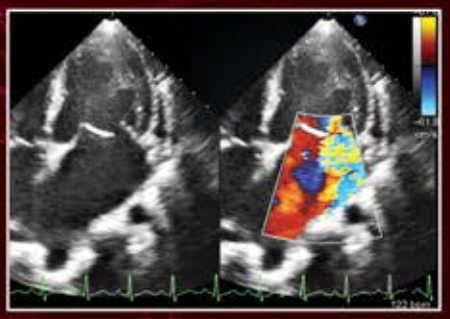
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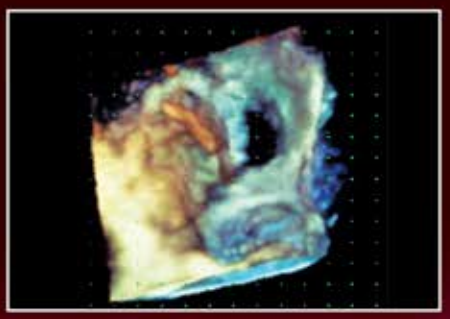
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Acute Rheumatic Fever and Chronic Rheumatic Heart Disease

2nd Edition







IB Vijayalakshmi

Foreword
George Cherian

JAYPEE

Video Content

Echocardiography for the diagnosis of carditis in acute rheumatic fever and chronic rheumatic heart disease.

- Dedication
- Revised Jones criteria, 2015.
- 6th revision of the Jones Criteria for the diagnosis of acute rheumatic fever in the era of Doppler echocardiography.
- Major changes in original Jones criteria.
- Clinical diagnosis of carditis.
- Echo can assess.
- Doppler findings in rheumatic valvulitis: Jones criteria, 2015.
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- Morphological findings on Echo in rheumatic valvulitis.
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- Physiological mitral regurgitation in PLX.
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- Pathological MR. (MR: mitral regurgitation)
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- Beaded appearance of mitral valve (histopathology comparing with Echo).
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- How specific are Vijaya's Echo criteria?
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- Unless valve regurgitation is associated with other features.
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- Both mitral and aortic valves are thickened.
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- Diagnostic of ARF with carditis. (ARF: acute rheumatic fever)
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- A 3-year-old girl with ARF. (ARF: acute rheumatic fever)
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- How Echo is superior?
- Aortic valve showing active valvulitis.
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- What to do if diagnosis is not certain?
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- BMV in juvenile MS. (BMV: balloon mitral valvuloplasty; MS: mitral stenosis)
- PTMC in juvenile MS (until 2016). (MS: mitral stenosis; PTMC: percutaneous transvenous mitral commissurotomy)
- Youngest child of MS. (MS: mitral stenosis)
- Mitral stenosis (MS), tricuspid stenosis (TS), and tricuspid regurgitation (TR) in a 3-year-old child.
- Shortest patient of MS to undergo BMV. (BMV: balloon mitral valvuloplasty; MS: mitral stenosis)

- A 12-year-old child with critical MS. (MS: mitral stenosis)
- Continuous wave (CW) cursor on tricuspid valve to demonstrate TS and TR. (TS: tricuspid stenosis; TR: tricuspid regurgitation)
- Juvenile MS/malignant MS. (MS: mitral stenosis)
- MVOA measurement by planimetry increased from 0.2 to 1.4 cm^2 after BMV. (BMV: balloon mitral valvuloplasty; MVOA: mitral valve orifice area)
- Post-BMV, the MVOA is better MV gradient reduced from 35/15 to 13/7 mm Hg. (BMV: balloon mitral valvuloplasty; MV: mitral valve; MVOA: mitral valve orifice area)
- Catheterization data of 12-year-old female of critical MS, height—130 cm.
- Post-BMV MR. (BMV: balloon mitral valvuloplasty; MR: mitral regurgitation)
- Post-BMV MR two jets in an 8-year-old girl. (BMV: balloon mitral valvuloplasty; MR: mitral regurgitation)
- Catheterization data of an 8-year-old female.
- Pre-BMV. (BMV: balloon mitral valvuloplasty)
- Post-BMV apparently good result.
- Do not miss the eccentric jet.
- Catheterization data.
- Restenosis.
- 16 Post-BMV, restenosis after 6 years. (BMV: balloon mitral valvuloplasty)
- Challenges of BMV in mitral restenosis. (BMV: balloon mitral valvuloplasty)
- Post-BMV restenosis.
- Post-BMV restenosis after 6 years.
- The eccentric MR with severe submitral fusion. (MR: mitral regurgitation)
- MVP, MS, and MR in an 8-year-old girl. (MR: mitral regurgitation; MS: mitral stenosis; MVP: mitral valve prolapse)
- Post-closed mitral commissurotomy and later BMV, RHD–MS, TS, severe TR, AS with AR. (AR: aortic regurgitation; AS: aortic stenosis; BMV: balloon mitral valvuloplasty; MS: mitral stenosis; RHD: rheumatic heart disease; TR: tricuspid regurgitation; TS: tricuspid stenosis)
- Commissural morphology.
- Valve morphology and subvalvular apparatus.
- Subvalvular stenosis.
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- Giant RA with severe TR. (RA: right atrium; TR: tricuspid regurgitation)
- Giant LA needs plication. (LA: left atrium)
- BMV during pregnancy. (BMV: balloon mitral valvuloplasty)
- Safe PTMC in pregnancy. (PTMC: percutaneous transvenous mitral commissurotomy)
- Echo-guided balloon across MV into LV. (LV: left ventricle; MV: mitral valve)
- BMV during pregnancy. (BMV: balloon mitral valvuloplasty)
- Contraindications to BMV. (BMV: balloon mitral valvuloplasty)
- Transthoracic echocardiography (TTE) versus transesophageal echocardiography (TEE) for thrombus in left atrial appendage (LAA).

