

## Rheumatic Heart Disease in Developing Countries: The Consequence of Inadequate Prevention

In economically developed countries, rheumatic fever and rheumatic heart disease have become uncommon health problems. In contrast, in Third World areas such as India, the Middle East, sub-Saharan Africa, and Latin America, rheumatic fever remains the leading cause of heart disease in children and young adults (1-3). The epidemiology of rheumatic fever and rheumatic heart disease in South Africa is particularly interesting because both of these disparate trends exist simultaneously in the same country. Among the white minority, who have experienced a more privileged socioeconomic and health care status under the apartheid system, rheumatic fever has decreased, as it has in economically developed countries (4). Among the socio-politically deprived black majority, the trends are comparable with those of Third World communities. Twenty-one years ago, a screening study (5) for rheumatic heart disease among 12 050 school children in Soweto (the large black ghetto area near Johannesburg) showed the highest reported prevalence of this disease at the time: 6.9 per 1000 children overall, with a maximum of 20 per 1000 among 7th and 8th grade children. The investigators (5) concluded that "a comprehensive prevention campaign is urgently needed, directed at both primary and secondary prevention of rheumatic heart disease."

In this issue of *Annals*, Marcus and colleagues (6) report on the frequency of pure mitral regurgitation among patients with rheumatic mitral valve lesions (hemodynamically severe) in "a developing country." That developing country is South Africa, and, coincidentally, two of the authors of the current study (6), as well as one of us (MJM), participated in the earlier Soweto study (5). The investigation by Marcus and colleagues (6) involved an enormous study population: 748 consecutive black patients with rheumatic heart disease who had mitral valve surgery at a major tertiary care hospital during a 3-year period (1983 to 1986). The patients were also young (median age, 25 years). A hospital-based consecutive sample cannot provide accurate prevalence data, but this study nevertheless shows the magnitude of rheumatic fever and rheumatic heart disease in the referral communities.

The large number of young patients with severe pure mitral regurgitation who required surgery attests to the virulent nature of rheumatic fever in many black South African children and adolescents. The authors do not provide information about the patients' rheumatic fever history. However, at the time of surgery, 60% of the patients in the first decade of life and 41% in the second decade had evidence of acute rheumatic fever activity

based on clinical, surgical, or histologic criteria (6). Such severe rheumatic heart disease can occur during the first episode of acute rheumatic fever. For example, one report (7) noted that during the recent outbreaks of rheumatic fever in the United States, 12 of 67 patients (18%) with carditis had congestive heart failure and that 2 required mitral valve surgery. However, this virulent pattern is more likely caused by the onset of rheumatic fever at a young age with frequent recurrences not prevented by penicillin prophylaxis, a pattern similar to the experience in the United States before antimicrobial drugs became available (8).

As Marcus and colleagues (6) point out, the juxtaposition of modern and sophisticated tertiary care facilities with the conditions that foster rampant rheumatic fever and rheumatic heart disease among black South Africans has made this landmark descriptive study possible. However, the situation also calls into question the distribution of health care resources in many developing countries. During the last two decades, many technological advances have occurred in the diagnosis and management of cardiac disease that have enhanced the immediate survival of patients with rheumatic heart disease. However, during the same period in many of these countries, little has been accomplished with respect to prevention of rheumatic fever. What happens in developing countries to patients with rheumatic heart disease after they have had mitral valve surgery? Will the health care systems and social conditions support the high level of care required by these patients to prevent repeated episodes of streptococcal pharyngitis, prevent recurrences of acute rheumatic fever, and prevent worsening of their rheumatic heart disease?

In developing countries, the large number of surgical procedures on young persons with rheumatic heart disease (6, 9, 10) has been described as "attempting to mop up the water on the floor while leaving the faucet open." Are the prevention strategies for this disease too complex, cumbersome, or costly for South Africa and other high-risk Third World countries? The decline in rheumatic fever and rheumatic heart disease in most of the Western World occurred before their origin and pathogenesis were fully understood. Many questions remain unanswered. Decreases in the frequency and, perhaps, virulence of streptococcal infections may occur after the general socioeconomic status and living conditions improve. Although this is an important goal, it is unlikely that many developing countries can substantially decrease their incidence of rheumatic fever at any time in the near future through such improvements.

