A
cute rheumatic fever (RF) continues to be a major health
problem at the dawn of the new millennium in many
parts of the world.1,2,3 Rheumatic heart disease (RHD), the
sequel of RF, is a very common cause of cardiovascular
mortality and morbidity,1,4 accounts for 35% to 40% of
cardiovascular disease-related hospital admissions, and is the
predominant indication for cardiac surgery in developing
countries.1,4 Although traditionally considered to be a disease
associated with poverty and overcrowding, RF continues to
persist, even among the prosperous middle-class population
in developed countries.7–9

Although RF is a systemic disease with multiorgan in-
volvement, none of its manifestations, except for carditis,
lead to permanent damage. Clinical cardiac involvement has
been reported in nearly one-third to almost all patients with
RF in various series and in up to 50% of patients in
progressive studies.10 Detection of active rheumatic carditis is
of great prognostic and therapeutic importance and is cur-
cently based on the Jones criteria. Not infrequently, the
diagnosis of carditis by the Jones criteria becomes difficult,
especially when carditis is the isolated manifestation of the
disease or when the rheumatic activity occurs on preexisting
RHD.11–13 It is important to develop a diagnostic strategy that
will improve our ability to diagnose rheumatic carditis and
allow us to apply existing criteria more efficiently.13,14 The
advent of modern, highly sensitive cardiac imaging modal-
ities, predominantly echocardiography/Doppler ultrasound
(echo-Doppler), has raised the question whether the Jones
criteria should be modified to incorporate these techniques.

Clinical Diagnosis of RF and Carditis
The Jones criteria were introduced in 1944 as a set of clinical
guidelines for the diagnosis of RF.15 The manifestations of
RF in the Jones criteria were divided into major and minor
categories (Figure). Suggested major manifestations were
least likely to lead to an improper diagnosis and included
carditis, joint symptoms, subcutaneous nodules, and chorea.
Historical evidence of RF or RHD also constituted a major
manifestation. Minor manifestations were considered sugges-
tive of RF but were not sufficient for the diagnosis and
included clinical signs such as fever and erythema mar-
ginatum, and laboratory markers of inflammation. Presence
of 2 major or 1 major and 2 minor manifestations provided
reasonable evidence of rheumatic activity. However, because
a previous history of definite RF or RHD was considered a
major criterion, presence of minor manifestations was suffi-
cient to establish the diagnosis of RF recurrence.

To improve specificity, these guidelines have been period-
ically modified.16–19 In the first modification,16 objectively
identifiable arthritis replaced joint symptoms as a major
manifestation and arthralgia was assigned to the minor
category. The history of previous RF or RHD was down-
graded to the minor category and therefore documentation of
a major manifestation became necessary for the diagnosis of
recurrence of RF. On the other hand, erythema marginatum
was recommended as a major criterion. Most importantly, the
evidence of preceding group A ß-hemolytic streptococcal
pharyngitis was added to the list of minor manifestations in
the modified Jones criteria.16 The evidence of a prior strep-
tococcal infection was considered essential for the diagnosis
of RF in the 1965 revision of the Jones Criteria, and it was
suggested that exclusion of clinical syndromes of nonstrept-
tococcal origin will further increase the accuracy of the
criteria.17 The increase in specificity adversely affected the
sensitivity,20 and 25% of the RF cases diagnosed by modified
criteria16 could not be diagnosed by revised Jones criteria.17
Such cases usually presented in the relatively late phase of the
disease or with delayed manifestations of RF, when antistrep-
tococcal antibody titers suggestive of preceding streptococcal
infection had already normalized. Therefore, the late mani-
festations of RF were subsequently exempted from the
requirement of elevated antistreptococcal antibody titers.18

In the setting of RF, diagnosis of a primary episode of
carditis is based on presence of a significant apical systolic
and/or basal diastolic murmur(s), clinical presence of pericar-
ditis, or unexplained congestive heart failure. Pericarditis and
congestive heart failure almost never occur in the absence
of valvular involvement.10 In a recurrence of RF, rheumatic
cardiac involvement almost invariably occurs if the initial
episode of RF involved the heart. The term mimetic carditis
was introduced to explain this phenomenon.21,22 For the
diagnosis of carditis in a recurrence of RF, the revised Jones