- LA body clot. (LA: left atrium)
- Spontaneous Echo contrast (SEC) on transesophageal echocardiography (TEE).
- Contraindications to BMV. (BMV: balloon mitral valvuloplasty)
- Periprocedural TEE and 4D Echo have gained great importance to assess paravalvular leak. (TEE: transesophageal echocardiography)
- Spontaneous Echo contrast with organized clot in LAA—relative contraindication. (LAA: left atrial appendage)
- TEE showing thrombus on interatrial septum—contraindication for BMV. (BMV: balloon mitral valvuloplasty; TEE: transesophageal echocardiography)
- Football in the heart.
- SBE prophylaxis. (SBE: subacute bacterial endocarditis)
- Echocardiographic assessment of aortic stenosis.
- Apical five-chamber view shows AS in a case of RHD with MS, MR, and TR. (AS: aortic stenosis; MR: mitral regurgitation; MS: mitral stenosis; RHD: rheumatic heart disease; TR: tricuspid regurgitation)
- Dextrocardia with severe AS and rheumatic MS. (AS: aortic stenosis; MS: mitral stenosis)
- Balloon dilatation of AS and MS. (AS: aortic stenosis; MS: mitral stenosis)
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- May–Thurner syndrome.
- Assessment of aortic regurgitation.
- M-mode AML flutter in AR. (AML: anterior mitral leaflet; AR: aortic regurgitation)
- Aortic regurgitation.
- Color Doppler.
- Diastolic flow reversal in descending aorta.
- Echo of diastolic flow reversal in descending aorta.
- Vena contracta width.
- AR with vegetation on AV. (AR: aortic regurgitation; AV: aortic valve)
- EF: 10–15%, inoperable. (EF: ejection fraction)
- Grading of MR by vena contracta width. (MR: mitral regurgitation)
- Tricuspid stenosis and regurgitation.
- Missed diagnosis can be disastrous for the patient.
- The disease in AV and TV is likely to progress despite BMV. (AV: aortic valve; TV: tricuspid valve; BMV: balloon mitral valvuloplasty)
- Post-BMV the MVOA is better MV gradient reduced. (BMV: balloon mitral valvuloplasty; MV: mitral valve; MVOA: mitral valve orifice area)
- Summary.
- Conclusion.
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- Borderline RHD. (RHD: rheumatic heart disease)
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- Congenital MV anomalies must be excluded. (MV: mitral valve)
- Criteria for pathological regurgitation.

- Test your skill—Case I.
- Parasternal long axis.
- Test your skill—Case II.
- What is the Echo score and what is the diagnosis?
- Test your skill—Case III.
- What do you see?
- Test your skill—Case IV.
- What is the diagnosis?
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- What is your decision?
- Is MR physiological or pathological? (MR: mitral regurgitation)
- What is the impression?
- What is the decision?
- Echo prevents damage at three levels.
- Carry home message.
- Conquer the unconquered.
- Acknowledgement.
- All working together for a cause.



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4

Can We Change the Epidemiological Trend of Rheumatic Heart Disease in India?

Smita Mishra

> *"Declare the past, diagnose the present, foretell the future."*
>
> —**Hippocrates**, 460–357 BC, Greek Physician

INTRODUCTION

Rheumatic fever (RF) is an immunologically mediated sequelae of relatively innocuous Group A β-hemolytic *Streptococci* (GABHS or GAS) throat infection. It is characterized by an inflammatory process involving collagen fibrils, which often results in pericardial inflammation and a lasting damage to heart valves.[1,2] The irreversible valvular damage, also known as rheumatic heart disease (RHD), is an important cause of cardiac failure and related premature mortality. Notably, streptococcal pharyngitis, a prerequisite to acute rheumatic fever (ARF), is the only common childhood bacterial disease without an effective vaccine. In this article, we will discuss the identifiable epidemiological determinants of ARF/RHD and analyze their potential to become the instrumental to induce a downward trend in the prevalence of the disease in India. Enlisted candidates for the task include factors responsible for virulence of the streptococci, environmental factors, and vulnerabilities of the human host. In last decade, many outstanding initiatives were taken to change the perspective largely. In this chapter, we will discuss how the collective efforts have made a difference in epidemiological trend of RF-RHD.

EPIDEMIOLOGICAL ASPECTS OF ACUTE RHEUMATIC FEVER AND RHEUMATIC HEART DISEASE: RECENT TRENDS

Because of the inhomogeneous healthcare delivery systems across the country, the magnitude of the problem remains obscured. According to a recently published report, RHD affects over 33 million individuals worldwide and has resulted in approximately 350,000 premature deaths/year.[3] In last two to three decades, a significant decline in clinical RF-RHD has been seen **(Table 1)**.[3-12] The Global Burden of Disease Study (GBDS) 1990–2016 showed a remarkable increase in prevalence of ischemic cardiovascular diseases and stroke in India between the aforementioned period; whereas there was decrease in the age-standardized disability-adjusted life-years (DALYs) rate of RHD, in all epidemiological transition level (ETL) state groups[4] **(Fig. 1A)**. Yet, when compared to the global average, RHD DAILY rate was 2.4 times of global average.[4] Lately, in studies using echo screening, a statistically significant higher prevalence of subclinical carditis (SCC) has been demonstrated, contesting the claim made by clinical studies

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TABLE 1: Epidemiological study and RHD prevalence in India.

