, et al. Evaluation of the Duke criteria versus the Beth Israel criteria for the diagnosis of infective endocarditis. Clin Infect Dis **1995**;21:905–9.
7. Arguello EA, Varini S, Romorini A, et al. Infective endocarditis in the Argentine Republic [abstract 152]. In: Third International Symposium on Modern Concepts in Endocarditis (Boston). **1995**.
8. Kanavos K, Antoniadou A, Venetis C, et al. Retrospective analysis of Duke's criteria in 60 cases of infective endocarditis [abstract 138]. Third International Symposium on Modern Concepts in Endocarditis (Boston). **1995**.
9. Del Pont JM, De Cicco LT, Vartalitis C, et al. Infective endocarditis in children: clinical analyses and evaluation of two diagnostic criteria. Pediatr Infect Dis J **1995**;14:1079–86.
10. Bayer AS. Revised diagnostic criteria for infective endocarditis. Cardiology Clinics of North America **1996**;14:345–50.
11. Hoen B, Beguinot I, Rabaud C, et al. The Duke criteria for diagnosing infective endocarditis are specific: analysis of 100 patients with acute fever or fever of unknown origin. Clin Infect Dis **1996**;23:298–302.
12. Dodds GA III, Sexton DJ, Durack DT, et al. Negative predictive value of the Duke criteria for diagnosis of infective endocarditis. Am J Cardiol **1996**;77:403–7.