Not everything that counts can be counted, and not
everything that can be counted counts.
Albert Einstein
Evolution of Jones Criteria. The manifestations of RF are categorized into major and minor groups. Two major or 1 major and 2 minor manifestations provide reasonable evidence of rheumatic activity. Major manifestations of RF include carditis, arthritis, subcutaneous nodules, erythema marginatum, and chorea. Previous history of RF or rheumatic heart disease (RHD) was considered a major manifestation in the original criteria, and the diagnosis of recurrence required just 2 minor manifestations. The historical evidence of RF and RHD was subsequently downgraded and has recently been completely withdrawn. Joint symptoms were considered major criterion in the original version but were divided into arthralgias (subjective) and arthritis (objective); arthritis continued as a major manifestation and arthralgia was placed into minor category. The erythema marginatum was initially considered minor evidence because of low incidence but was subsequently upgraded owing to high specificity. Most importantly, preceding evidence of streptococcal infection was added to original list initially as minor manifestation, but it was subsequently recommended as a prerequisite for the diagnosis of RF. Some minor, less relevant features have been dropped.

criteria recommended demonstration of evidence either of pericarditis or an obvious change in previous clinical cardiac findings. Changes in the cardiac findings included appearance of a new murmur and change in the previous murmurs or an obvious increase in cardiac size in the clinical context of RF. The diagnosis of rheumatic carditis by Jones criteria becomes difficult when carditis is the isolated manifestation of RF. This is true especially when carditis is subclinical, when it is apparent but supportive noncarditic criteria for diagnosis of RF are not fulfilled, or when the previous cardiac findings are not known for documentation of interval change in cardiac findings during the recurrence of disease. These difficulties led to a major change in the 1992 update of Jones criteria wherein the previous history of RF or RHD was excluded from the list of minor manifestations, limiting the applicability of the Jones criteria only to primary episodes of RF. This change represented a return to the intent of the original proposal of Jones, which did not require strict application of the criteria for the diagnosis of a recurrence of RF.

The diagnosis of carditis therefore remains a problem, and the solution is obviously not the formulation of yet another set of clinical criteria. The development of laboratory aids of incremental diagnostic use is desirable. Because valvulitis constitutes the sine qua non of rheumatic carditis, echocardiographic documentation of valvular regurgitant lesions should, theoretically, be of significant help.

Does Echocardiography Perform Better than Clinical Examination in the Detection of Carditis?

Clinically manifest mitral regurgitation (MR) and aortic regurgitation (AR) are diagnostic of acute rheumatic carditis. The rheumatic carditis is rarely diagnosed in the absence of valve regurgitation and precordial auscultation has been the usual modality for the diagnosis of MR and AR. However, studies done even in the golden era of cardiac auscultation have shown that valvular regurgitation may not always be detected by routine clinical auscultation. Recent studies have shown that clinical auscultation may be a dying art, especially in countries where RF is declining. Not more than one third of the Internal Medicine Residency programs in the United States teach cardiac auscultation in a structured way. The residents detect significant mitral regurgitation in less than half of the cases. Skill levels do not significantly improve with increasing periods of clinical training; even cardiology fellows have not demonstrated superior diagnostic ability for the identification of cardiac murmurs. Fifty percent of the chiefs of cardiology responded to a survey conducted in the United States in 1993; 79% agreed that after 3 years of training, many cardiology fellows are still deficient in bedside clinical skills. The auscultatory skills have declined compared with those reported in the 1960s. All this suggests that the clinical diagnosis of rheumatic carditis may not be made with sufficient confidence. Echo-Doppler examination identifies valvular regurgitation not detectable with clinical examination, allowing visualization of valve structure, and allows detection of unrelated causes of valve dysfunction, such as mitral valve prolapse. It is important to note that the incremental utility of echo-Doppler would be inversely proportional to the clinical skills. In the Irvington House reports, a number of patients with no clinical evidence of cardiac involvement in the first attack of RF developed cardiac involvement on follow-up. A concerted effort by experienced clinicians in subsequent enrollments led to better recognition of carditis in the index attack and thus better predicted the development of residual heart disease.

