How can we prevent rheumatic heart disease? Still a challenging question

Abstract

**Background.** This review of literature considers the factors that bear most importantly on the pathogenesis of Acute Rheumatic Fever and on the strategies for its diagnosis, prevention and management.

**Methods and results.** A systemic review of the literature was performed. It focuses mainly on diagnosis. Rheumatic fever resulting from group A B-haemolytic Streptococcus infection continues to be prevalent and an important cause of morbidity and mortality in developing countries. Arthritis followed by carditis and chorea, are the main problematic major isolated manifestations of the disease. Evidence of asymptomatic carditis has been increasing; however, abnormality identified by echodoppler evaluation is not considered as a criterion for diagnosis of ARF. No single laboratory test can confirm the diagnosis of RF; however, some tests help to characterize the inflammatory process and provide evidence of a preceding streptococcal infection.

**Conclusion.** Rheumatic fever is still a community problem. There are a lot of gray cases. Diagnosis is difficult even with Jones Criteria. There is over lapse of issues. Carditis and Arthritis is a sign of other systemic illness like Sickle Cell Anemia, Rheumatoid Arthritis, Henochschialin Purpura and Reactive Tonsillitis, although the history is different. In acute stage, if no thorough history was taken from the patient, sign of Carditis and Arthritis is minimal and will mislead patient to seek late medical advice. So, what does evidence base tell us when we have gray cases? The diagnosis is not clear and it does not fulfill the Jones Criteria. There is need for follow up as the patients are seen in General Clinic and in ER. They should be alert to early referral to pediatrician and Multidisciplinary approach where Cardiologist should help to identify the problem is essential.

Introduction

Rheumatic Fever remains one of the primary causes of acquired heart disease worldwide. A resurgence of ARF since 1984 prompted the medical community to review the early signs and symptoms of an illness that was considered to be uncommon.[1]

By the 1980’s, the incidence rate of acute rheumatic fever had fallen to approximately 1 to 2/100 000 in the United States with sporadic local epidemic rates as high as 18 to 45/100 000.[2] In their decision analysis, Lieu et al[3] assumed a rate of acute rheumatic fever after untreated pharyngitis of 0.288%, a high rate that may have been justified by the sporadic local epidemics of acute rheumatic fever seen in the mid-80’s. Since that time, however, sporadic epidemics of acute rheumatic fever have not been widely reported in this country. In this analysis, it is estimated that the
The probability of a child developing acute rheumatic fever after an untreated GABHS (Group A B-Hemolytic Streptococcus) pharyngitis is 0.03%, one tenth of that used Lieu et al. [3]

In the past 50 years, ARF has emerged as a major contributor to cardiovascular morbidity in India. Despite the paucity of clear information regarding secular trends, the few available community surveys indicate that there are at present more than 1 million patients with RHD. Even a conservative estimate of the incidence of RF suggests that at least 50,000 new episodes occur every year. The younger age of onset (juvenile RHD) seen in India is a special feature of both public health and clinical importance. These patterns of RF and RHD, which may be similar to those in other developing countries, underscore the importance of effective public health strategies for prevention and control.

It is a major problem in the high risk areas of the tropics, countries with limited resources and in communities with minority indigenous populations. As many as 25-45% of cases worldwide appear in those nations. Although individuals of any age group may be affected, most cases are reported in persons aged 5-15 years. No sex predilection exists. The prevalence of RHD in Saudi Arabia as reported by al-Sekait MA, et al (1999), was 24 per 10,000 schoolchildren (6-15 years). The prevalence was higher in rural areas and in females.

Etiology and Pathogenesis

In the first half of the twentieth century, the group A streptococcus (GAS) was established as the sole etiologic agent of acute rheumatic fever (ARF). In the century’s latter half, the clinical importance of variation in the virulence of strains of GAS has become clearer.

