Rheumatic and Nonrheumatic Valvular Heart Disease
Epidemiology, Management, and Prevention in Africa
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Background—Unlike the Western world, valvular disease ranks among the major cardiovascular afflictions in Africa. Acute rheumatic fever and chronic rheumatic valvular disease in their most virulent form are still commonly encountered and impose a huge burden on limited healthcare resources.

Methods and Results—We performed a systematic review of the literature with PubMed using rheumatic fever, rheumatic heart disease, valvular disease, warfarin anticoagulation, and pregnancy as search items. Literature emanating from Africa was emphasized. Epidemiology, current concepts on pathogenesis, and aspects of the medical and surgical management of this disease as seen from an African perspective are presented. The association of pregnancy with mitral stenosis is common and may be fatal if not managed appropriately. A practical approach to these patients is presented to optimize maternal and fetal outcome. Pregnant patients with mechanical valves require careful attention to ensure maternal survival and prevent fetal warfarin embryopathy. Prolonged subcutaneous heparin and frequent monitoring of the partial thromboplastin time are impractical in this setting, and the merits of different anticoagulation regimens are discussed. Congenital submitral aneurysms are a unique cause of mitral regurgitation, with the vast majority of cases originating from sub-Saharan Africa. Although the precise etiology is as yet unclear, the clinical and echocardiographic features are sufficiently characteristic to allow a preoperative diagnosis to be made. Transesophageal echocardiography allows much better definition of the size and anatomic relationships of the aneurysm. Surgical resection can be difficult but is usually curative. Mitral valve prolapse and endocarditis constitute the remaining frequent causes of valvular disease and are discussed briefly.

Conclusions—The spectrum and presentation of valvular disease in Africa are uniquely different from elsewhere. Together with socioeconomic issues and the HIV pandemic, this fact makes it imperative that further epidemiological and clinical studies be undertaken and guidelines developed that are appropriate to the practice of medicine on the African continent. (Circulation. 2005;112:3584-3591.)

Key Words: echocardiography ■ rheumatic heart disease ■ valves ■ valvuloplasty

It was Pliny the Elder (AD 23 to 79) who wrote that out of Africa (comes) always something new: “Ex Africa semper aliquid novi.”1 The scope and magnitude of cardiovascular disease in Africa are vastly different from those of Europe or North America. Nowhere is this more evident than with valvular disease. In contrast to the developed nations, where valvular disease is largely degenerative in origin, in Africa it is almost always the result of infectious disease, either directly, as in infective endocarditis, or indirectly, as in acute rheumatic fever.2 Whereas valvular disease in developed nations afflicts the elderly, is insidious in onset, and is frequently associated with other comorbidities, in Africa valvular disease is encountered in the young, not infrequently in children of school-going age or young females of child-bearing potential, and with a course that is much more rapid. These peculiarities have far-reaching implications for the assessment and management of valvular heart disease in Africa. Unfortunately, most of the research and all of the guidelines on the management of valvular disease originate from Europe and North America, and their relevance to Africa is questionable. Much of Africa is a population in transition, rural to urban, traditional to modern, and a clearer understanding of the epidemiology and changing patterns of cardiovascular disease is desperately needed to allow better planning of healthcare delivery.

The physician practicing in Africa is commonly faced with certain issues in the management of valvular disease that his counterpart elsewhere rarely encounters. These are highlighted and briefly discussed in the following section.

Epidemiology of Streptococcal Pharyngitis, Acute Rheumatic Fever, and Chronic Rheumatic Heart Disease
Although neither streptococci nor their products can be found in the heart of patients with acute rheumatic fever or chronic
rheumatic heart disease and no animal model exists, there is sufficient circumstantial evidence to implicate antecedent pharyngitis due to group A streptococci in the pathogenesis of this disease. It is intriguing to note, however, that although there has been no apparent or documented decline in group A streptococci pharyngitis, the incidence of acute rheumatic fever in industrialized countries has dropped precipitously to below 1/100,000, whereas in Sudan it exceeds 100/100,000. Although these differences may in part reflect less overcrowding and more effective antibiotic treatment of group A streptococci pharyngitis in Western countries, differences both in the frequency of infection with rheumatogenic M-protein serotypes and in their virulence may be important.