In the Utah outbreak of RF, whereas carditis was confirmed by auscultation in 53 of the 74 patients (72%) with RF, Doppler evidence of MR was demonstrated in an additional 14 patients (19%) who were clinically considered to have isolated arthritis or pure chorea. In another report from the same group, asymptomatic cardiac involvement was detected in 47% of RF patients presenting with polyarthritis. Folger et al, from a middle-eastern country, also demon-
strated significant valvular involvement with color flow Doppler examination in the patients with RF, polyarthritis, and no clinical evidence of carditis.29,32 On the other hand, a large prospective study of RF from India did not find evidence of Doppler regurgitation in the patients without clinical evidence of carditis.34 The discrepancy in the diagnostic utility of echo-Doppler among these studies can be best explained by the presumption that patients in developing countries seek medical attention in relatively late phase of disease, when clinical valvular involvement is well manifested. This contention is supported by a recent study from New Zealand in which Doppler evidence of valvular involvement was observed in 100% of patients with RF compared with 79% on clinical auscultation.30 However, all patients with only echo-Doppler evidence of valvular regurgitation demonstrated audible murmurs in the next 2 weeks. Echo-Doppler, therefore, may allow earlier diagnosis but ultimately may not prove to be superior. In addition, the ability of echo-Doppler to detect subclinical recurrence of carditis in the presence of preexisting rheumatic heart disease remains obscure, unless there is an obvious interval change in echo-Doppler findings. This presupposes that a previous echocardiogram is available for comparison, probably an unreasonable expectation in the developing countries which bear the brunt of disease.

Can Echocardiography Reliably Differentiate Echocardiographic Valve Regurgitation (Physiological) from Minor Degrees of Pathologic Valvular Regurgitation?

Echo-Doppler evidence of trivial-to-mild valvular regurgitation is commonly observed in the normal population.35 The prevalence of MR in normal people may range from 38% to 45% and that of tricuspid regurgitation from 15% to 77%.36 Importantly, echo-Doppler aortic regurgitation has also been reported in normal people.37 The prevalence of regurgitation in normal people may be exaggerated on color-Doppler examination. The likelihood of transient valvular regurgitation may further increase in populations suspected to have RF, such as in clinical setting of patients with polyarthralgia, who may be febrile and thus have hyperdynamic circulation. A number of studies have described the characteristics of and differences between benign valvular regurgitation and organic rheumatic valvular dysfunction.38,39 A holosystolic jet of MR is tacitly accepted as pathologic if it is visible in 2 echo planes and extends beyond the plane of valve leaflets.30,31 In the absence of a gold standard for the diagnosis of carditis, the sensitivity and specificity of these echo-Doppler findings cannot be prospectively evaluated. In the New Zealand study, although all controls who were febrile had normal echo-Doppler studies, valvular regurgitation was also seen in 2 of the 3 patients (leading to the diagnosis of carditis) who were eventually not confirmed even to have RF.30 Furthermore, Doppler evidence of pulmonary and tricuspid regurgitation, reported in some studies, cannot be used to diagnose carditis because these findings are not uncommon on echo-Doppler in normal subjects29,32,36 and isolated involvement of these valves is unlikely in RF. Thus, although echo-Doppler is a powerful tool for diagnosing pathologic valvular regurgitation in RF, a fair amount of overlap with regurgitation in normal people (physiological) cannot be avoided.

Use of serial echocardiographic studies has been proposed to facilitate identification of organic valvular involvement.29 Although documentation of persistent abnormalities, involvement of multiple valves, and disease progression may improve the specificity of abnormal echocardiographic findings, they may cause a delay in the diagnostic process. More recently, nodular structures on inflamed valves have been observed on transthoracic echocardiographic examination,34 which appear to be the ultrasonic counterparts of pathologic valvular vegetations seen at autopsy and have been suggested as an evidence of carditis in RF. The utility of diagnosis of valvular nodules needs to be validated prospectively. Transesophageal echocardiography, particularly multiplane echocardiography, can be expected to demonstrate these nodules more clearly, but there is no data to support this assumption at the present time.

Can the Detection of Echo-Detectable Carditis Translate into Clinical Benefit?

