

CURRENT OPINION

Rheumatic heart disease control: the time for a paradigm shift

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ABSTRACT

Rheumatic heart disease (RHD) is a completely preventable, life-threatening complication of group A streptococcal pharyngitis and the commonest cause of acquired heart disease in children and young adults in low- and middle-income countries. Conventional control measures are faced with many obstacles including the difficulty of early diagnosis of bacterial pharyngitis and acute rheumatic fever (ARF) leading to late presentation with established RHD which is not curable. Recent evidence confirmed the role of echocardiography screening of asymptomatic children in the early detection of 'latent' RHD. Benzathine penicillin prophylaxis was shown to be effective in halting the progression of latent RHD. There is enough evidence to warrant the implementation of control strategies that use lower thresholds for the diagnosis of group A streptococcal infection and ARF and we believe that it is high time to introduce an echocardiography screen-to-treat policy in endemic areas.

KEYWORDS

Rheumatic heart disease; Control; Echocardiography; Screening; Latent.

Rheumatic heart disease (RHD) is a completely preventable life-threatening sequel of a relatively simple infection with Group A beta-haemolytic streptococcus (GAS) that results in acute rheumatic fever (ARF). If not treated early, ARF can result in carditis leading to permanent, incurable destruction of heart valves which rapidly progresses to heart failure and death. The estimated prevalence of RHD is 40 million people with the maximum burden in South Asia and sub-Saharan Africa [1]. RHD has almost disappeared from developed countries since the 1940s except for pockets in marginalised communities. Thereafter, the disease was neglected for many decades leading to flaring in low-income countries. Global control measures were initiated in the 1990s by the World Health Organisation (WHO) but soon they ceased and were almost non-existing till mid-year 2000 [2]. In the year 2007, echocardiographic (echo) screening of large cohorts of asymptomatic people revealed a huge burden of subclinical disease [3]. Simultaneously, control initiatives were introduced by many organisations including the Pan African Society of Cardiology (PASCAR) [4], and the World Heart Federation (WHF) [5]. In 2018, WHO issued a resolution for RHD which

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61	signifies and is expected to be the start of a global	training and public education in highly endemic	105
62	campaign against RHD [6].	areas [13,14].	106
63	THE ERA OF ECHO-DIAGNOSED	Further studies documented that subclinical	107
64	CARDITIS	RHD can progress to the clinical stage. However,	108
65	Since 2004, the WHO recognised that echo can	the role of antibiotic prophylaxis in halting the	109
66	diagnose RHD in patients without clinically	progression of the disease was not confirmed [15].	110
67	detected signs [6]. With the rapid improvement	In 2022, a randomised controlled study from	111
68	of echo technology, smaller (portable) echo	Uganda proved that Benzathine penicillin G	112
69	machines became available which resulted in	(BPG) can stop the progression of subclinical	113
70	echo screening of asymptomatic people revealing	RHD paving the way for establishing an echo-	114
71	a striking discrepancy between clinical and	based control program [16].	115
72	echo-diagnosed RHD [2]. The echo prevalence	<i>RHD control: the conventional policies and</i>	116
73	was found to be several folds higher than that	<i>their limitations</i>	117
74	discovered by auscultation. Subsequently, many	There had been many models for RHD control	118
75	studies from several highly endemic countries	including the PASCAR and the WHF [5,17].	119
76	revealed similar findings unmasking a huge	Most of the objectives of these models depend	120
77	burden of subclinical disease [7–10]. These	on primary prevention (targeting early diagnosis	121
78	findings led to the re-classification of RHD into	and treatment of GAS), secondary prevention	122
79	the following categories:	(targeting early diagnosis and treatment of ARF)	123
80	1. <i>Subclinical</i> (echo diagnosed/ silent/latent)	and tertiary prevention which aims to prevent	124
81	RHD	complications of established RHD. However,	125
82	2. <i>Clinical asymptomatic</i> RHD with heart	many limitations exist to these parameters as	126
83	murmurs (early RHD)	shown in Figure 1.	127
84	3. <i>Clinical symptomatic</i> (severe/late) RHD	<i>Time for a paradigm shift</i>	128
85	presenting with heart failure or other	Due to the described limitations in the	129
86	complications (such as stroke and endocarditis)	conventional model of RHD control, and the new	130
87	In 2012, the WHF published guidelines for the	evidence indicating the benefit of BPG in halting	131
88	diagnosis of subclinical carditis that included two-	the progression of echo-diagnosed RHD, a need	132
89	dimensional echo, colour and spectral Doppler	for a paradigm shift in RHD control is evident.	133
90	criteria from two echo views [11]. However, these	The followings are the main features of the	134
91	criteria need either a standard or portable echo	suggested model (Figure 2) and the tools needed	135
92	machine with spectral Doppler which limited their	to implement it (Figure 3) [18].	136
93	use in remote areas. Subsequent studies tested a	<i>Setting simple algorithm for diagnosis and</i>	137
94	focused protocol modified from the WHF criteria	<i>treatment of GAS pharyngitis</i>	138
95	using handheld echo machines and a single echo	In the absence of a reliable and affordable test	139
96	view. The protocol utilises two-dimensional and	for GAS pharyngitis, it is widely accepted to	140
97	colour Doppler echo, omitting spectral Doppler	use protocols for the diagnosis of bacterial	141
98	which allowed more accessibility in remote areas.	pharyngitis. The stricter the rules, the more likely	142
99	The protocol was found to have a reliability of	for them to miss positive cases of GAS; therefore,	143
100	98.7% for definite and 94.7% for borderline	it is desirable to use the most sensitive criteria in	144
101	disease [12]. Using this focused protocol, we	RHD endemic areas [19]. Stratification of patients	145
102	established RHD control sites based on echo	according to their susceptibility to ARF/RHD	146
103	screen-to-treat policy in the nine states in Sudan.	is useful, this has been applied to New Zealand	147
104	The programs were coupled with health worker		

