

Continued Challenge of Rheumatic Heart Disease The Gap of Understanding or the Gap of Implementation?

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Two decades ago, the American streptococcal researcher Floyd Denny reflected on the history of research, management, and prevention of rheumatic fever (RF) and rheumatic heart disease (RHD) since T. Duckett Jones's pivotal paper outlining the diagnostic criteria for RF [1,2]. He paraphrased Milton Markowitz's description of the years between 1950 and 1980, respectively, as the decade of discovery (when the most important findings about methods to prevent RF were made), the decade of dissemination (during which the message about these approaches, particularly primary prophylaxis, was widely practiced in the United States), and the decade of dissonance (during which limitations of these approaches were noted, but also when RF began to disappear from the United States) [3]. Denny went on to label the 1980s as the decade of dismay, because of the return of RF and of severe group A streptococcal infections in some regions of the United States.

Those labels aptly summarized 40 critical years for RF and RHD, particularly in the United States. But with the passing of a further 2 decades plus, it may be appropriate to take a more global view of RF and RHD. As interest in RHD waned in wealthy countries between the 1970s and the 1990s, in parallel with reducing rates of disease in those same countries, attention of the cardiology community turned to the escalating epidemic of ischemic heart disease, while infectious diseases specialists focused on the human immunodeficiency virus, malaria, tuberculosis, and the emergence of antibiotic-resistant bacteria.

But it was during this period that the problem of RF and RHD in developing countries became increasingly recognized. In 1985, Dr. Alan Bisno stated: "While rheumatic fever has become a rare disease in many parts of the United States... the disease continues to devastate many of the poorer and most densely populated areas of the globe" [4]. Although it was not clear if RF had always been a problem in these countries, just under-recognized, or if in fact there had been a real increase in the disease in recent years [5], interest began to shift to RF and RHD in low- and middle-income countries.

Led by the World Health Organization [WHO], a global program of RHD control was established in 16 countries and later expanded to 22 in the mid-1980s [6]. Although underfunded, this global program had some remarkable achievements: the concept of register-based control programs was borne, as was the idea of screening school-aged children for RHD; the WHO published the first global guideline on RHD; and some pilot programs managed to persist and even later report dramatic reductions in disease burden [7,8]. But by

2000, the WHO global program was abandoned. This development, combined with the lack of new researchers emerging from the United States and other affluent countries, signaled the nadir of global interest in RF/RHD.

But since then, a new era has begun, notable for the emergence of voices from regions where RF/RHD remains a major problem. Research, policy, and advocacy are now dominated by individuals, and some organizations, working in low- and middle-income countries (particularly in sub-Saharan Africa, South Asia, the Pacific, and Latin America), or in wealthy countries where RHD remains prevalent in subgroups (often indigenous or other populations living in poverty, such as in Australia and New Zealand). This remarkable transformation has resulted in increased advocacy for so-called comprehensive approaches to RF/RHD control, encompassing primary and secondary prevention, treatment of established RHD, and broad education and health promotion strategies [9]. It has led to some traditional views being challenged, including the classic teaching that streptococcal skin infection has no role in RF pathogenesis [10], molecular mimicry may not be the basis of disease [11], and even the Jones criteria have been found to be wanting in places where RF remains a scourge [12,13]. This "southern shift" has also seen a new generation of RF/RHD researchers coming from these countries, many conducting high-end genetic, epidemiological, clinical, and pathogenesis research.

The new era has also resulted in wonderful collaborations on a global scale. Efforts to develop RF vaccines have researchers from countries such as the United States, Australia, and New Zealand collaborating with researchers in Mali, Nicaragua, Fiji, India, and South Africa [14]. A truly global effort resulted in a pivotal publication of agreed criteria for the echocardiographic diagnosis of asymptomatic RHD [15], and an ongoing collaboration to increase uptake of these guidelines and ensure that protocols for RHD screening are evidence-based, practical, affordable, and supported by essential secondary prophylaxis programs.

New organizational leadership had emerged during this era as well. The gap left by a waning of activity and interest from WHO has been partly filled by the World Heart Federation, which has recently published 5 targets to achieving control of RF/RHD by 2025 [16]. Organizations such as NCD Child have also included RHD in their agendas. As more players come into the field, and hopefully organizations that have RHD as their major focus, and if the current sense of collaboration and collegiality continues to be fostered, then the prospects of real progress in RF/RHD control are excellent over the coming 2 decades.

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The new era of RF/RHD was encapsulated at the recent World Congress on Paediatric Cardiology and Cardiac Surgery, held in Cape Town in February 2013. This conference had a major focus on RHD, and that agenda was dominated by participants from low- and middle-income countries. This issue of *Global Heart* is dedicated to RF/RHD and largely arises from presentations made at the 2013 World Congress on Paediatric Cardiology and Cardiac Surgery.

We still have a long way to go to control RF and RHD. All indications are that the disease burden figures commonly cited (more than 15 million cases and more than 200,000 deaths annually) will be shown to be dramatic underestimates when the 2010 Global Burden of Disease, Injuries, and Risk Factors reports its updated data on RHD over the next 12 months. There continue to be no low- or middle-income countries with coordinated, national control programs. We still do not have a RF vaccine, although the recent announcement that the Australian and New Zealand governments are jointly sponsoring a program to fast track development of a RF vaccine gives hope that this may be achievable.

But we must keep in mind that, although there are still gaps in our knowledge about understanding the pathogenesis of RF, the role of skin infections, the relevance of so-called borderline RHD detected on echocardiography, and others, the major gap is one of implementation [17]. There is no doubt that, if we put into practice the knowledge we already have, the majority of deaths from RHD around the world, as well as the new cases that continue to occur, could be prevented right now. This requires implementation science, but it also requires advocacy, awareness, commitment, coordination, and resources. At least the new era means that the future of RF/RHD science and control is in good hands.

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