An important contribution of echo-Doppler could reside in the identification of the group of patients who do not show clinical cardiac involvement during an attack of RF. In a large echocardiographic prospective study, patients without echocardiographic evidence of valvular regurgitation did not develop valve dysfunction on 6-month follow-up.34 The follow-up time was short and raises the question of whether one can reassure such patients of a benign prognosis that may allow early discontinuation of secondary prophylaxis.

Although exclusion of the diagnosis of carditis can be significantly facilitated by employing echo-Doppler as a primary diagnostic modality, use of echo-Doppler for uncovering the diagnosis of subclinical carditis needs evaluation of the following issues:

1. Would the detection of subclinical carditis alter the management strategy?

Echocardiography is unlikely to modify acute management of RF regardless of whether mild carditis is present or absent. The use of corticosteroids is not indicated in patients with mild carditis and the management is limited to symptomatic treatment.

2. If management is not altered, should the finding of echocardiographic subclinical carditis help in better assessment of prognosis?

All the data of benign prognosis in patients without carditis have essentially come from clinical studies.23,24,40–47 If the incremental utility of echo-Doppler is indeed limited to the detection of subclinical carditis,34 then a large proportion of patients with echo-detectable carditis must have been included in the low risk noncarditis group in previous clinical studies. The good prognosis in the so-called noncarditis group suggests that the included group of echo-detectable carditis probably did not suffer adversely by the misclassification. It is likely that the majority of patients with the milder forms of rheumatic carditis would resolve with adequate prophylaxis,23,24,40–42,46–48 and it is not certain if the additional detection of nonclinical echocardiographic carditis will be of prognostic significance. However, Folger et al found that 4 of
the 6 patients with Doppler-only evidence of valve involvement continued to show valvular regurgitation 18 to 36 months later.29 One of these had a normal valve on follow-up and then redeveloped an abnormality suggesting a recurrence of RF possibly related to inadequate penicillin prophylaxis.

3. If echocardiography is not likely to significantly alter either acute management or prognostication, then should it influence the long-term prophylaxis strategy? Some of the patients without clinical carditis in an index attack do develop carditis and cardiac damage in the subsequent recurrences.23 It is possible that these patients had suffered from subclinical carditis in the index attack which was too mild to be detected clinically. Echo-Doppler is likely to identify this subset, which would support a somewhat longer duration of secondary prophylaxis. There is no clear evidence for this scenario, however, and the American Heart Association (AHA) expert group does not presently favor the diagnosis of carditis based on Doppler echocardiography in absence of clinical criteria to support the diagnosis.12,49

4. Finally, if echocardiography is used as a primary diagnostic modality, will the epidemiological face of RF be completely altered? Unlike a 50% prevalence of carditis by clinical auscultation in patients with RF, echo-Doppler demonstrates carditis in a much larger population. How useful is a test that identifies a test characteristic in a very large proportion of the whole population? Should we just accept that carditis is a universal phenomenon in RF and dispense with routine echocardiography? Since the echo-detectable subgroup has not yet been characterized prognostically and does not radically affect the therapeutic measures, one might, with equal facility, assume that a patient has carditis unless proven otherwise instead of undertaking an echocardiogram (with its added cost) and (probably) ending up with the same long-term clinical outcome as in those identified with echocardiography. There is little evidence at present that we need to incur the cost and effort to identify subclinical disease of unclear significance notwithstanding the intellectual purity of diagnosis allowed by the use of echo-Doppler. Thus, if echo-Doppler is to be used to diagnose carditis, then fairly strict criteria must be developed (and used) that reasonably excludes valve regurgitation which can be seen in normal people.

Should Echo-Carditis Be Accepted as a Major Manifestation in the Jones Criteria in the Absence of Clinical Evidence of Carditis?

Although echo-Doppler has paramount importance in the diagnosis and management of most valvular disorders, its incorporation in the Jones criteria for the diagnosis of RF will need some caveats and can be best considered on the basis of epidemiological burden of disease and socio-economic status of various countries.