Author	*Place*	*Year*	*Age (years)*	*Population studied*	*Prevalence (per 1,000)*
ICMR[5]	Ballabhgarh (rural)	1982–1990	5–15	13,509	2.9
Padmavati[6]	Delhi (urban)	1984–1994	5–10	40,000	3.9
Agarwal et al.[7]	Aligarh	1995	All	3,760	6.4
Grover et al.[8]	Ambala (rural)	1988–1991	5–15	31,200	2.1
Lalchandani et al.[9]	Kanpur (combined)	2,000	7–15	3,953	4.5 (rural: 7.4) (urban: 1.2)
Jose and Gomathi et al.[10]	Vellore (rural)	2001–2002	5–18	229,829	0.68
Mishra et al.[11]	Gorakhpur (urban)	2003–2006	4–18	118,212	0.5
A Bharani et al.[12]	Indore (urban)	2004–2007	5–15	25,676	0.46

(ICMR: Indian Council of Medical Research; RHD: rheumatic heart disease)

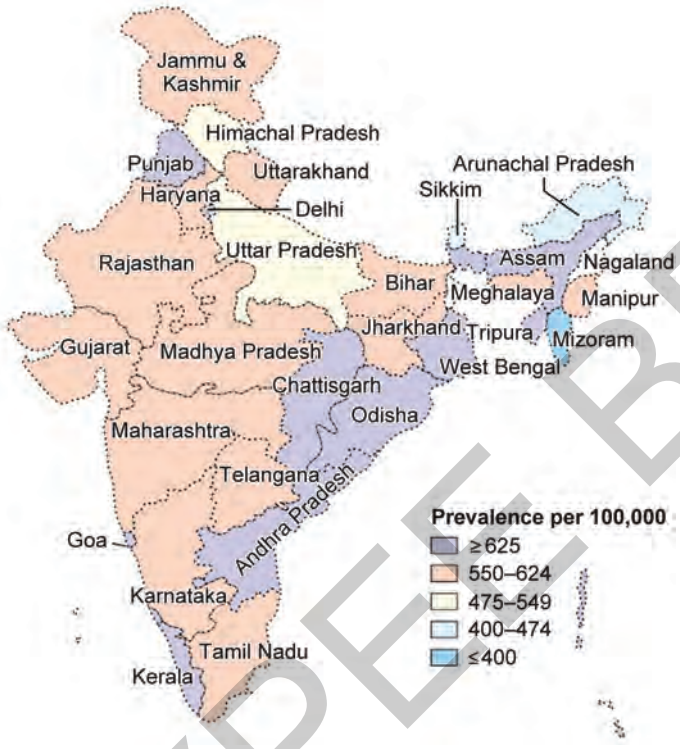


FIG. 1A: Rheumatic Heart Disease in India: Global Disease Burden studies 2016[4].
Source: India State-Level Disease Burden Initiative CVD Collaborators. The changing patterns of cardiovascular diseases and their risk factors in the states of India: the Global Burden of Disease Study 1990-2016. Lancet Glob Health. 2018;6(12):e1339-51

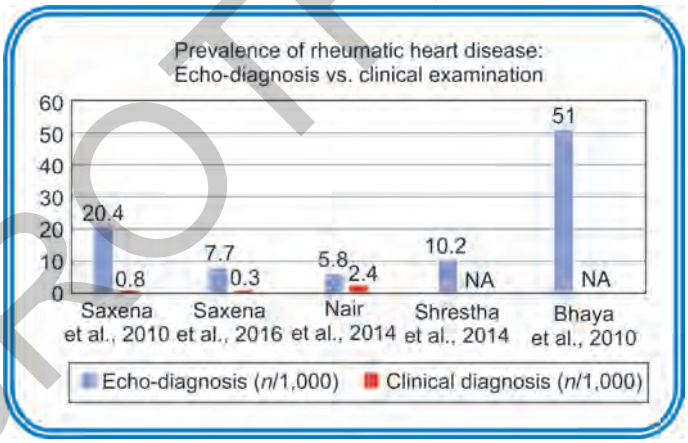


FIG. 1B: Comparative Data of Prevalence of carditis: Echo-diagnosis and clinical diagnosis.[13-17]

that prevalence of RF-RHD has substantially gone <1/1,000 population.[13-17] But, a downward trend has been observed in prevalence of SCC [20.3/1,000 (2010) vs. 7.7/1,000 (2016)] when study was resumed in same area after 5–6 years **(Fig. 1B)**.[14,17] Correspondingly, Negi et al. reported a two-point survey study, carried out among the school children (urban and rural area) of Shimla, over a gap of about 15 years and confirmed five-fold decline in the prevalence of RF-RHD.[18] Authors attributed the declining trend to the improvement in the socioeconomic state, access, and affordability of healthcare services, change in health-seeking behavior of the community leading to timely treatment of acute pharyngitis. It has been observed that concerted ICMR (Indian Council of Medical Research) studies led to change in health-seeking behavior of the concerned population. Arguably, indices of human development are the major determinants of the RF prevalence and they grossly vary across the country. Therefore, available Indian data from the selective studies may not be considered as reasonable representation of the country as a whole.[4,16-18]

Rationally, Australian New Zealand guidelines of ARF/RHD altered the Jones clinical criteria to improve the sensitivity, in the area with high prevalence.[19,20] No such consideration has been shown in Indian studies done before the creation of World Heart Foundation.