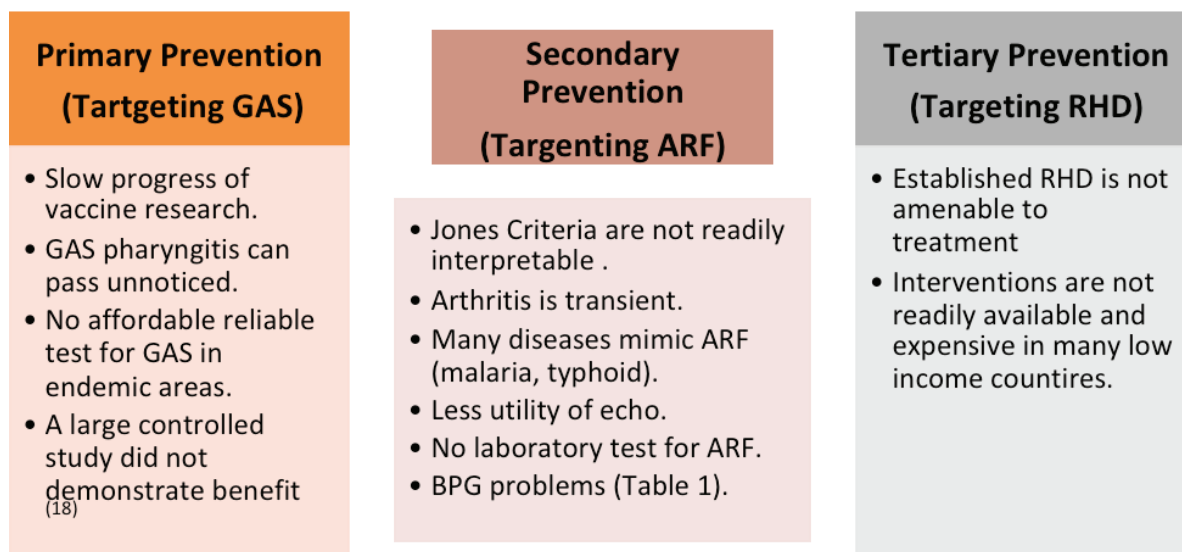


Figure 1. Limitations of conventional RHD control policies. ARF, Acute rheumatic fever; BPG, Benzathine penicillin G; GAS, Group A streptococcal infection; RHD, Rheumatic heart disease.