Despite remarkable increases in our knowledge of the biology of the Group A streptococcus and of the human host and despite important observations about the epidemiologic association between group A streptococci and the human host, the pathogenic mechanism responsible for the development of acute rheumatic fever remains unknown. There have been two basic theories attempting to explain the development of this sequel to group A streptococcal pharyngitis: a toxic effect produced by an extracellular toxin of group A streptococci on target organs such as myocardium, valves, synovium, and brain; and an abnormal immune response by the human host. The most popular hypotheses are those that postulate and abnormal immune response by the human host to some still, undefined component of the group A streptococcus. The resulting antibodies might then cause the immunologic damage leading to clinical manifestations. (James Todd)

The concept of specific rheumatogenic strains of group A streptococci (GAS) has been difficult to establish, because the actual pathogenesis of acute rheumatic fever
(ARF) remains hypothetical. It required the first 6 decades of 20th century to establish firmly that pharyngeal infection with GAS alone causes all of the manifestations of acute and recurrent attacks of rheumatic fever (RF). Not all strains of GAS do so, however; more than 50 years ago, Rebecca Lancefield and others demonstrated marked variation in the virulence of GAS strains by their content of M protein and by their degree of hyaluronate encapsulation. The relevance of strain virulence to the pathogenesis of ARF is not yet appreciated by most clinicians. In the past several decades, it has become clear that the great majority of throat infections due to GAS do not cause ARF at all, but rather that the strains that do so are unusually virulent. They cause ARF with an attack rate that varies with the intensity of the host’s immune response Stetson CA. The relation of antibody response to rheumatic fever. In McCarty M, ed. Streptococcal infections. New York: Columbia University Press, 1954:208–18., which in turn is related to the virulence of the infecting strain [3]. Widdowson JP, Maxted WR, Grant DL, et al. The antibody responses in man to infection with different serotypes of group A streptococci. J Med Microbiol 1974; 7:483–95.

New understanding of the pathogenesis of ARF would have an immediate effect on primary prevention strategies and vaccine development.[9]

How can we prevent rheumatic heart disease?

As cited by the AHA (American Heart Association) the best defense against rheumatic heart disease is to prevent rheumatic fever from ever occurring. By treating strep throat with penicillin or other antibiotics, doctors can usually stop acute rheumatic fever from developing.[1]

If their heart has been damaged by rheumatic fever, they're also given a different antibiotic when they undergo dental or surgical procedures. This helps prevent bacterial endocarditis, a dangerous infection of the heart's lining or valves.

Prophylaxis

It is essential to employ continuous antibiotic prophylaxis to prevent recurrences of rheumatic fever due to subsequent streptococcal infection.

Treatment of GAS pharyngitis is in a state of some turmoil. On the one hand, the emergence of throat flora resistant to antibiotics (gratefully, not GAS, but particularly Streptococcus pneumoniae and Staphylococcus aureus) is a consequence of overuse of antibiotics for treatment of nonbacterial respiratory infections [49] Schwartz B. Preventing the spread of antimicrobial resistance among bacterial respiratory pathogens in industrialized countries: the case for judicious antimicrobial use. Clin Infect Dis 1999; 28:211–3. On the other hand, fear of the return of RF has made many expert committees reluctant to compromise on the 10-day oral penicillin regimens that are required to prevent RF after rheumatogenic GAS pharyngitis [50Bisno AL, Gerber MA, Gwaltney JM Jr, et al. Diagnosis and management of group A streptococcal
pharyngitis: a practice guideline. Infectious Diseases Society of America. Clin Infect Dis 1997; 25:574–83. ]]. Most unfortunate is the insistence by some authors that antibiotic regimens produce total eradication of GAS pharyngeal carriage, an outcome virtually impossible to achieve. Preventive antibiotic treatment of rheumatogenic GAS pharyngitis never achieved better than 90%–95% eradication of organisms from the throat. From extensive clinical observations, clones persisting after adequate therapy have limited pathogenetic potential. In order to achieve more-efficient eradication, some authors recommend that broad-acting cephalosporins or other antibiotics (e.g., clindamycin, azithromycin) replace penicillin. Some regimens are recommended for only 5 days. These recommendations carry greater risk for emergence of resistance of vulnerable pathogenic throat flora, are more expensive, and are unnecessary. Five days of oral penicillin V, 500,000 U b.i.d., usually cures GAS pharyngitis clinically, but it will not prevent RF when the infection is due to a rheumatogenic strain. When there is no longer a threat of RF in the community, some authorities recommend that, for mild sore throats, neither diagnostic tests nor antibiotic therapy are necessary. Where RF is no longer prevalent, negative RADT result that reliably excludes GAS may justify not prescribing antibiotics. This strategy may be the most practical and cost-effective approach to primary prevention in some regions of this country and, similarly, in those countries where ARF is no longer observed. In my own view, however, when a clinical diagnosis of GAS pharyngitis is suspected, a diagnostic test should be made, initially with an RADT and, if the results are negative, with a follow-up throat culture. If results of either are positive, a full 10 days of oral penicillin V therapy or an injection of bezathine penicillin G (when compliance is dubious or RF is still a problem in the community or region) represents the most reliable guideline for the primary prevention of RF and the intrafamilial spread of virulent strains. This view is also consistent with most current guidelines [50–52American Academy of Pediatrics. Group A streptococcal infections. In: Pickering LK, ed. Red book: report of the Committee on Infectious Diseases. 25th ed. Elk Grove Village, IL: American Academy of Pediatrics, 2000:526–36 ].