PATHOGENESIS (FIGS. 2 AND 3)

Primarily, RF is related to the GABHS throat infection but some case series have found a relationship with streptococci causing pyoderma and reactive arthritis, particularly

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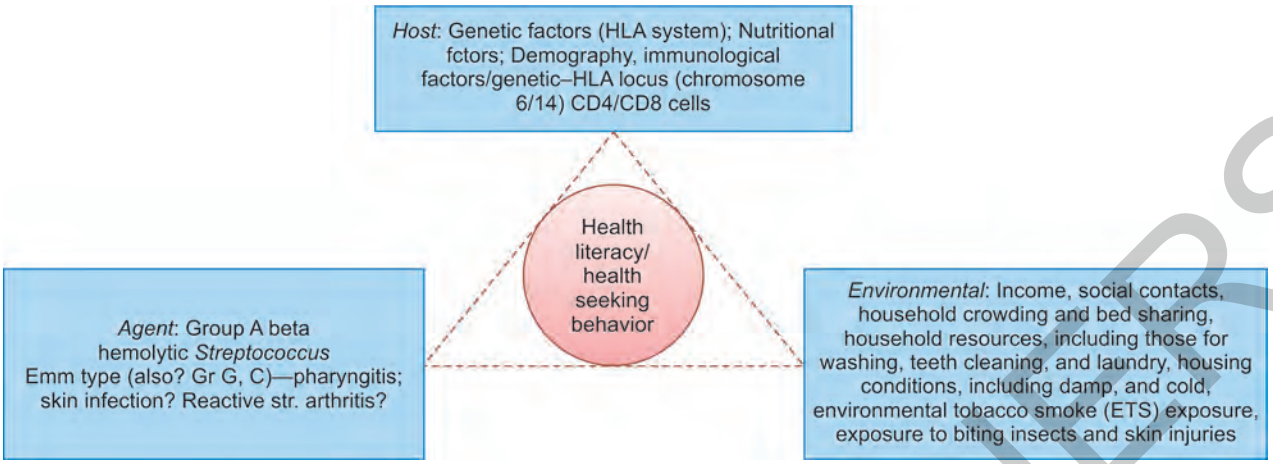


FIG. 2: Rheumatic fever—epidemiological triangle and determinants of disease.[19-21]
(HLA: human leukocyte antigen)

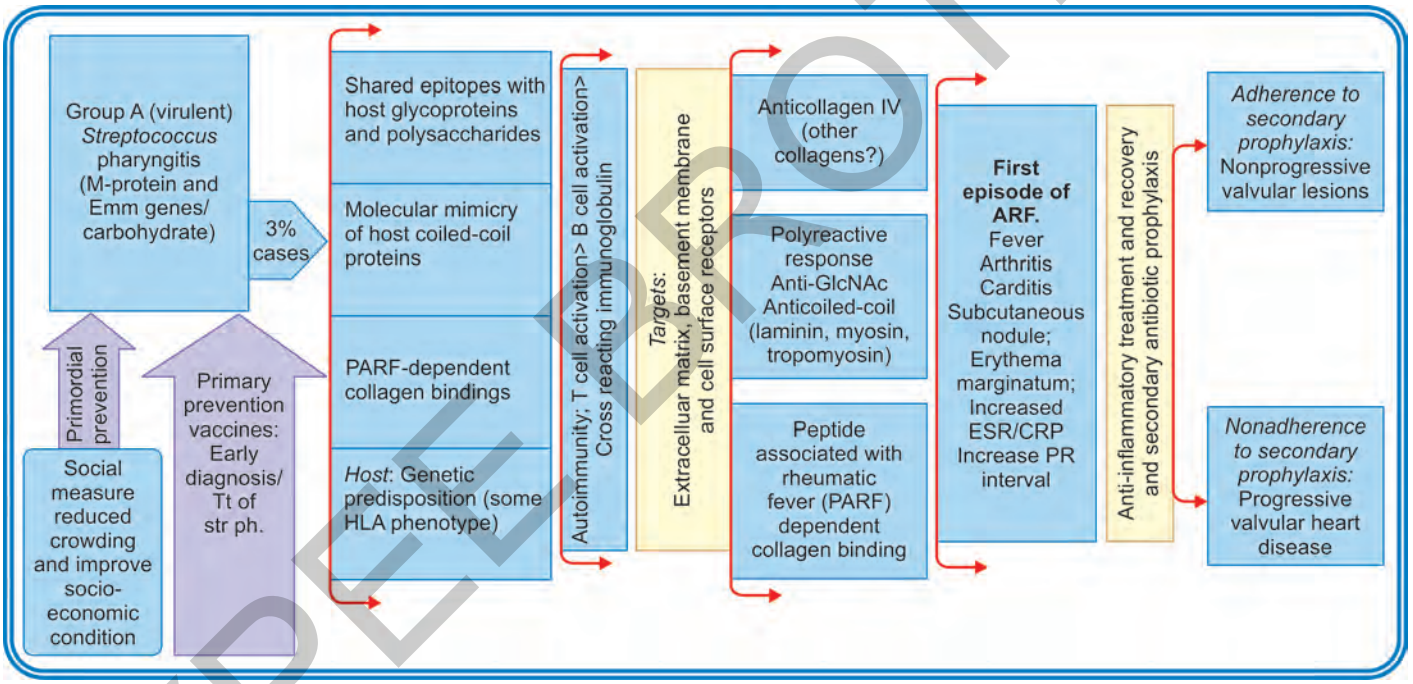


FIG. 3: Pathogenesis of rheumatic fever and level of prevention.[19-21]
(ARF: acute rheumatic fever; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate)

in aborigine population of Australia and New Zealand **(Fig. 2)**. Pathogenesis of ARF/RHD is discussed elsewhere in book, but it is well established now that the RF results from amplified immunological response against the many candidate proteins of host, having molecular mimicry with GABHS bacterial protein **(Figs. 2 and 3)**.[19-24] Classical epidemiological triad (agent, host, and environment) is difficult to discern in ARF as agent leaves immunological trail and remains invisible at the time of clinical appearance of the ailment. Moreover, understanding of epidemiological model is important to strategize an effective control program. Additionally, ARF has a variance in the outcome of different organs passing through the analogous inflammatory process. Presence of the autoantibodies against the collagen I of the cardiac valves indicated possibility of alternative pathways responsible for valvular damage in ARF-RHD.