The definitive form of primary prevention of rheu-

matic fever would be a streptococcal vaccine that uses the surface M protein. The development of a safe and effective streptococcal vaccine has been hindered by two major obstacles. First, although a limited number of the more than 80 distinct serotypes are rheumatogenic, an effective vaccine would still have to be a highly complex mixture of M proteins from multiple serotypes. Second, M protein contains epitopes that cross-react with human tissue. Antibodies directed against these epitopes could actually produce rheumatic fever. Using new molecular techniques, investigators appear to be on the verge of overcoming this obstacle; however, it will still be many years before an inexpensive, safe, and effective group A streptococcal vaccine is available (11).

Currently, the only way to prevent first attacks of rheumatic fever is to appropriately treat the previous episode of streptococcal pharyngitis. Because it is impossible to identify persons at risk for developing rheumatic fever after an episode of streptococcal pharyngitis, prevention of first attacks of rheumatic fever requires a primary health care system readily accessible to everyone, the widespread availability of antibiotics, and culturally relevant health education of the population and their health care workers. The ability to substantially decrease the incidence of rheumatic fever in economically underprivileged populations through a concerted effort to treat streptococcal throat infections was shown in two landmark studies (12, 13). In the first study (12), diagnosis of streptococcal pharyngitis with throat cultures and treatment with oral or intramuscular penicillin, as part of a comprehensive primary health care program in inner-city Baltimore, led to a statistically significant decrease in the incidence of rheumatic fever. In the second study (13), which was done in Costa Rica, throat cultures were eliminated as a prerequisite for treating pharyngitis because of the cost and the difficulty in follow-up. To avoid poor compliance with oral antibiotic regimens, a single injection of benzathine penicillin G was selected as the standard mode of therapy for all children with symptoms and signs suggesting streptococcal pharyngitis. These measures were part of a comprehensive primary health care program begun in the 1970s. During the next decade, this program resulted in the virtual elimination of rheumatic fever from Costa Rica. Because this simplified primary prevention program is not only highly effective but also inexpensive and safe, it offers a good model for developing countries such as South Africa that have a high prevalence of rheumatic heart disease and limited resources.

A more cost-effective and attainable goal is the prevention of recurrent attacks of rheumatic fever (secondary prevention), and this should be the first priority of prevention. Although oral antibiotic regimens can be effective, it has been known for almost 50 years (14) that monthly injections of benzathine penicillin G are the most effective method for preventing recurrences. The change in the morbidity and mortality rates for patients with rheumatic heart disease in economically developed countries has been due largely to the decrease of rheumatic fever recurrences (15). The World Health Organization has instituted trial rheumatic fever

prevention in 16 Third World countries, including 3 in Africa: Mali, Zambia, and Zimbabwe. These programs involve early detection of rheumatic fever and rheumatic heart disease, secondary prophylaxis, and health education of the population and health care providers. Preliminary results from this cooperative study (16) have shown a decrease in rheumatic fever recurrences among patients maintained on secondary prophylaxis of monthly injections of benzathine penicillin G. The fear of serious allergic reactions has been a barrier to the use of this agent in many Third World countries, but a recent international study (17) showed that anaphylaxis is rare in patients with rheumatic fever receiving long-term benzathine penicillin G.

Developing countries face many challenges, and the problems of rheumatic fever and rheumatic heart disease will have to compete for limited resources with other more immediate and urgent health concerns such as malnutrition, diarrheal disease, tuberculosis, and infection with human immunodeficiency virus. However, strategies for preventing rheumatic fever should be incorporated into the plans for an accessible primary health care system for all the citizens of these countries. Among the developing countries, South Africa, as it stands on the threshold of its new political future, has a unique opportunity to adopt these strategies. We hope that in the next 20 years, a substantial decrease will occur in the prevalence of rheumatic heart disease.

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