Streptococcal vaccines. We will probably not eradicate RF from the world without a GAS vaccine. James Dale and associates have prepared a recombinant multivalent vaccine composed of the end-to-end combination of the type-specific epitopes representing some of the most common M serotypes in which rheumatogenic strains are usually found [36] Dale JB. Multivalent group A streptococcal vaccine designed to optimize the immunogenicity of six tandem M protein fragments. Vaccine 1999; 17:193–200. . Trials of efficacy in humans are currently underway. Oral immunization with similar vaccines also seems promising, because an M type–specific IgA response to this route of immunization has been well demonstrated. In view of how much M antigen is swallowed in the course of a GAS sore throat, the oral route for production of protective IgA may be the most effective one. And in light of the number of M serotypes (190), we must focus on those known to contain strains of greatest pathogenetic potential.

Laboratory Investigations.

Many of the patients diagnosed as having ARF during these epidemics had no recognizable prodrome that would have brought them to medical attention. A history
of symptomatic pharyngitis often was absent. It is important to remember that the throat culture frequently is negative by the time rheumatic fever develops. These facts emphasize the need to consider ARF in the appropriate clinical setting and use the streptococcal enzyme tests to establish a diagnosis. Chronic rheumatic heart disease was common in young children who presented with carditis. Long-term follow-up is necessary to determine the outcome for young children with subclinical echocardiographic evidence of valvular disease [11]. *Pediatrics* 2003;112:1065–1068; *rheumatic fever*. Cardiac involvement often is established by finding of a new murmur of mitral or aortic insufficiency. Mitral regurgitation, heard best at the apex, is generally of moderate-to-high intensity throughout systole. Aortic insufficiency is a basal diastolic murmur that is usually high-pitched and blowing and decreases in intensity toward the end of diastole. A possible association of PANDAs with rheumatic heart disease, such as seen in long-term follow-up of patients with chorea, should also be carefully studied.

Documentation of Inflammation. Leukocytosis with neutrophilia and mild to moderate anaemia are found. Haemoglobin levels below 90g/l are usually associated with severe carditis. Lymphocytosis and severe anaemia suggest a differential diagnosis that includes leukemia and sickle cell anaemia.

Acute phase reactants are always elevated at the onset of acute RF. The erythrocyte sedimentation rate (ESR) is elevated in the first weeks of the disease, and higher levels are found among patients with cardiac involvement. C-reactive protein (CRP) is elevated at the onset of the acute phase and tends to disappear at the end of the second or third week. Both ESR and CRP are affected by anti-inflammatory medications. Acid alpha-l-glycoprotein and alpha-2-globulin are elevated in the acute phase of heart disease and remain elevated for a prolonged time. Their levels are not influenced by anti-inflammatory medications and they have been used to monitor RF activity.

Detection of streptococcal Infection. Group A streptococcus is isolated by culture of throat swab in only 15-20% of patients and these may be due to both the latency period between infection and the onset of RF symptoms and the prior use of antibiotic. Non-invasive carriage of group A streptococcus contributes to the low sensitivity of throat culture in diagnosing a preceding infection. Rapid antigen detection tests from throat swabs have the same limitations as cultures with specificity of 95% but lower sensitivity.

Elevated titers of anti-streptolysin O (ASO) confirm invasive streptococcal infection but approximately 20% of patients with RF may not have this antibody. In these cases, determination of anti-hyaluronidase, ant-deoxyribonuclease B (Anti-Dnase B) and/or anti-streptokinase antibodies may be essential for the diagnosis of recent infection. However, in most developing countries only the ASO test is available in public hospitals. Therefore, serial determinations of ASO at 15-day intervals are recommended. The Streptozyme test simultaneously detects several antibodies to the streptococcus; however, it has not been shown to have any advantage over the ASO titre.