The prevalence of chronic rheumatic heart disease has been estimated mainly from surveys of school-going children and varies from 2.7/1000 in Nairobi to 14.3/1000 in Kinshasa. In a survey of 12,050 black school children in Soweto, South Africa, in 1975, McLaren et al found a prevalence of 6.9/1000 with a maximum of 20/1000 in seventh- and eighth-grade children. With an improvement in the standards of living in the Soweto population, we have observed a distinct decline in the incidence of acute rheumatic fever presenting to Baragwanath Hospital (M.R. Essop and V.T. Nkomo, unpublished data, 2004). Unfortunately, increasing urbanization with the creation of large ghettos and, in war-torn countries, migration of large segments of the population into refugee camps result in overcrowding, close person-to-person contact, and poor healthcare facilities, all of which have been shown to be the most consistent predisposing epidemiological factors for rheumatic fever.

Acute Rheumatic Fever With Carditis
Although interest in acute rheumatic fever in North America has been renewed with the recent description of several outbreaks in geographically distinct areas, in Africa acute rheumatic fever is still seen regularly in its most fulminant form, affecting children as young as 6 years, manifesting with severe refractory heart failure, and often requiring valve replacement in childhood. The pathophysiology of acute rheumatic fever, as it pertains to the heart, essentially relates to the mechanism and consequences of valvular regurgitation and the issue of left ventricular contractile function.

Valvular Dysfunction in Acute Rheumatic Fever
Although valvular regurgitation is frequently the hallmark of rheumatic fever with carditis and is the forerunner of the long-term complications of this disease, until recently little has been known about the mechanism of valvular dysfunction. Furthermore, an appreciation of the pathology and pathophysiology of valvular regurgitation is germane to any surgical endeavor to restore competence of the mitral and aortic valves. Neither postmortem analysis nor observations made intraoperatively in a flaccid nonbeating heart are able to appreciate the dimensions and spatial relationships of the valvular and subvalvular components of the mitral valve. Echocardiography is an easily applied, noninvasive technique with excellent resolution and has made a unique contribution to the understanding of the pathogenesis of valvular regurgitation in rheumatic carditis. In a detailed echocardiographic analysis of 73 young patients (mean age, 13 years) with acute carditis and severe mitral regurgitation, Marcus et al demonstrated varying degrees of prolapse of the anterior mitral leaflet in 94% (Figure 1). Echocardiographically detected prolapse, defined as failure of leaflet edge coaptation during systole, was confirmed in every patient at the time of surgery. An increase in the mitral annular diameter, mainly of the posterior annulus, was the primary cause for leaflet prolapse. The mean mitral annular diameter in their patients was 37 mm compared with a diameter of 23 mm in a control group matched for age and sex. Further support for this hypothesis was provided by the fact that despite the young age of this group of patients, relatively large-diameter annuloplasty rings or mechanical prostheses could be inserted in the mitral position. Elongated chordae to the anterior mitral leaflet, but without rupture, was another feature of severe mitral regurgitation in rheumatic fever (Figure 1). It is probable that both primary involvement by the rheumatic process and secondary exposure to increased tensile stresses during ventricular systole contribute to elongation of the chordae. Apart from some shortening of the posterior mitral leaflet caused by stretching of the annulus, leaflet morphology appeared remarkably normal. Thus, severe mitral regurgitation in rheumatic fever was the result of annular dilatation and chordal elongation with resultant prolapse and was not, at least in the early stages, caused by abnormalities of the leaflets themselves. Color Doppler is useful in quantifying the severity of mitral regurgitation and almost invariably shows a posteriorly directed jet confirming anterior leaflet prolapse. The abnormalities of the mitral valve that have been described are characteristic of patients with rheumatic fever and severe mitral regurgitation. In an unselected group of patients presenting with rheumatic fever and carditis, Vasan et al were able to document mitral valve prolapse in only 9% of patients classified as experiencing a first attack of carditis and in 16% with recurrent carditis. The severity of mitral regurgitation in these patients is unfortunately not documented. In their series, leaflet thickening and nodules possibly representing verrucous vegetations were the most frequent echocardiographic abnormality. Other series have noted a higher
incidence of mitral valve prolapse. Wu et al\textsuperscript{10} noted mitral valve prolapse in 30\% of their patients with rheumatic fever and mitral regurgitation. Mitral valve prolapse also correlated with a larger cardiac size and a less favorable long-term outcome. In a series of patients receiving rheumatic fever prophylaxis with less than moderate mitral regurgitation, Lembo et al\textsuperscript{11} found an 80\% incidence of echocardiographically detected mitral valve prolapse.