Host Factor and Role of Genetics

Several inheritable factors augmenting or altering the immunological response have been identified, explaining the prevalence of RF in only 3% population exposed to GABHS pharyngitis.[19-24] Auckland et al. reported a major susceptibility locus for RHD in human leukocyte antigen

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(HLA) region (human HLA locus, on chromosome-6) of Indian and Fijian population.[24]

VANISHING ACT OF RHEUMATIC FEVER IN DEVELOPED WORLD: LESSON LEARNED

World Health Organization describes ARF–RHD as a disease grounded in the poverty.[25,26] The virtual disappearance of ARF/RHD in western world has been a landmark, which could not be replicated in a few of developed countries and in most of the developing countries. Industrialized nations now have an average annual RF incidence of <0.5/100,000 and RHD prevalence of <0.05/1,000.[19-26] Knowing the complex nature of RF–RHD and its unabated presence in other part of world needed a thorough analysis particularly in view of the fact that RHD-related mortality dipped-down by 50% before the advent of effective antibiotics such as sulfonamide and penicillin **(Fig. 4)**.[27] Following theories were put forward by Dr L Gordis:[27] (1) Decreased prevalence of streptococci, in general in USA; (2) decreased prevalence of rheumatogenic variants; (3) decreased virulence of bacteria as was evident by decreased severity of then prevailed scarlet fever; (4) disappearance of cofactors needed to produce RF; (5) emergence of effective antibiotic therapy; (6) better medical care; and (7) host factors including nutrition, genetic predisposition, etc. There was an upswing in incidence after 1985, drawing attention to the temporal shift of virulent strains and also identification of type of M proteins associated with carditis.[28]

CONTROL OF RHEUMATIC FEVER IN DEVELOPING WORLD

For a country such as India, primordial prevention, i.e., controlling environmental, economic determinants or sledge–hammer use of antibiotics for pharyngitis without getting into discretion of exact diagnosis, has feasibility issues. Hence, ARF–RHD control program has targeted so for, the re-infection with agent or GABHS. **Table 2** is the comprehensive review of these factors.[17-24]

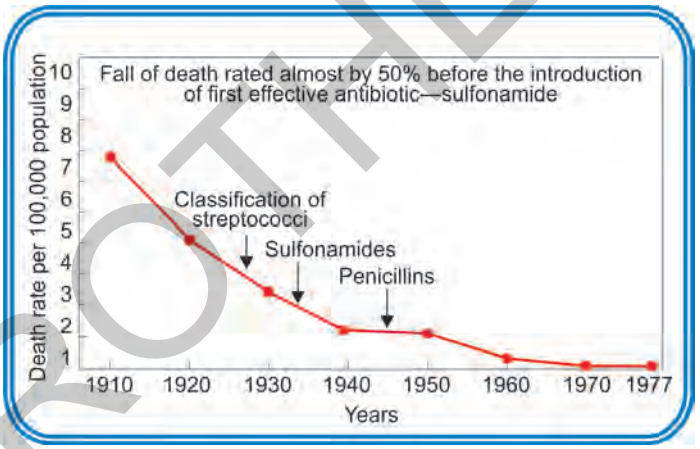


FIG. 4: Crude death rates from the ARF/RHD (USA) 1910–1977.

Source: Gordis L. The virtual disappearance of rheumatic fever in the United States: Lessons in the rise and fall of disease: T. Duckett Jones Memorial Lecture. Circulation. 1985;72:1155-62.

TABLE 2: Agent, host, environment, and health system: the determinants of diseases.

Direct and indirect results of interaction of the environmental/agent/host health system determinants on rheumatic fever and rheumatic heart disease[4]

Determinants	*Effects*	*Impact on RF and RHD burden*
Socioeconomic and environmental factors (poverty, undernutrition, overcrowding, and poor housing)	• Rapid spread of group A streptococcal strains • Difficulties in accessing healthcare	• Higher incidence of acute streptococcal pharyngitis and suppurative complications • Higher incidence of acute RF Higher rates of recurrent attacks
Health system-related factors: • Shortage of resources for health care • Inadequate expertise of healthcare providers • Low level awareness of the disease in the community	• Inadequate diagnosis and treatment of streptococcal pharyngitis • Misdiagnosis or late diagnosis of acute RF • Inadequate secondary prophylaxis and/or noncompliance with secondary prophylaxis	• Higher incidence of acute RF and its recurrence • Patients unaware of the first RF episodes • More severe evolution of disease • Untimely initiation or lack of secondary prophylaxis • Higher rates of recurrent attacks with more frequent and severe heart valve involvement and higher rates of repeated hospital admissions and expensive surgical interventions
Virulence of bacteria (M protein 1, 3, 5, 6, 14, 18, 19, 24, Emm variety, etc.)	Predisposes for immunological response	Increased chances of ARF
Vulnerable host (genetic predisposition, malnutrition, etc.)	Valvular disease	Higher rates of recurrent attacks with more frequent and severe heart valve involvement

(ARF: acute rheumatic fever; RF: rheumatic fever; RHD: rheumatic heart disease)

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In order to define relationship between GABHS infection, ARF–RHD and socioeconomical determinants, Coffey et al. made an extensive and systematic literature review of 1,164 relevant observational and experimental studies.[29] Significant associations between socioeconomic factors and risk of Group A streptococci and ARF/RHD were found in 57.1%, and 50% studies, respectively. The majority of studies included in this meta-analysis found reasonable causal association with nutritional status, crowding, dwelling characteristics, education, and employment status of parents or patients, despite of heterogeneity in quality of evidence.