Chest Radiograph and Electrocardiogram (ECG). The chest radiograph and ECG may be abnormal in only 30% of patients with carditis. The chest radiograph usually shows cardiomegally only in patients with myocarditis or moderate to severe pericardial
effusion. On ECG, repolarization abnormalities characterized by prolonged PR and QT intervals can be observed. These abnormalities are not unique to RF and could be present in Systemic Juvenile Idiopathic Arthritis or Systemic Lupus Erythematosus. A persisting, prolonged PR interval is usually a manifestation of cardiac fibrosis rather than an active process, whereas a persisting prolonged QT interval is a manifestation of severe disease and a less favourable outcome. Low-voltage QRS complexes and abnormalities of the ST interval may be seen with pericarditis.

**Echocardiography (EC) and Doppler methods.** Most cases of rheumatic carditis are not severe enough to be symptomatic, and the diagnosis of isolated carditis has previously depended on auscultation alone [14, 15, 16, 17]. Approximately 80% or more of the cases of mitral regurgitation detected by EC are also readily diagnosed by the auscultation of experienced clinicians. The remaining “subauscultatory” cases are those with the mildest degree of mitral or aortic regurgitation. If, indeed, they are rheumatic in origin, 180% of these valvular lesions are likely to heal without scarring (see “Treatment,” below); however, the sensitivity of EC may detect degrees of valvular regurgitation within physiologic range, and not functionally significant, especially in children and in very thin, active individuals with highly elastic valve leaflets and rings. Although EC, particularly accompanied by Doppler studies, offers greater sensitivity and specificity for the assessment of valvular regurgitation, it need not be considered essential for the diagnosis of RF by experienced primary care physicians, especially in settings where the disease is common and medical resources are limited [13, 14]. Nonetheless, cardiologists proficient in echo-Doppler technology now use this method routinely to distinguish abnormal from physiologic valve leaks more sensitively and accurately than by auscultation alone. Despite the relatively good prognosis of “silent” rheumatic mitral regurgitation, EC does, indeed, provide an accurate assessment of the presence and severity of valvulitis, especially in an era when cardiac auscultation has been taught less extensively and is used with less confidence by young clinicians. In any case, it is doubtful that a diagnostic tool that is as powerful as EC will be neglected in the assessment of valvular disease wherever the instrument is available and certainly where its expense may not be too great a concern. In my view, whether or not subauscultatory mitral regurgitation can be accepted as the sole criterion of carditis in the absence of other major manifestations of RF remains at issue and is certainly dependent on the experience of the examining cardiologist, not only with the technique of EC, but also with the diagnostic criteria of RF [14,16,17]. Whether the Jones criteria should be modified to incorporate these techniques is being debated with differences of opinion tempered by considerations of availability and cost benefit of EC to developing countries, since outcomes of the treatment and management of such minimal valvular inflammation may not differ significantly, whether they are detected or not [14].

**Problematic Isolated Major Manifestations**

**Carditis.** Rheumatic carditis is virtually always associated with the murmurs of valvulitis [8, 13]. Isolated myocarditis or pericarditis without valvulitis is rarely, if ever, due to RF. Thus, the finding of valvular involvement is critical and is aided by noninvasive imaging methods.
**Isolated polyarthritis.** Where ARF is uncommon, the diagnosis of isolated polyarthritis is problematic because of the large differential diagnosis [13]. Polyarthritis is, however, recognizable early in the rheumatic attack when streptococcal antibodies are at peak elevation. Therefore, the absence of significant increase in GAS antibodies at the onset of polyarthritis is a useful negative predictor of the diagnosis of ARF, and it suggests a reactive arthritis due to another infection, such as rubella, Lyme disease, the enteric organisms causing Reiter’s disease, ankylosing spondylitis, and so forth. When GAS antibodies are increased, however, the diagnosis of ARF remains presumptive, requiring months of close observation, because such elevations may have been only coincidental GAS infections that were not causally related [8, 13, 18]. Symptoms of chorea present late (unlike arthritis or carditis), usually months after the initial pharyngitis. The process is self-limiting and reversible.

**Poststreptococcal reactive arthritis (PSRA).** What is at issue is whether to recognize PSRA as a separate disease from the polyarthritis clearly associated with RF [19, 20]. The characteristics of PSRA that are not typical of ARF are persistence of arthritis for several months, nonmigratory polyarthritis, poor response to NSAIDs.