Differentiation of rheumatic mitral valve prolapse from degenerative or myxomatous mitral valve disease is important (Figure 2). Rheumatic prolapse always involves the anterior leaflet, whereas myxomatous prolapse has a predilection for the posterior leaflet. Myxomatous leaflets are thickened, voluminous, and redundant with significant systolic bulging or billow toward the left atrium. In contrast, the leaflets in rheumatic carditis with mitral regurgitation show minimal thickening, redundancy, or billow.

Despite careful auscultation, valvular regurgitation may sometimes be inaudible. In these cases echocardiography may play a useful role in enhancing the detection of carditis. Thus, Doppler echocardiography was the sole means for the diagnosis of carditis in 25\% of the patients in one series\textsuperscript{5} and increased the diagnosis of carditis based on the Jones criteria from 72\% to 91\% in another.\textsuperscript{12} Furthermore, functional murmurs in young, febrile, and anemic patients are quite common. By differentiating these from the murmur of mitral regurgitation, Doppler echocardiography could potentially reduce the rate of false-positive diagnoses. The American Heart Association Guidelines for the Diagnosis of Rheumatic Fever published in 1992\textsuperscript{13} do not encourage the use of echocardiography as the sole criterion for the diagnosis of carditis. Although there is some justification for this, including the possibility of overdiagnosis and the lack of prospective studies evaluating the role of echocardiography, there is an emerging body of evidence emphasizing the utility of Doppler echocardiography for the diagnosis of rheumatic carditis,\textsuperscript{14} and we would concur with Veasy\textsuperscript{14} and the World Health Organization recommendations\textsuperscript{3} that echocardiography has the potential of being a useful diagnostic tool in the assessment and management of these patients.

**Left Ventricular Function in Acute Rheumatic Fever**

Although histological evidence of myocarditis is present in 32\% to 95\% of autopsy cases,\textsuperscript{15} it is not clear that these features are related to abnormalities of left ventricular contractile function. It is both our experience\textsuperscript{16} and that of others\textsuperscript{17} that left ventricular dilation and heart failure rarely occur in the absence of hemodynamically significant mitral regurgitation with or without accompanying aortic regurgitation. In patients with active rheumatic carditis presenting with overt heart failure, functionally severe mitral regurgitation and its anatomic correlate of annular dilation, chordal elongation, and prolapse of the anterior mitral leaflet have been observed sufficiently frequently by us\textsuperscript{5} to be regarded as a pathoanatomic hallmark of the disease. To clarify the relative contribution of volume overload induced by valvular regurgitation and myocardial dysfunction caused by rheumatic myocarditis to the overall degree of left ventricular dilation, we analyzed left ventricular dimensions and function noninvasively in a group of young patients with documented active rheumatic carditis before and after successful isolated mitral or combined mitral and aortic valve replacement.\textsuperscript{16} Prompt reduction in left ventricular dimensions and preservation of fractional shortening after isolated mitral or combined mitral and aortic valve replacement provided good evidence that rheumatic carditis was not accompanied by myocardial contractile dysfunction to any significant degree. Distinction between left ventricular dilatation and congestive heart failure arising as a consequence of contractile dysfunction resulting from rheumatic myocarditis or volume overloading associated with valvular regurgitation has important clinical implications because the definitive treatment of severe regurgitant lesions is prompt surgery.