A DECADE OF EMERGING GLOBAL LEADERSHIP TO CONTROL RHEUMATIC FEVER: POLICY, GUIDELINES, AND DATA COLLECTION (2011–2020)

In 2010–2011, while writing this chapter, we discussed multiple barriers posing as the gaps in the policies, guidelines, and health delivery system. However, in last 10 years, developing world has seen the joint-leadership coming from Australia, New Zealand, India, South Africa and many other countries leading to coordinated efforts and tandem walking with the various global agencies. This new uprising in the public health perspectives brought in a new zeal and energy while pursuing the goals, which were once thought to be unachievable. This enterprising global leadership perhaps may be tributed for the negative epidemiological trends in India and other places. Many important events, which have empowered the efforts to control RF-RHD, are as follows:

- Publication of new guidelines from Australia and New Zealand dissociating itself from the traditional approach of American Heart Association (AHA)/WHO/Indian guidelines.[19,20]
- Onset of Global Burden of Diseases, studies and massive collection of epidemiological data allowing comprehensive analysis of the etiological and pathological factors.[4]
- Carapetis et al., while collecting, comprehending, and coordinating related data from all parts of globe, steered a constructive drive among the developing countries, which has dodged the "savior" role of developed countries.[19,20-23]
- World Heart Federation emerged as the biggest challenger for the traditional dominance of west as the policymakers. WHF has the moto to reduce death by 25% in under 25 years age group from RHD up to 2025.[30,31]
- Echocardiography, which was unjustly denied its promising role in the RF control/prevention program, could be recruited in the toolbox of clinical Jones criteria.[13-20,30,32]
- *Portable echocardiographic machines*: India suffered a setback due to rising female feticide prevalence, which culminated into preconception—Prenatal Sex Determination (PNDT) Test Act, prohibiting generous use and portability of ultrasound (US) machines. However, countries with poor health infrastructure were benefitted by introduction of handy, portable US machine.
- *Publication of revised Jones criteria 2015 by AHA*: These criteria are inspired by global trends as discussed above and are evidence of path-breaking transformation in policymaking and advocacy.[32]
- *Role of institutions in India*: Formation of rheumatic consortium (2014), an initiative by All India Institute of Medical sciences under the banner of Pediatric Cardiology Society of India and Cardiology Society of India, is another milestone to create an advocacy for the RF/RHD in India and neighboring countries.[33]
- CSI (Cardiology Society of India) position paper on heart failure guidelines was a unified Indian effort to gather data on specific conditions relevant to the Indian context, which included RF and heart disease.[34]
- *United Nation's Sustainable Development Goals*:[35,36] We will discuss subsequently that how Sustainable Developmental Goal-2030 (SDG-2030) and SDG score are the wholesome package to control RF–RHD without even mentioning it.

DESIGN OF A COMMUNITY OUTREACH MODULE[19-26]

Management of GABHS Pharyngitis[19,20-23,37]

Early recognition and treatment with appropriate antibiotics for desired duration is utmost important both for the general population and part of prevention strategy for recurrence of RF. Yet, a sledgehammer approach to treat all cases of sore throat as GABHS pharyngitis cannot be advocated.[21]

Epidemiological Module[19-23,37]

Tables 2, to 4 provide comprehensive compilation of various epidemiological determinants of RF-RHD and preventive/management strategies.

A successful model is desired for dispensing the epidemiological information and solutions for RF–RHD. Restricted access of the healthcare delivery systems in certain territories may be responsible for both—presence of statistical blind spots for epidemiological data and undulating prevalence status of RF–RHD. Specially designed, unit-specific, module-based investigational and interventional programs are needed to meet the need of tribal colonies, urban slums, and remote rural India. These regions with the poorest healthcare infrastructure need to be prioritized. An ideal Community Outreach Module has to have following components:[36]

- The proactive, sensitized state, and central government
- Medical colleges/civil hospitals and associated ancillary services recruitment in the program

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- Involvement of professional academic association such as Indian Academy of Paediatrics, Cardiological Society of India, Pediatric Cardiological Society of India, and Indian Medical Association

TABLE 3: Prevention of ARF-RHD.[3,15,17,19-27]

Collection of epidemiological data	In view of AHA 2015 revised clinical criteria, risk stratification of a population in a geographical area is required and therefore epidemiological accurate data collection is utmost important to design and execute a control program of ARF and RHD
Prevention of ARF and RHD	I. *Primordial prevention*: By modulating socioeconomic factors—alleviation of poverty, better housing, avoid crowding as spelled out in sustainable development goals adopted by UN
	II. *Primary prevention*: This can be done by developing and researching for a cost-effective vaccine, early diagnosis and adequate treatment of sore throat by GABHS infection
	III. *Secondary prevention*: Early diagnosis of RF and secondary prophylaxis preferably with benzathine penicillin G and to ensure the adherence
	IV. *Tertiary prevention*: The goal of early, effective and adequate anti-inflammatory treatment and management of valvular heart disease

(ARF: Acute rheumatic fever; GABHS: group A β-hemolytic *Streptococcus*; UN: United Nations; RHD: rheumatic heart disease)

- Paramedic training for benzathine penicillin G (BPG) injection and anaphylaxis management
- Role of research organizations such as Indian Council of Medical Research in collecting epidemiological data and improving the health-seeking behavior of society
- Tertiary prevention of progressive VHD with timely intervention is also important. It also gives opportunity to secure native valve for longer duration avoiding the financial burden and need of long-term anticoagulation
- To provide patient education for strict INR monitoring to avoid restenosis of prosthesis as well as overt episodes of accidental bleeding.

Feasibility and Scope of RF/RHD Control Program in the Time of Pandemic COVID-19

Pandemic 2019 has brought socioeconomic crisis in addition to the health calamities. It has decreased gross domestic product (GDP) by –23% in India and increased the number of people below poverty line and hampered the screening programs.[38]

On the other hand, it improved the hygiene, blocking the transmission of droplet infection, due to increased use of masks and hand-hygiene. During the pandemic, resilience of health infrastructure in India was also proved to be fairly good. Therefore, scope of primordial prevention has risen recently like never before.

ROLE OF WORLD HEALTH ORGANIZATION[24,25]

In 2018, World Health Assembly launched a coordinated program to respond the zealous global drive, and to upgrade

TABLE 4: ARF/RHD prevention and control program: Role allocation.