The 1992 update differs from prior versions in its strong focus on identifying acute episodes of rheumatic fever. Whereas previously two major or one major and two minor criteria were required to fulfill the diagnostic profile, evidence of a preceding streptococcal infection (such as an elevated antistreptolysin O (ASO) titer) in addition to two major or one major and two minor manifestations now are needed for diagnosis. In addition, increased antibodies to the bacterial product streptolysin O (ASO) were seen to be strongly associated with previous throat infection and less so with skin infection, whereas anti-DNAase B (ADB) titres responded to either throat or skin infection [21].

**Sydenham’s chorea.** Sydenham’s chorea, similarly, may occur as an isolated manifestation, and frequently recurs following new streptococcal pharyngitis. After puberty, it is almost entirely limited to women. Like polyarthritis, it is most often evanescent—over in a few weeks—but occasionally, it may be stubborn and persist for many months. The pathogenesis of chorea, which is similar to the synovitis of polyarthritis, seems to be associated with immune complex disease produced by nondestructive antoantibodies localized to the basal ganglia and striatal system of the brain [59 Swedo SE. Sydenham’s chorea: a model for childhood autoimmune neuropsychiatric disorders. JAMA 1994; 72:1788–91. , 6060. Moore DP. Neuropsychiatric aspects of Sydenham’s chorea: a comprehensive review. J Clin Psychiatry 1996; 57:407–14]. Severe chorea seems to respond occasionally to treatment with iv IgG [61Perlmutter SJ, Leitman SF, Garvey MA, et al. Therapeutic plasma exchange and intravenous immunoglobulin for obsessive-compulsive disorder and tic disorders in childhood. Lancet 1999; 354:1153–8.]. It seems to be closely related to the so-called PANDAs (postinfectious autoimmune neurological diseases). These include tics, Tourette’s syndrome, and obsessive-compulsive behavior, all of which have been observed in some patients during or after an attack of rheumatic chorea [60]. Of course, patients with PANDA that did not express choreiform movement and were not previously referred to RF centers were more often referred to pediatric neurologists. PANDAs are now known to be often associated with
Secondary Prevention

For prevention of rheumatic recurrences, continuous antibiotic prophylaxis is now recommended by health authorities throughout the world [4]. McLaren MJ, Markowitz M, Gerber MA. Rheumatic heart disease in developing countries: the consequence of inadequate prevention. Ann Intern Med 1994; 120:243–5. Monthly injections of 1.2 million units of benzathine penicillin G are the most stringent regimen. In some populations with a high prevalence of RF, however, some observers have reported that the last week of the month is not completely covered by this regimen, and they choose to administer it every 3 weeks [45, Meira ZM, Mota C de C, Tonelli E, Nunan EA, Mitre AM, Moreira NS. Evaluation of secondary prophylactic schemes, based on benzathine penicillin G, for rheumatic fever in children. J Pediatr 1993; 123:156–8. 46Lue HC, Wu MH, Wang JK, Wu FF, Wu YN. Three- versus four-week administration of benzathine penicillin G: effects on incidence of streptococcal infections and recurrences of rheumatic fever. Pediatrics 1996; 97: 984–8.]. One should be sure, in any case, that the commercial formulation of the drug contains the full dose of 1.2 million units of benzathine penicillin G, and that it is not like the commonly marketed, confusing formulations, which contain smaller amounts of benzathine penicillin G mixed with shorter-acting penicillin G compounds. Where ARF is no longer prevalent, oral penicillin V, 600,000 U b.i.d., now suffices. For that matter, sulfdiazine, 0.5 g b.i.d., is also effective and inexpensive and thus useful for secondary (but not primary) prevention. How long to continue these regimens is a matter of clinical judgment, with recognition of the major variables that affect the decision: (1) how frequently RF occurs among cohorts, (2) how recent and severe the rheumatic attack, and (3) the presence and severity of rheumatic heart disease. In a community in which RF has not appeared for many years, patients who have had polyarthritis alone and who reach adult life without rheumatic valvular disease are at lower risk Penicillin prophylaxis has been safely suspended after several years of treatment when rheumatogenic streptococci have been shown to have disappeared from the community [1Stollerman GH. Rheumatic fever. Lancet 1997; 349:935–42. 47] Dajani A, Taubert K, Ferrieri P, Peter G, Shulman S. Treatment of acute streptococcal pharyngitis and prevention of rheumatic fever: a statement for health professionals. Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease Council on Cardiovascular Disease in the Young, the American Heart Association. Pediatrics 1995; 96: 758–64. Following a new GAS infection, patients with isolated polyarthritis who were observed prospectively in long-term follow-up studies developed recurrences with an attack rate greater than that of the 3% noted for first RF attacks in the military population. In a classic 5-year
follow-up study that stratified recurrences by various risk factors, patients without rheumatic heart disease developed recurrences after GAS infections, with attack rates that varied from 4% in patients with a 2-tube increase in ASO titer to 36% in those with a 4-tube rise [48] Taranta A, Wood HF, Feinstein AR, Simpson R, Kleinberg E. Rheumatic fever in children and adolescents: a long-term epidemiological study of subsequent prophylaxis, streptococcal infections, and clinical sequelae. IV. Relation of the rheumatic fever recurrence rate per streptococcal infection to the titers of streptococcal antibodies. Ann Intern Med 1964; 60 (Suppl 5):47–57. With such a relatively high propensity to recur, particularly by the challenge of more severe GAS infections, these patients with isolated polyarthritis have been considered rheumatic subjects. The recurrent attack rate was, of course, still higher in patients with polyarthritis who have rheumatic heart disease. The risks of travel should be considered, particularly for patients with rheumatic heart disease—especially travel to so-called “undeveloped countries” in which close contact with indigenous populations may be anticipated.