**Repair Versus Replacement for Rheumatic Mitral Regurgitation**

There has been a dramatic paradigm shift in the management of mitral regurgitation with a recommendation for earlier surgery in minimally symptomatic patients with relatively well-preserved left ventricular dimensions and function, providing that the valve can be repaired. This strategy may be appropriate in patients with degenerative mitral regurgitation, which is ideally suited to a repair technique and which is the most common type of disease encountered in developed countries. The benefits of mitral valve repair, however, may not be as obvious in patients with a rheumatic etiology. In the setting of active rheumatic carditis, in which the leaflets may look relatively normal on macroscopic examination intraoperatively, progressive fibrosis and leaflet deformity from frequently present microscopic inflammatory cell infiltration may preclude a durable long-term result. Even in chronic rheumatic mitral regurgitation in the absence of active cardi-
tis, the results of valve repair have been disappointing compared with results in patients with a nonrheumatic etiology. In a long-term evaluation of 254 young patients with rheumatic mitral regurgitation undergoing mitral valve repair from our institution, reoperation was required in 27%, and overall freedom from valve failure was only 66% after a mean follow-up of 5 years. Furthermore, multivariate analysis showed active rheumatic carditis at the time of surgery to be the only predictor of valve failure and need for reoperation. The results for mitral valve repair for rheumatic mitral regurgitation from Carpentier et al looked somewhat better, and we can only speculate that more aggressive disease, as evidenced by a younger mean age and higher incidence of active carditis in our patients, accounts for the difference. Notwithstanding these differences, mitral valve repair offers significant advantages over valve replacement in terms of need for anticoagulation and risk of prosthetic valve thrombosis. In choosing between repair and replacement for rheumatic mitral regurgitation, additional variables that need to be factored into the decision-making process include the presence of chronic atrial fibrillation, concomitant aortic valve disease, and preoperative left ventricular dysfunction. Thus, mitral valve repair would be futile in patients with atrial fibrillation or in those who need concomitant aortic valve replacement, in whom long-term warfarin anticoagulation would be required in any case.

The impact of mitral regurgitation and corrective mitral valve surgery on preoperative and postoperative left ventricular function, respectively, has been investigated in great detail. Mitral valve replacement has been consistently associated with a reduction in left ventricular ejection fraction, and this decline has been abrogated with mitral valve repair or replacement but with preservation of the chordal apparatus. These data have served to underscore the importance of the subvalvular apparatus for preserving cardiac function and have formed the basis for earlier surgery in patients in whom a repair can be guaranteed. In developing countries, many patients are seen for the first time when adverse echocardiographic characteristics such as an ejection fraction <60% or an end-systolic diameter >45 mm are already present. The results of mitral valve replacement under these circumstances have been clearly documented to be poor, and an often-asked question is whether mitral valve repair, although more difficult with rheumatic disease compared with degenerative disease, would not be preferable in these patients. In an analysis of 274 patients undergoing mitral valve repair, Matsumura et al found the echocardiographic predictors of a poor postoperative outcome to be numerically similar to if not identical to those previously defined for mitral valve replacement. This is disappointing because given the well-known benefits of valve repair in terms of preservation of chordal-ventricular continuity, one would have anticipated that postoperative left ventricular function could be guaranteed at lower preoperative ejection fractions or higher end-systolic diameters.

In summary, the choice between mitral valve repair and replacement for rheumatic mitral regurgitation in an African setting can be difficult. It is our belief that mitral valve repair may be considered if the surgeon is confident that he or she is able to perform a successful repair, active carditis as judged by serology or intraoperative observation is absent, sinus rhythm is present, there is no need for concomitant aortic valve replacement, the patient is a female of child-bearing age, and monitoring of warfarin anticoagulation is difficult; it may also be possibly considered in the patient with advanced preoperative left ventricular dysfunction in whom mitral valve replacement is contraindicated. In all other patients, mitral valve replacement is appropriate, but the timing of surgery is of crucial importance.

Timing of Surgery for Mitral Valve Replacement
Because mitral valve repair avoids many of the disadvantages of replacement with a mechanical prosthesis, the threshold for surgery has been progressively lowered. For mitral valve replacement, however, the guiding principle is not to operate too early, incurring unnecessarily the potential complications of a mechanical valve, nor to operate too late, when the potential for recovery of left ventricular function is lost. The question of how early is too early and how late is too late was investigated by Wisenbaugh et al in a cohort of 66 patients with mainly rheumatic mitral regurgitation undergoing valve replacement with chordal preservation. In a stepwise Cox proportional hazards analysis, the only independent predictor of postoperative death was preoperative end-systolic diameter. The probability of death or severe heart failure increased abruptly at a preoperative end-systolic diameter of 51 mm. A good outcome was predicted at a preoperative end-systolic diameter of 40 mm. On the basis of these data, together with observations of others, the optimal time for surgery would be when the end-systolic diameter is between 40 and 50 mm. When the end-systolic diameter is <40 mm, a policy of watchful waiting is safe, and when it is >50 mm, valve replacement is contraindicated and valve repair may be more appropriate.

