

# RHEUMATIC HEART DISEASE AND THE ASAP PROGRAMME: FRESH INSIGHTS INTO AN OLD DISEASE

*Rheumatic heart disease continues to affect and kill millions of children, adolescents and young adults in the developing world.*

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*Her specific interests are imaging modalities, adult congenital heart disease, preventive cardiology and global health. These have led to her particular research interest: rheumatic heart disease and echocardiographic screening in asymptomatic schoolchildren. She feels passionately that rheumatic heart disease, a preventable chronic disease of childhood, can be controlled in developing countries using a multi-pronged approach. Her planned dissertation is entitled 'The case for screening for rheumatic heart disease'.*

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Acute rheumatic fever (ARF) is the immune-mediated sequel of an innocuous Group A streptococcal throat infection and occurs in 0.3 – 3.0% of children between the ages of 3 and 15 who have untreated sore throat.<sup>1</sup> Although ARF involves skin, subcutaneous tissue, brain and joints, only the devastating effects on the heart valves are permanent and associated with a number of serious sequelae. This is thought to affect about 60% of new cases of rheumatic fever per year. Current estimates suggest that 62 – 78 million individuals worldwide may have rheumatic heart disease (RHD), which could potentially result in 1.4 million deaths per year from the disease and its complications.<sup>2</sup> These individuals are predominantly children, adolescents and young adults who live in poor and under-resourced areas of the world.

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## Current epidemiology

The prevalence of RHD has steadily been decreasing over the past decade with only an aged population with existing disease being seen in the developed world and very few incident cases. This reflects the effect of improved public health measures such as sanitation, better housing and reduced overcrowding, and occurred before the widespread introduction of antibiotics. However, in the developing world, particularly in sub-Saharan Africa, Asia and the Australasian indigenous populations, a very different pattern exists, with RHD being endemic and matching that of the developed world decades ago.<sup>3</sup> This is demonstrated by high reported incidences of ARF in many regions of the world. Recent systematic reviews have found that the incidence of ARF is >10/100 000 in some regions of Eastern Europe, the Middle-East, Asia and the Pacific regions.<sup>4,5</sup> The highest recorded incidence of ARF is from the Western Pacific, averaging 100/100 000 people. This is partly due to improved recognition and extreme vigilance as well as better reporting in these small island nations.<sup>6</sup> However, recent landmark studies have highlighted the existence of a RHD 'iceberg', using echocardiography to identify subclinical disease and demonstrating a prevalence of asymptomatic disease almost 10 times higher than previously thought.<sup>7,8</sup> This has resulted in a reversal of the trends in RHD prevalence in the world with reported data now

seeming to suggest that RHD prevalence is increasing in all areas of the world except in Europe.<sup>5</sup> This is related in part to the method by which RHD is being diagnosed, i.e. using echocardiography as opposed to auscultation, as well as the effect of increased treatment, availability of surgery and longer survival.<sup>9</sup>

Screening for asymptomatic RHD has given rise to debate, including the validity of the findings,<sup>7</sup> the criteria chosen to define RHD,<sup>10,11</sup> as well as important public health issues. These relate to the ability of developing countries to manage the scores of patients who will be detected, the appropriate treatment for these patients and the cost-effectiveness of screening. Currently, screening is underway in virtually all regions of the world where the disease is prevalent and an urgent call for further and extensive research in this area to answer some of these questions has been made.<sup>12</sup>

## Clinical burden of disease

It is important to note the high burden of established RHD in developing countries. *De novo* cases of established RHD comprised almost 10% of the burden at a tertiary cardiac centre in Soweto, South Africa,<sup>13</sup> while complications relating to RHD, such as stroke, infective endocarditis and heart failure,<sup>14</sup> are still strongly evident in clinical practice. In a recent study from a university hospital in Dakar, Senegal, a review determined that 92% of women hospitalised for heart disease during pregnancy presented with RHD. Rheumatic mitral stenosis was by far the most frequent cause of heart disease during pregnancy, accounting for 64% of all cases. Of importance was the reported maternal mortality of 34%, while the mortality rate in the group with severe mitral stenosis was just under 50%.<sup>15</sup> The perinatal mortality rate was over 25%, with a neonatal mortality rate of 8%. Infective endocarditis is also a known complication of RHD, due to the damaged valves and the pro-thrombotic state of the patient. In Turkey, 36% of patients presenting with native and prosthetic valve endocarditis had RHD.<sup>16</sup> In recent reviews,<sup>17,18</sup> RHD was found to be the second most significant contributor to cardiac failure in sub-Saharan Africa. In the absence of the newer, more effective drugs, access to surgery, and improved myocardial protective strategies together with the health resources of the developed world, cardiac failure is associated with a vastly different outcome.<sup>18</sup> A case fatality rate of 24% in a review of childhood heart failure among the study population demonstrated the poor outlook for children with heart failure in the developing world. Poor prognostic indices identified included the presence of underlying RHD.<sup>19</sup>