Treatment

Antibiotic therapy can be initiated before laboratory results are available. Treatment should be discontinued if test results are negative. The IDSA notes that rheumatic fever can be prevented even if treatment is postponed for up to nine days after symptom onset. [22]

Because of proven safety and efficacy, narrow spectrum, and low cost, penicillin remains the treatment of choice for patients who are not allergic to the drug. Once-daily amoxicillin therapy could become an alternative regimen if the results of preliminary investigations confirm efficacy. In young children, amoxicillin is often used in place of oral penicillin V. [22] For recurrent acute pharyngitis, Benzathine penicillin G 1.2 million units intramuscularly remains the treatment of choice for prophylaxis and is administered every 3 or 4 weeks. [24] For patients who have carditis but no residual heart disease, prophylaxis is continued for 10 years or well into adulthood (whichever is longer). Those patients who have residual heart disease from carditis are treated at least until age 40 or may receive lifelong prophylaxis.

Patients with severe carditis are often treated with corticosteroids, but studies of the effects of corticosteroids in the treatment of rheumatic carditis have shown conflicting results [10,11]. A 2003 meta-analysis from the cochrane database concluded that there was no significant difference in outcome when corticosteroids and aspirin treatment were compared [23].

This prophylactic regimen does not substitute for the standard bacterial endocarditis prophylaxis required for patients who have rheumatic heart disease.

Cost-Effect

In Tompkins’ assumption, the per patient cost of acute rheumatic fever and RHD is estimated to be USD14 674.[30] In 1993, North et al [29] obtained an average patient
cost of New Zealand Dollars 19 226. If North’s estimate is converted into USD and adjusted at 3.5% annual inflation rate, the per patient cost in 1997 is estimated to be USD18 600. In this analysis, the cost of ARF and RHD is estimated as USD20 000.

Kenneth H. Webb[25], recommended a high-sensitivity antigen test strategy than the treat-all strategy. Use of the high-sensitivity antigen test was the least expensive of the strategies using a diagnostic test, in terms of total (encounter plus complication) costs. In terms of cost per streptococcal complications prevented, the high-sensitivity antigen test strategy was also the most cost-effective under most circumstances currently seen in the United States.

Summary and conclusion

In the near future the burden that heart failure will impose on the emerging economies is likely to increase dramatically. There is an urgent need for properly conducted population based studies in these countries to establish the true size of the problem and the relative importance of the different aetiologies. This will help inform appropriate health policy within these countries. Preventive and public health strategies will need to be specific to the local epidemiological characteristics. As countries go through epidemiological transition and undergo socio-economic development, the epidemiology is likely to become increasingly similar to that of Western Europe and North America.[27]

Finally, what can we look forward to in the future? There are some obvious limitations in our ability to completely eradicate rheumatic fever with antibiotics. There has been progress in purifying and characterizing streptococcal M protein, the antigen that elicits antibodies that confer immunity to the streptococcus.[28] However, the availability of a vaccine is not imminent.

Progress has also been made in identifying a genetic marker for rheumatic fever susceptibility. The genetic marker could be useful to identify susceptible individuals in families with a history of rheumatic fever.

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