Pregnancy and Valvular Disease
The high rate of teenage pregnancies combined with an endemic prevalence of rheumatic disease in developing countries results in cardiac disease being the most important comorbid state during pregnancy. Of crucial importance in the management of the pregnant cardiac patient is to be able to identify those at greatest risk and institute appropriate surveillance and therapy in these patients. Of all of the rheumatic valvular lesions, mitral stenosis is not only the most frequent but also the one most likely to lead to a potentially serious outcome. In Africa, it is not uncommon for previously occult mitral stenosis to be discovered for the first time during pregnancy. This is easily understood when one considers the interaction between the physiological cardiovascular adjustments to pregnancy and the hemodynamics of mitral stenosis. The availability of new therapies has engendered some controversy even in the optimal management of the nonpregnant patient with mitral stenosis. This controversy is compounded in the pregnant patient because the risks to the fetus of drug therapy, radiation exposure during percutaneous mitral balloon valvuloplasty, or anesthesia with or without cardiopulmonary bypass during surgical commissurotomy need to be considered.
In the management of these patients, we have found it useful to identify 3 groups of patients: (1) the patient with known mitral stenosis who desires to be pregnant; (2) the patient who is already pregnant with well-compensated mitral stenosis; and (3) the patient who is in a critical hemodynamic state and usually in an advanced stage of pregnancy or recently postpartum.

Patients with mitral stenosis contemplating pregnancy usually have a mobile noncalcific valve and should be offered either percutaneous balloon valvuloplasty or closed mitral valvotomy depending on local experience. This approach preempts the expected hemodynamic deterioration and obviates the need for pharmacological therapy during pregnancy. Careful judgment is required in the occasional patient with calcific mitral stenosis in whom the only therapeutic option is mitral valve replacement. If symptoms are minimal and adverse prognostic factors such as atrial fibrillation and pulmonary hypertension are absent, a policy of intensive medical therapy may be safer than mitral valve replacement. However, should mitral valve replacement before pregnancy be necessary, we are in agreement with Oakley that selection of bioprosthesis valves to avoid the need for anticoagulation is not a suitable alternative to metallic valves because of their accelerated degeneration during pregnancy and the consequent need for repeated mitral valve surgery.

Optimal management of the already pregnant patient with compensated mitral stenosis requires careful assessment of the risk-benefit ratio to mother and fetus of standard pharmacological therapy (diuretics and \( \beta \)-blockers) versus percutaneous balloon valvuloplasty. \( \beta \)-Blockers are safe and well tolerated by both mother and fetus and by reducing heart rate significantly ameliorate the hemodynamics of mitral stenosis. \( \beta \)-Blockers not only may have a beneficial hemodynamic effect but, by inhibiting episodes of paroxysmal atrial fibrillation, may also prevent the formation of left atrial thrombi. The vast majority of patients in our experience can be carried successfully through pregnancy and the puerperium by judicious use of these drugs combined with a diuretic in those with accompanying shortness of breath.

Since the first case reports in 1988 of mitral balloon valvuloplasty during pregnancy by Safian et al. and Palacios et al., numerous publications have confirmed the technical feasibility and hemodynamic improvement after this procedure. Although percutaneous balloon valvuloplasty may be seen as an attractive alternative to medical therapy, 2 shortcomings make it difficult to recommend unconditionally. The first, severe mitral regurgitation, is not specific to pregnancy, has an incidence of \( \approx 8\% \), and is largely unpredictable. Of more specific relevance to pregnancy is the risk of fetal distress and irradiation during balloon valvuloplasty. Fetal bradycardia has been observed in several studies, but this is usually transient, with no apparent adverse effect. Using film badge dosimeters, Lung et al. were able to show that abdominal radiation was \(< 0.2 \text{ mSv} \). Although this is well below the 5-mSv radiation limit recommended for pregnant women, the real risk of even such low radiation levels to the fetus in the long term is as yet unknown. On the basis of these data, we agree with Ribeiro and Al Zaibag that mitral balloon valvuloplasty should only be attempted in patients in whom symptoms are not adequately controlled on optimal medical therapy or in cases in which close follow-up during pregnancy, labor, and delivery is not possible. Mitral balloon valvuloplasty is best done beyond 20 weeks of gestation, when irradiation risk to the fetus is less by experienced physicians, with adequate abdominal and pelvic shielding, and in an abbreviated form omitting left ventricular cineangiography and detailed pressure and shunt evaluations to complete the procedure in as short a time as possible. In cases in which balloon valvuloplasty cannot be performed, closed mitral valvotomy is a suitable alternative.