## Mortality due to ARF/RHD

Mortality rates calculated from reported case fatality ratios in recent published reports reveal that the highest estimated mortality from RHD comes from Pakistan (3.7/100 000), while Mauritius has the highest mortality rates from ARF (4.32/100 000).<sup>20</sup> This review used vital registration data to obtain mortality rates, and noted that these data were largely not available in Africa, resulting in a possible under-estimation of the mortality rates for most of Africa. Gunther *et al.* stressed this point in a letter to the *Lancet* in 2006, where they pointed out that in a rural Ethiopian community<sup>21</sup> the annual mortality rate of patients with RHD was 12.5%, 10 times that of the mortality rate used by Carapetis and colleagues to estimate the worldwide annual mortality (233 000 - 294 000) from RHD in 2005.<sup>22</sup> It is clear that contemporary robust estimates of mortality and morbidity rates, as well as those related to complications, are urgently needed from the highest prevalence areas to have a more accurate assessment of the true disease burden.

## Global strategies to eliminate RHD in the 21st century: the ASAP call to action

Prevention of RHD starts with improving the health of the population in which the disease occurs. The foci of traditional public health principles include infectious diseases, maternal and child health and occupational and environmental exposure. RHD fits very well into this model as it is an infectious disease, communicated in close environments and of particular risk to children and young adults. It is often referred to as a barometer of access to healthcare and indicative of social injustice and poverty.<sup>23</sup> However, beyond primordial prevention in terms of social upliftment and improving access to basic health, lies the primary prevention of streptococcal sore throat, secondary prophylaxis as delivered within a registry-based programme and tertiary cardiac services with surgery and interventions.<sup>24,25</sup> Currently, a significant amount of work (and money) is being directed at attempting to develop a vaccine against Group A Streptococcus.<sup>26</sup> All of these can be seen as being within the realm of 'traditional' public health strategies. However 'new' public health principles, with increasing emphasis on the complexity of health-related issues and the focus on interdisciplinary approaches, may be the answer to controlling this disease and planning cost-effective and community-appropriate interventions to stem RHD in the countries needing it the most. The ASAP (Awareness, Surveillance, Advocacy and Prevention) programme is one such initiative,<sup>27,28</sup> drawing on different disciplines to plan a multi-pronged approach to attack this disease on all fronts, incorporating public health principles to target health

promotion and prevent disease while advocating for appropriate interventions. The ASAP programme, launched in 2006, followed a call for action from key players in Africa's healthcare and political realms in response to the persistent health burden attributable to RF/RHD and has agreed to a pledge of action to reduce it.<sup>29</sup> The programme targets efforts to raise *Awareness*, establish *Surveillance* systems, *Advocate* for increased resources for treatment, and to promote *Prevention* strategies, using a community-based, bottoms-up approach. The ASAP programme has been an example of programmes initiated, run and organised by countries most affected by the disease.<sup>30,31</sup>

## The four pillars of action

### Awareness

An important element of the comprehensive ASAP programme is to create awareness of the disease and its effects on millions of people worldwide, especially in resource-limited conditions. It is well known that as the incidence of RF waned in the developed world, so did the awareness of and attention to this global public health problem.<sup>32</sup> This has consequently resulted in limited funding for RHD activities, decrease in research and publications, and reduced mention of RHD in textbooks published in more affluent parts of the world.<sup>33</sup> Improving community awareness has been demonstrated by programmes incorporating public education campaigns into their RHD control strategies to be a vital element.<sup>34,35</sup> We have evidence from initiatives instituted in various parts of the world, both in the past and currently,<sup>35</sup> that comprehensive programmes incorporating awareness-raising can not only control RHD but also create a global RHD agenda and construct a platform for collaboration. Communication and health promotion as a means of raising and maintaining awareness is an essential part of an effective RHD control and prevention programme.

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### Surveillance

Despite the staggering burden of RHD and the subsequent complications in those affected by the disease, no contemporary data exist documenting the presentation,

clinical course, complications and treatment practices among patients. Recent reviews have bemoaned the fact that these data either do not exist in sub-Saharan Africa, or are not of high-enough quality to be included in systematic reviews.<sup>4</sup> The Rheumatic Heart Disease Global Registry (REMEDY) was recently launched with a view to bridging this knowledge gap. Firstly, this registry will involve sites from Africa, the Middle-East and Asia in an attempt to document contemporary practice and identify risk factors and possible areas of intervention. Initial results from REMEDY demonstrate a significant hospital-based burden of disease as well as huge deficits in secondary prophylaxis and anticoagulation strategies, and reinforce the need for political commitment and urgent action.