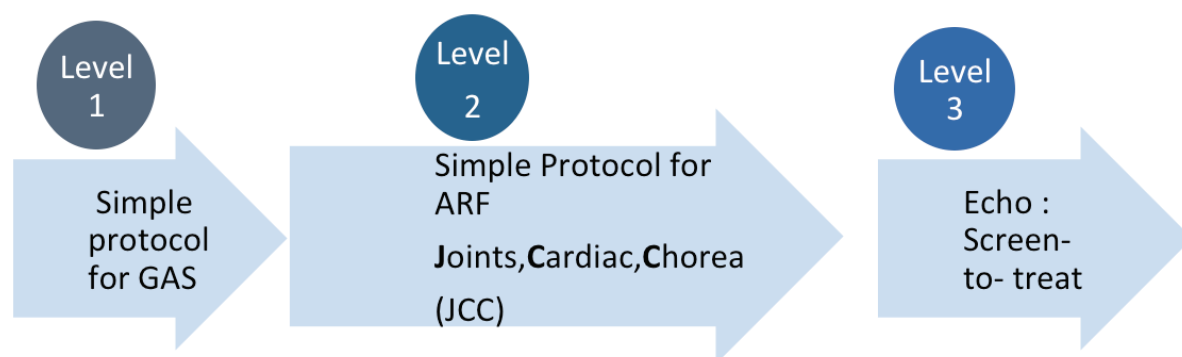


Figure 2. Suggested policy for RHD control. ARF, Acute rheumatic fever; GAS, Group A streptococcal infection; JCC, Joint, cardiac, chorea.

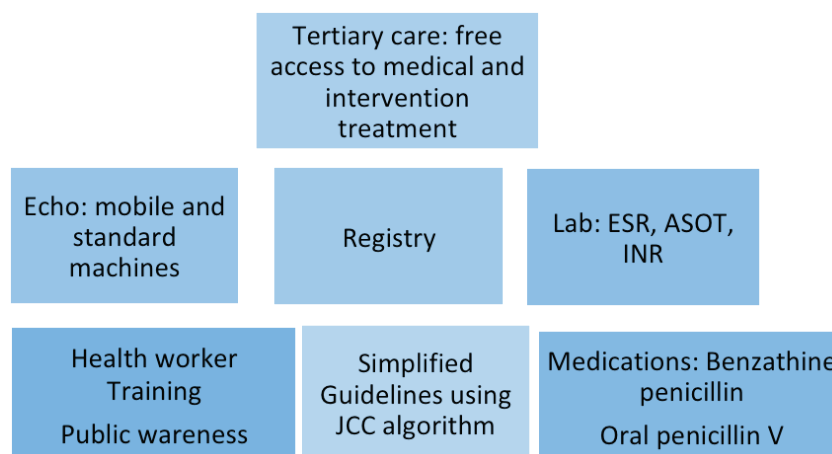


Figure 3. Tools needed to implement RHD control. ASOT, Antistreptolysin O titre; ESR; Erythrocyte sedimentation rate, INR; International normalisation ratio; JCC, Joint, cardiac, chorea.

148 GAS protocols. In high-risk categories, empiric diagnosis at the referral hospital where an echo is 180
 149 treatment of sore throat is advised [20]. expected to be done by specialists. 181

150 The standard treatment for GAS pharyngitis is *Echo screen-to-treat policy in endemic areas* 182
 151 one injection of BPG or a 10-day course of oral This indicates **active surveillance** for RHD in 183
 152 penicillin [21]. However, BPG is preferred due to endemic areas by screening asymptomatic school 184
 153 its better bactericidal effect as well as guaranteed children using portable/handheld echo machines. 185
 154 compliance. Therefore, the minimum number of The operators can be trained physicians or other 186
 155 clinical symptoms and signs together with the use health professionals who can record the images 187
 156 of a single injection of BPG is recommended in for later review by cardiologists. Positive cases 188
 157 order to improve the primary prevention of ARF/ need to be started immediately on BPG and 189
 158 RHD. referred to the next level of care for re-evaluation. 190

