

Secondary penicillin prophylaxis for latent rheumatic heart disease: A naïve realism?

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The past has no power over the present moment.

–Eckhart Tolle

Rheumatic heart disease (RHD) continues unabated in many economically disadvantaged areas of the world. Even so, the severity of rheumatic fever and subsequent RHD has undergone a change that has not been adequately understood. In the Bland and Jones report of 20-year follow-up of 1000 children with ARF, 30% had died from the disease.^[1] The ravages of advanced RHD cannot be undermined, but the epidemiology of RHD has many unsolved mysteries. The decline in the prevalence of RHD began before the discovery of penicillin and has largely paralleled the improvements in socioeconomic status. Nevertheless, in the absence of any better strategy, secondary penicillin prophylaxis with monthly benzathine penicillin injection has been rigorously advocated as the mainstay of the RHD control strategy. This has been emphasized so much in the collective conscience of the cardiology community that questioning its role would be considered blasphemous. However, the emerging data on the utility of secondary penicillin prophylaxis in latent RHD require that the question be examined imminently before any well-meaning society might be tempted to suggest implementing monthly benzathine penicillin injections to children with latent RHD.

The literature on secondary penicillin prophylaxis, although voluminous, is not conclusive. It is not widely appreciated that the three-most quoted studies for the efficacy of secondary penicillin prophylaxis lacked a control group! [Table 1]. The Cochrane review on the subject also lamented on the low quality of the available evidence.^[2] It is obvious that penicillin injection might

prevent a streptococcal infection and a recurrence, but that is not quite the same as the efficacy of altering the course of RHD in the population. The ravages of RHD certainly worsen with recurrences, but a lot of morbidity of RHD is the result of a severe first episode.^[6] People who did not develop severe carditis in the initial episode do not develop severe carditis subsequently, as a rule.^[7] Further, patients with mitral stenosis go on to worsen without a history of recurrent episodes; and patients with severe juvenile mitral stenosis do not suffer from obvious recurrent episodes although such has been presumed for them.^[8] Patients with rheumatic chorea develop mitral stenosis on follow-up without a history of recurrent episodes and possibly despite prophylaxis with penicillin in some cases. Further, typical Aschoff nodules that are pathognomonic of rheumatic fever are often seen in atrial appendages of patients operated on for mitral valve lesions with no clinical signs of activity,^[9] and it may be reasonable to suppose that some of these patients would be on penicillin prophylaxis as well. As such, the role of patient-related factors has not been studied at all, and those might influence disease progression. In sum, all these data suggest that secondary penicillin prophylaxis might not be as important in all patients with RHD, and a more nuanced approach is warranted. The sledgehammer approach with secondary penicillin prophylaxis could have arguably been justified in the earlier era when the cardiac treatment was just not available, but to carry the analogy to the children with borderline RHD and latent RHD is unwarranted.

Technological advances have made earlier detection of RHD possible, and studies have shown that up to 1%–3% of school children might have a latent RHD on screening

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Table 1: Most quoted studies for secondary penicillin prophylaxis

Author	Number of patients	Follow-up (years)	Control group
Stollerman GH ^[3] (1955)	410	1.7	None
Tompkins DJ ^[4] (1971)	115	5	None
Majeed HA ^[5] (1992)	64	12.3	None

in endemic areas. The natural history of these children remains ill-defined; even so, the trial data suggest that secondary penicillin prophylaxis in them would prevent the progression of RHD.^[10] An NNT of only 13 patients over 2 years appears a very attractive proposition to avert a potentially lethal RHD.^[10] That too, when none of the patients in the control group developed rheumatic fever! The purpose of this communication is to suggest that this conclusion does not reflect the realism but results from the mere statistical treatment of images of borderline significance, or by chance.

Physicians working in the endemic areas of RHD realize that mild latent RHD and borderline RHD do not progress at 26% and 9.8% in 2 years as found in these studies.^[10,11] At this rate, given the prevalence of 1%–3% of school children with latent RHD, one would have many more children with RHD than we currently have. Notably, in these studies, nearly 50% of children improved with or without penicillin prophylaxis. Hence, with the trajectory of healing in around 50% of patients in 2 years, many more are expected to heal (with or without prophylaxis). Thus, on the one hand, we accept that the prognosis of children with latent RHD remains undefined, and on the other hand, we emphatically conclude that the progression of RHD is averted by penicillin injection in this patient population, notwithstanding the incongruity of the argument! It should be remembered that no patient in this trial developed rheumatic fever and it is unlikely that all patients (n=33) had an episode that they did not recognize. Thus, another conclusion of the trial data could be that latent RHD might progress without an additional episode of rheumatic fever and that penicillin might prevent this progression by pleiotropic effects hitherto unrecognized! Thus, the trial result is simply a reductionistic view of the data. It may also be pointed out that 30% of patients in this study needed reclassification from the initial impression. Many physicians have voiced their reservations about the diagnostic certainties of morphologic criteria utilized in the screening studies. The results of this trial need to be confirmed by others.

The impact of penicillin prophylaxis needs to be systematically studied in the modern era using modern methodology rigorously. Its utility in children with borderline RHD (that is, 75% of the participants in the GOAL trial^[10]) is not established and appears improbable due to several reasons. The trajectory of the evolution of latent RHD shows spontaneous improvements in

many children. The diagnostic criteria of borderline RHD remain less than perfect and may be subjected to disagreements among the experts.

However, no one disagrees that receiving monthly benzathine penicillin injection is a very painful experience. The impact of this treatment, which is not easily accessible to low-income families, and also causes pain, isolation, and labeling on the psyche and life of the child, needs to be examined in totality. Had RHD been a disease of a more affluent society, this archaic mode of treatment would have been modified much earlier. A comprehensive look at the entire issue suggests that penicillin prophylaxis for the latent RHD would repeat the “tonsillectomy story” in the history of medicine.^[12]

Children from low-income families with latent RHD deserve better.

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Conflicts of interest

There are no conflicts of interest.

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