Role of government	***Role of medical colleges/civil hospitals and associated ancillary services***	***Role of IAP and pediatricians***	***Role of paramedics***
• RF-RHD prevention program needs to be accepted as government program • Set-up goals and budget allocation • Sensitize healthcare system • Procure BPG and ensure turnover • Cardiac patients must be considered as physically handicapped and given facilities for treatment • Introduce insurance policies	• To run RHD prevention program • To run regular rheumatic clinic from pediatric department • Training program for medical and paramedical staff • To sensitize them for secondary prophylaxis • Research/thesis at 5–7 years interval or creation of registries	*Role of IAP*: • To ensure the participation at all levels • To improve awareness by publications • IAP branches can bring out their program for helping the patients *Role of pediatricians*: Only pediatricians can successful run supervised RHD prevention program	*Must know*: • Doses and how to dilute the benzathine penicillin • Be trained for IM injection and learn precautions • How to do sensitivity test • Be trained in recognizing and managing anaphylaxis • Be trained to handle life support • Record keeping • *RHD card:* Entry for every injection like in vaccination/ INR monitoring card

(ARF: acute rheumatic fever; BPG: benzathine penicillin G; IAP: Indian Academy of Pediatrics; RHD: rheumatic heart disease)

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and accelerate the preventive program. WHO has taken following initiatives:

- To establish RF/RHD prevention and health promotion in schoolchildren in as many countries as possible, wherever RF/RHD remains a major public health problem
- To urge Ministries of Health in all of these countries, as well as nongovernmental organizations and donor agencies, to intensify their efforts to promote and support the establishment of at least a local/provincial program on RF/RHD prevention and control
- It is working on developing and upgrading guidelines in view of recent publications
- WHO has owned the responsibility to ensure a steady, quality supply of BPG.

INITIATIVE TAKEN BY INDIAN ACADEMIC OF PEDIATRICS[37]

Indian Academy of Pediatrics (IAP) took the initiative by organizing a consensus meeting on pediatric RF–RHD (2007) and published its guidelines (2008) based on the survey among the pediatricians about the knowledge attitude and practice. Pediatricians are major stakeholders for the efficient implementation of RF control program as this disease mostly affects pediatric (<20 years) population. Following recommendations were made:

- Recognition and prompt treatment of GABHS pharyngitis
- Early recognition of ARF–RHD
- Secondary prophylaxis (SP) preferably with long-acting BPG. Alternative treatment with oral penicillin and erythromycin was recommended in penicillin-sensitive patients.
- It also provided guidelines on diagnosis and management of valvular lesions, infective endocarditis, rhythm issues, etc.
- Consensus guidelines were published in "Indian Paediatrics" a journal religiously followed by all pediatricians of country.
- IAP also approached to various pharmaceutical companies, ICMR, and government to improve the supply of BPG in the country.
- On behest of IAP, BPG was included in the list of essential drugs in 2011.[39]

ROLE OF INDIAN COUNCIL OF MEDICAL RESEARCH AND JAI VIGYAN MISSION MODE PROJECT AND NATIONAL HEALTH MISSION[4,18,21,40,41]

The Indian Council of Medical Research initiated community control and prevention of RF/RHD through hospital-based passive surveillance and implementation of SP under Jai Vigyan Mission Mode Project from 2000 to 2010. Changing socioeconomic state, improved living conditions, and improving connectivity and access to healthcare centers after liberal economic policies and introduction of National Rural Health Mission (Now—National Health Mission) helped in better delivery of healthcare system. Jai Vigyan Mission Mode Project on community control of RF/RHD had four arms—(a) epidemiology; (b) molecular typing of rheumatogenic strains; (c) RF/RHD registries; and (d) development of a vaccine against streptococci.

Nevertheless, none of the ICMR research projects were based on troubled and under developed states such as Bihar, UP, MP, North Eastern regions and Jammu and Kashmir state or the tribal belts. The results of the molecular and vaccine-related research remained unknown.

SUSTAINABLE DEVELOPMENTAL GOAL 2030, SDG SCORE, AND RF CONTROL PROGRAM[35,36]

The RF/RHD is both a biological and a social problem. Its public health importance is not only a direct result of its high occurrence rates (mortality, prevalence, and incidence), but also the population affected (children and young adults). Its economic consequences, both in healthcare related costs and in indirect costs to society (often resulting in premature death or disability), are very significant.[41]

The United Nations (UN-1945) is an international organization currently made up of 193 countries, which takes an active role in designing and developing the global policy issues. Sustainable Developmental agenda 2030 (2015) is an ambitious 17th point plan to promote sustainable development in all countries of the world. It has been broadly accepted that to have a sustained development, world has to have a multilayered proposal to sort-out the intertwined issues related to the health, education, climate change, poverty, and economic growth **(Box 1)**.

Mitigation of the poverty, the food security (Goals 1 and 2), reducing maternal mortality rate (target 3.1), universal health coverage (target 3.8), improving housing, and hygiene (Goal 11) are grossly desired goals to reduce the transmission of streptococci and prevalence of ARF/RHD. Eventually, control of any endemic issue depends on engagement of committed people, well-researched, and precise policies, which must convert into carefully defined programs. It has been appreciated globally that the good policies have a lot of impact globally, regionally, and nationally when they dribble down into good action and execution, locally.

It is important to acknowledge that India is in endemic RF zone, carrying the moderate-to-high risk for RF. India secured 117th position in global SDG scale much lower in comparison with most of its neighboring countries: Shri Lanka—94th; Nepal—96th; Myanmar—104th; and Bangladesh—109th.[36] All developed countries and China stand within the SDG score of 50, which also implicates better human development indices in these countries.

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BOX 1 Proposed health-related targets:[35,36] Sustainable Development Goal, 2030.