159 *Lowering the threshold for diagnosis and*
 160 *treatment of ARF* *Expected limitations and suggested solutions* 191
BPG and oral penicillin 192

161 In primary and secondary care settings, it might BPG is the cornerstone drug for the treatment 193
 162 be cumbersome for health workers to refer of GAS and secondary prevention of ARF with 194
 163 to Jones Criteria due to their complexity and proven efficacy for both conditions. The drug has 195
 164 multiple items. The main objectives of the 2015 inherent problems which face the patients as well 196
 165 update of the Jones Criteria were to include echo as health workers (Table 1). However, there is 197
 166 as a major criterion and to lower the threshold for currently no ideal alternative to BPG, moreover, 198
 167 diagnosis of ARF in endemic areas by including GAS is still sensitive to it with no reported 199
 168 mono arthralgia and introducing a new category resistance. WHO and other health organisations 200
 169 of ‘probable ARF’ which indicates the use of a are urged to improve the supply of BPG and 201
 170 combination of symptoms suggestive of ARF oral penicillin in RHD-endemic countries. 202
 171 without fulfilling the whole criteria [22]. The most Protocols for safe administration need to be made 203
 172 common symptoms of ARF are **joint** and **cardiac** available and training of health workers should be 204
 173 symptoms followed by **chorea (JCC)**. Therefore, intensified in endemic areas. 205
 174 health workers can be trained to treat any of these
 175 symptoms as probable ARF, start BPG and refer
 176 to the next level of care. On the other hand, many
 177 endemic diseases can mimic ARF which leads to
 178 overlapping of diagnoses, however, the clinical
 179 picture and investigations will reveal the correct

Over-diagnosis of ARF 206

The new protocol entails the diagnosis of any 207
 joint symptom as ARF, and this can lead to 208
 overdiagnosis as there are many other causes 209

Table 1. Problems of BPG and suggested solutions. 210

Problem	Suggested solution
The drug is heavy	-Dissolve in the recommended volume of diluent
The drug may obstruct the needle	-Use a large bore needle - Avoid cold diluent
The drug is painful	Use local anaesthetic as a diluent
Patients fear allergy	Allergy is rare, ask patients to report previous reactions
Health workers fear reactions	Use a protocol for health worker training
The drug can lead to sudden collapse	-Avoid using in uncontrolled heart failure -Patients need to have oral fluids to avoid dehydration before the injection
Drug supply shortage	Global efforts to improve availability

211 of acute arthritis in children. In an endemic
212 area, malaria and typhoid fever as well as viral
213 infections can lead to joint symptoms that can
214 mimic ARF. Health workers tend to diagnose
215 these ‘mimickers’ more often than ARF as has
216 been observed during daily practice. It is safer
217 to start BPG prophylaxis and send the patient
218 for an echo while investigating the cause of joint
219 symptoms. A specified protocol is needed to
220 direct health workers to the right diagnosis and
221 treatment.

222 *Over-diagnosis of RHD by echo*

223 Training of health workers needs to be guided by
224 protocols set by expert cardiologists. The health
225 workers performing echo could be physicians or
226 non-physicians; task shifting utilising nurses and
227 other health professionals has been tested in some
228 countries with acceptable results [23,24]. After
229 the screening echo, patients need to be referred
230 for evaluation by a trained cardiologist to re-
231 evaluate the diagnosis and treatment which will
232 decrease the potential for overdiagnosis.

233 CONCLUSION

234 Echo has reshaped the spectrum of RHD unmasking
235 a huge burden of subclinical carditis. Evidence
236 has shown that BPG stopped the progression of
237 subclinical RHD. The conventional approach to
238 controlling RHD has many limitations. A new
239 approach utilising fewer criteria for ARF and
240 active echo surveillance is suggested.

241 CONFLICT OF INTERESTS

242 The authors declare that they have no competing
243 interests.

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246 ETHICS APPROVAL AND 247 CONSENT TO PARTICIPATE

248 Not applicable.

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