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### Advocacy

A critical element of establishing the true burden of disease lies in case detection of both ARF and RHD. In South Africa, where disease notification is mandatory, a review of notifications has demonstrated that the legal requirement to notify has not been sufficiently stressed nor has notification been correctly implemented, resulting in poor capture of the burden of ARF.<sup>36</sup> Studies have shown that ARF is underdiagnosed in primary healthcare clinics in developing countries and that there is an increasing burden of RHD on autopsy in the same population.<sup>37</sup> It is therefore extremely encouraging that, together with the Directorate of Surveillance

and the Department of Health, a pilot of web-based notification will use RF/RHD as sentinel diseases to explore an online method of submitting notifications. (Personal communication: Mark Engel). Acute RF is a notifiable condition in South Africa and it is a legal requirement that healthcare practitioners at the point of first contact notify patients with ARF/RHD.

A key priority area is creating political awareness of the disease and building organisational structures to promote control activities which will be supported by national funding and concerted political will. In September 2011 the second UN summit centred on health-related issues was held in New York, focusing on non-communicable diseases. RHD, as a neglected non-communicable disease that is completely preventable by simple and inexpensive means, was one of the focus diseases and attention by the NCD alliance (Non-communicable Diseases Alliance) and WHF (World Heart Federation) will be the impetus for increased political will and urgent action.

### **Rheumatic mitral stenosis was by far the most frequent cause of heart disease during pregnancy, accounting for 64% of all cases.**

#### **Prevention**

RHD is a preventable disease using simple, proven and inexpensive antibiotics. Primary prevention consists of treating sore throat in a timely and effective manner. Early diagnosis and appropriate treatment with antibiotics of Group A Streptococcus pharyngitis provide an opportunity for prevention of ARF and RHD.<sup>38</sup> Intramuscular penicillin remains the drug of choice in developing countries and has been shown to reduce ARF by 60%.<sup>1</sup> However, many such countries face huge challenges in terms of the availability of penicillin, both oral and intramuscular preparations. This is a critical area for future research as secondary prophylaxis is a vital element of any register-based RHD control

programme. Efforts to improve delivery of penicillin and increase penicillin levels using other forms of penicillin would improve acceptability of concordance with prophylaxis.<sup>39</sup> Finally, tertiary prevention in terms of surgery is an unattainable and unaffordable luxury for many countries afflicted by RHD. It was recently reported that a comprehensive control programme could be run on a fraction of the price that a surgical programme would cost.<sup>40</sup> The ASAP programme therefore strongly supports the adoption of a comprehensive prevention and control programme for ARF and RHD, incorporating primary and secondary prevention, as critical to underpin the efforts in many parts of the world to stem the tide of this devastating disease.

#### **Summary**

RHD has not been called a 'disease of social injustice' without good reason.<sup>23</sup> It has long fallen between the cracks, and without commercial interests or dynamic action groups to drive intervention it remains a neglected disease. This has resulted in the lack of political will to significantly improve awareness and education of the disease in communities, schools and hospitals. The onus therefore falls on the medical community to take up the challenge of advocating for the return of diseases of the poor, such as RHD, to the political agenda. The ASAP programme was developed as a response from concerned practitioners from all over Africa in the face of an overwhelming burden of a preventable disease. The primary objective of this programme remains the creation of a simple modular but comprehensive model for RF/RHD control in Africa, building on the best evidence-based interventions, to be adopted by national departments of health and countries/organisations with a combined commitment to reducing the burden of disease attributable to RF/RHD. Focusing on the four pillars of action in the fight against ARF/RHD will provide a framework for the community, politicians and physicians to work together to control this preventable disease from continuing to wreak havoc among the poor in the world.

References available at [www.cmej.org.za](http://www.cmej.org.za)

## **IN A NUTSHELL**

- Rheumatic heart disease (RHD) continues to affect and kill millions of children, adolescents and young adults in the developing world.
- There remains a high burden of established RHD in developing countries.
- The diagnosis of RHD is now predominantly made by using echocardiography.
- The evidence exists for significant under-diagnosis as well as under-reporting of acute rheumatic fever (ARF).
- RHD is a neglected disease of poverty.
- Surgery remains a luxury in many parts of Africa.
- The ASAP programme, launched by the Pan-African Society of Africa in 2006, is a focused action plan using awareness, surveillance, advocacy and prevention to galvanise efforts, identify and strengthen interventions and create political will to stem the tide of RHD.
- The REMEDY project seeks to bridge the gap between lack of data regarding distal sequelae of RHD and morbidity and mortality data in low- and middle-income countries.
- There is conclusive evidence that intramuscular penicillin is the most effective agent for primary and secondary prevention.
- ARF is a notifiable condition in South Africa and it is a legal requirement that health care practitioners at the point of first contact notify patients with ARF/RHD.