Pregnant patients with mitral stenosis who are in a critical hemodynamic state with pulmonary edema, hypotension, and right heart failure pose a considerable therapeutic challenge and constitute a situation in which maternal survival takes precedence. A rapid trial of intravenous diuretics and inotropic therapy, amiodarone for atrial fibrillation, and direct current cardioversion if necessary should be instituted. Failure of significant clinical improvement is an indication for urgent intubation and ventilation and mechanical relief of mitral stenosis. The choice of balloon valvuloplasty, open or closed surgical commissurotomy, or mitral valve replacement should be dictated by echocardiographic valve characteristics and local expertise and should be performed as expeditiously as possible. A fetal mortality of \( < 10\% \) may be expected during procedures requiring cardiopulmonary bypass.

**Anticoagulation for Mechanical Prostheses**

Thromboembolism and bleeding may lead to catastrophic complications in patients with mechanical valves, requiring careful monitoring of warfarin anticoagulation. In developing countries, warfarin anticoagulation presents many logistic difficulties, including poor compliance, lack of facilities in close proximity to monitor the international normalized ratio (INR), and the large number of females of child-bearing age who become pregnant. In a tertiary care setting, as ours was, using low-level warfarin anticoagulation, defined as a target INR of 2 to 2.5 in combination with dipyridamole, Kontozis et al. documented excellent results with the St Jude bileaflet prosthesis in 200 young rheumatic patients with a mean age of 31 years and 867 patient-years of follow-up. The linearized rates of thromboembolism and major bleeding were 1.5\% per patient-year and 1.3\% per patient-year, respectively, with no incidence of prosthetic valve obstruction. Butchart et al. found a similar experience using low-level anticoagulation in patients with Medtronic Hall prostheses. On the basis of this experience, it is our current practice to recommend low-level warfarin anticoagulation combined with aspirin or dipyridamole to all patients with modern-generation mechanical valves except those with a history of previous thromboembolism or those with additional risk factors such as atrial fibrillation or left ventricular dysfunction.

An alternative approach that avoids the need for monitoring INR is the use of fixed-dose warfarin. After a dose-finding phase, Buchanan-Lee et al. randomized 296 patients from an impoverished rural South African population to fixed-dose warfarin with no measurement of INR or adjusted dose warfarin according to INR. After a mean follow-up of 2.4 years, no differences in mortality were observed, but the...
fixed-dose group had a significantly higher incidence of thromboembolic events (13 versus 4), leading the authors to conclude that fixed-dose warfarin is only an alternative in cases in which anticoagulation control is impractical. Areas of ongoing investigation include the utility of the cytochrome P450 CYP2C9 gene polymorphism to predict warfarin resistance and the use of new direct antithrombin agents that obviate the need for monitoring anticoagulation.

Pregnancy is a hypercoagulable state, and adequate anticoagulation for those with mechanical valves is essential. Apart from concerns that heparin may not offer sufficient protection against prosthetic valve thrombosis and the risk of maternal bleeding is increased, prolonged therapy and the attendant need to monitor the activated partial thromboplastin time are impractical in Africa. Even conversion to heparin in the first trimester, when the risk of warfarin embryopathy is highest, is difficult because most patients have not had preconceptual counseling and arrive on warfarin already late in the first trimester. In our experience and that of others, the best outcome for both mother and fetus is guaranteed by administration of warfarin throughout pregnancy until the 38th week, at which time the patient is admitted for conversion to intravenous heparin and elective cesarean section. The rate of fetal wastage may be high, but warfarin embryopathy is uncommon, possibly because of the lower doses of warfarin that may be used with modern mechanical valves that are less thrombogenic.

**Nonrheumatic Valvular Disease in Africa**

**Mitral Valve Prolapse**

Also known as Barlow’s syndrome, myxomatous mitral valve disease, or the click-murmur syndrome, this entity was first described in South Africa by Barlow and Bosman in 1966. In its most typical form, 1 or more scallops of the posterior mitral leaflet are thickened and redundant and prolapse in systole into the left atrium (Figure 3). The controversy about the prevalence and significance of mitral valve prolapse may be explained by several factors, including the method of diagnosis (clinical versus echocardiographic), nonuniform echocardiographic criteria, and referral or sample bias. Barlow’s original observations were based on auscultation and ECG abnormalities. Although echocardiography has contributed tremendously in furthering anatomic, functional, and diagnostic concepts in this disease, we view with concern the large numbers of patients labeled as having mitral valve prolapse solely on the presence of trivial mitral regurgitation on color Doppler. We strongly agree with Nishimura and McGoon that in the absence of the typical clinical findings, stringent echocardiographic criteria should be adhered to when this diagnosis is made. The classification into classic (associated with leaflet thickening) and nonclassic (no leaflet thickening) is also useful because serious morbidity in terms of worsening mitral regurgitation, endocarditis, and stroke is confined largely to the former.