Developed Countries

Since echocardiographic is currently the best modality to identify valvular involvement, it will have a role in countries with widespread access to health care and with low burden of RF (eg, the United States). Less than 115 cases of RF were seen in the United States in 1994 and RF no longer remains a reportable disease.50 The incidence may be higher among immigrants from developing countries who are living in lower socio-economic conditions in the United States. In this situation, the patients are almost always seen during first attacks of RF and the additional cost and workload imposed by routine echocardiograms is small and should be outweighed by its advantages. There is a significant prognostic implication of finding a normal heart or finding unrelated causes of cardiac murmurs in this population. In addition, with suboptimal auscultation skills,25,26 an echo-Doppler study will quickly resolve the question of whether absence of a clinically detectable murmur is truly so. This will protect patients with clinical carditis from being misclassified as patients with a more benign prognostic class and protect them from inadequate secondary prophylaxis regimens. Even if echocardiography overestimates subclinical carditis, given the good medical follow-up in these countries, serial echocardiographic studies should resolve the significance of such valve dysfunction and optimize secondary prophylaxis program. Although there is a trend toward abbreviated periods of prophylaxis in developed countries, the minimum recommended period is sufficiently long to protect patients while the significance of subclinical carditis is being resolved. Therefore, detecting subclinical carditis and even mislabeling a minority of patients with RF as having carditis for a short period of time until their clinical situation is resolved would not seem to inconvenience or overtreat the RF patients.

Developing Countries

On the other hand, the clinical scenario is strikingly different in developing countries.2,3,6,51 The incidence of RF and prevalence of RHD is very high, whereas access to medical care and echocardiography are limited, and the disease is more aggressive which merits prolonged prophylaxis. First attacks are rarely witnessed; many patients present with recurrences and are likely to have established heart disease. Nonrheumatic causes of valvular murmur are proportionally less common, given a wide prevalence of RHD. Physical examination is the most commonly used modality of diagnosis; clinicians encounter a large burden of valvular heart disease and are likely to keep up their auscultation skills (although this has not been tested). In the prospective echocardiographic study reported from India, clinical examination accurately triaged patients with and without cardiac involvement and echocardiography did not provide incremental diagnostic utility in a large medical center.34 This diagnostic facility is not widely available in developing nations and centers equipped with such facilities are far away from majority of the rural population. Furthermore, the cost and additional workload imposed on tertiary care centers with the universal use of echocardiography in RF episodes will need to be resolved. Detecting echo-detectable rheumatic carditis is costly and probably will not change the management strategy significantly because prophylaxis is initiated in both groups, that is, in those with or without carditis. An echocardiogram could be better utilized at the time of discontinuation of prophylaxis. The AHA and World Health Organization recommend a finite period of prophylaxis,2,52 which is longer in patients with clinical RHD. A number of recent studies
have shown that RF can recur in adults not on prophylaxis,53 recurrences are higher in patients with RHD and each recurrence further damages the heart. Thus, echocardiography might have a role in the detection of RHD before discontinuation of secondary prophylaxis (because the presence of RHD at this time will constitute an indication for life-long prophylaxis).5,25 Echocardiography during acute attack therefore cannot be recommended as a routine modality for investigating RF in developing countries at present. It is needless to emphasize that the role of echocardiography in the diagnosis and management of established RHD remains unquestioned in any population. The AHA 1995 recommendations for duration of secondary prophylaxis indeed includes clinical or echocardiographic evidence of valvular disease.54

Conclusions

Echocardiography/Doppler ultrasound may have a place as a major criterion in the Jones Criteria in the United States, and possibly in the other developed countries, provided strict criteria are established and are used for the diagnosis of pathological valve involvement. Jones criteria are universally used and any major alterations in their application should strongly consider that most of the patients with RF live in developing countries, possibly under the sponsorship of the World Health Organization. Echo-Doppler can always be used and any major alterations in their application should be strongly considered. It is likely to be intellectually satisfying but practically not possible. Prospective, well-controlled studies are needed in developing countries, possibly under the sponsorship of the World Health Organization. Echo-Doppler can always be given a progressively greater role if these prospective studies demonstrate distinctly superior prognostic value of echo-detectable carditis. Dr Jones’ major contribution was to create a set of criteria that was easy to use, diagnostically accurate, and applicable worldwide. There is a major need for more objective evidence of the value of echocardiography/Doppler ultrasound in this clinical situation.

References


**KEY WORDS:** rheumatic heart disease ■ endocarditis ■ mitral regurgitation ■ arthritis ■ streptococcal infections