**Congenital Submitral Aneurysm**

Left ventricular submitral aneurysms occur infrequently and have been reported predominantly from sub-Saharan Africa. Left ventricular submitral aneurysms are recognized to be the third most common cause of severe mitral regurgitation after rheumatic heart disease and myxomatous degeneration. The etiology is uncertain but is thought to be caused by a congenital weakness in the mitral anulus. The aneurysms typically arise from the posterior mitral anulus, are often multiloculated and serpiginous, and bulge in an extracardiac direction or into the left atrium (Figure 3). Severe mitral regurgitation occurs because of undermining of the leaflets and papillary muscle or sometimes rupture of the aneurysm into the left atrium. Atrial arrhythmias are common, and myocardial ischemia may sometimes occur because of compression of the left circumflex coronary artery. Surgery is indicated in all cases with ligation of the neck via a left atrial approach and a mitral annuloplasty.

**Infective Endocarditis**

In Africa, the high prevalence of largely rheumatic valvular disease, combined with inadequate antibiotic prophylaxis, results in an unusually high incidence of infective endocarditis. The large number of patients with infective endocarditis, together with the life-threatening nature of the disease and the need for protracted pharmacological therapy and surgery in a large proportion of patients, places a huge economic burden on already limited healthcare resources. Clearly, any endeavor to reduce the medical and financial impact of this disease should be directed at (1) the prevention of rheumatic valvular disease with primary and secondary antibiotic prophylaxis; (2) prevention of endocarditis with adequate antibiotic prophylaxis in at-risk patients with known valvular disease; and (3) expeditious diagnosis and treatment of patients with endocarditis. Physicians often confuse rheumatic fever prophylaxis with infective endocarditis prophylaxis, and it is important to emphasize that a patient receiving daily oral penicillin or monthly intramuscular penicillin for prevention of acute rheumatic fever still requires additional antibiotic coverage when exposed to procedures requiring endocarditis prophylaxis.
Prevention of Rheumatic Valvular Disease

In a continent faced with famine, overcrowding, war, retroviral and other communicable diseases of epidemic proportions, lack of basic amenities such as provision of clean water and electricity, poor health services, lack of education, and political ineptitude, the prospects for a comprehensive program to eliminate rheumatic heart disease are grim. A recommendation in South Africa 30 years ago that a comprehensive prevention campaign was urgently needed has remained largely unheeded.

The reasons for the declining incidence of rheumatic fever in the Western world are not entirely clear but in part probably relate to less overcrowding and better sanitation and general living conditions, all of which result in a reduction in infectious diseases in general and streptococcal infections in particular. Although living standards for blacks in postapartheid South Africa have improved somewhat, we concur with McLaren et al that it is unlikely that most developing countries could substantially decrease their incidence of rheumatic fever through improvements in living standards.

It is unlikely that a vaccine against rheumatogenic streptococcal strains will be available in the near future, and currently, prevention of the first attack of rheumatic fever by early treatment of streptococcal pharyngitis (primary prevention) or prevention of recurrent attacks of rheumatic fever (secondary prevention) is the only way to prevent rheumatic heart disease. Secondary prevention is a more cost-effective and attainable goal than primary prevention. A recent systematic review of the most effective antibiotic regimen for secondary prophylaxis confirms the World Health Organization recommendation of 3 weekly intramuscular injections of benzathine penicillin.

Africa faces many difficulties, and the challenge of preventing and treating the scourge of rheumatic heart disease is enormous. If we are to rise to this challenge, we need to establish the scope and magnitude of the problem with large, properly conducted epidemiological trials, and health authorities must be urgently convinced of the need to institute efficient and readily accessible programs for the primary and secondary prevention of rheumatic heart disease.

Disclosures

The authors report no conflicts of interest.

References

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