- *Goal 1*: End poverty in all its forms everywhere
- *Goal 2*: End hunger, achieve food security and improved nutrition and promote sustainable agriculture

Sustainable Development Goal 3: Ensure healthy lives and promote well-being for all ages:

- *3.1* by 2030 reduce the global maternal mortality ratio to less than 70 per 100,000 live births
- *3.3* by 2030 end the epidemics of AIDS, tuberculosis, malaria, and neglected tropical diseases and combat hepatitis, water-borne diseases, and other communicable diseases
- *3.4* by 2030 reduce by one-third premature mortality from noncommunicable diseases (NCDs) through prevention and treatment, and promote mental health and wellbeing
- *3.b* support research and development of vaccines and medicines for the communicable and noncommunicable diseases that primarily affect developing countries, provide access to affordable essential medicines and vaccines, in accordance with the Doha declaration which affirms the right of developing countries to use to the full the provisions in the TRIPS agreement regarding flexibilities to protect public health and, in particular, provide access to medicines for all
- *3.c* increase substantially health financing and the recruitment, development and training and retention of the health workforce in developing countries, especially in LDCs and SIDS
- *3.d* strengthen the capacity of all countries, particularly developing countries, for early warning, risk reduction, and management of national and global health risks
- *11. Make cities and human settlements inclusive, safe, resilient, and sustainable*

Source: https://rhdaction.org/prevention/primordial-prevention

ROLE OF ADVOCACY AND NEW GUIDELINES

Jones Clinical Criteria: The Holy Grail for Rheumatic Fever

"Rheumatic heart disease is a global health issue which should not even exist in the 21st century, yet it continues to limit the lives and opportunities of individuals across the world. We must seize every opportunity we can to eliminate this preventable disease."

—Dr Salim Yusuf, President World Heart Federation[30,31]

Clinical Jones criteria, revised or modified several times in last many decades, are the pivotal for clinical diagnosis.[32,42] In a nutshell, review of various publications suggests following limitations of the jones criteria.[4,17-33]

- These major and minor criteria were not universally present. Even if they were present but were not conspicuous enough to be identified easily.[19,20,32]
- *Diagnosis of pancarditis*: It is known since beginning that ARF affects all three layers of heart but essentially valvulitis is the hallmark of rheumatic carditis. The pericarditis and myocarditis in isolation are not specific for RF. The clinical Jones criteria for carditis had described murmur of ARF as follows: (i) an apical systolic murmur, which does not change with posture or respiration; (ii) parasternal high-pitch diastolic murmur (aortic regurgitation); (iii) a third murmur—mid-diastolic apical [carry Coomb's or murmur of mitral stenosis (MS)]. The issues with diagnosis of carditis were multiple: (a) early carditis usually does not produce classical murmur; (b) there is gradual decline in auscultatory skills of physicians; (c) the murmurs may not be of rheumatic origin in about 60% pediatric population even in endemic zones due to high prevalence of benign (Still's murmur) and small ventricular septal defects; (d) unjust prescription of secondary BPG prophylaxis by zealous physicians while other physicians may ignore presence of several fold higher incidences of SCC (by echo imaging) in comparison to the clinical carditis; (e) RF may present only with fever and subclinical valvulitis and may be missed initially. It may present subsequently with MS, a late sequelae, which occur very quickly following RF in 40–50% cases. The patients with MS may not have other components of clinical criteria.
- Polyarthralgia is common than the polyarthritis in the high-prevalent area.
- Chorea is usually associated with carditis but it has a late and insidious onset and does not give opportunity to diagnose carditis early.
- Erythema marginatum and subcutaneous nodule are specific but are relatively infrequent. They are likely to be missed in routine clinical examination.

Judicious Application of Echo Imaging: Role of World Heart Federation (Table 5)

The American Heart Association and WHO guidelines declined the idea to include echo imaging for the diagnosis of carditis for following reasons: (1) overestimation of regurgitant lesions due to the absence of guidelines to differentiate the physiological and pathological valvular lesions; (2) cost escalation of mass screening due to echocardiography.

These contradictions and controversies compelled researchers, cardiologists, pediatric cardiologists, and epidemiologists to come under one umbrella and develop the recommendations applicable in the diverse group of patient population.[32,33] Carapetis J and group became key to create a combined group of researchers, pediatric/adult cardiologists, epidemiologists, and specialists from all relevant specialties. Over the period of time, multiple epidemiological studies from the affected countries emphatically demonstrated:[13-23,30,31] (1) prevalence of SCC is several folds higher than the clinical carditis; (2) the SCC has a potential to progress into moderate-to-severe carditis

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TABLE 5: World Heart Federation criteria for echocardiographic diagnosis of RHD (2012).[31]

Echocardiographic criteria for individuals aged ≤20 years:	
Definite RHD (either A, B, C, or D)	A. Pathological MR and at least two morphological features of RHD of the MV B. MS mean gradient ≥4 mm Hg* C. Pathological AR and at least two morphological features of RHD of the AV D. Borderline disease of both the AV and MV
Borderline RHD (either A, B, or C)	A. At least two morphological features of RHD of the MV without pathological MR or MS B. Pathological MR C. Pathological AR
Normal echocardiographic findings (all of A, B, C, and D)	A. MR that does not meet all four Doppler echocardiographic criteria (physiological MR) B. AR that does not meet all four Doppler echocardiographic criteria (physiological AR) C. An isolated morphological feature of RHD of the MV (for example, valvular thickening) without any associated pathological stenosis or regurgitation D. Morphological feature of RHD of the AV (for example, valvular thickening) without any associated pathological stenosis or regurgitation echocardiographic criteria for individuals aged >20 years
Echocardiographic criteria for individuals aged >20 years:	
Definite RHD (either A, B, C, or D)	A. Pathological MR and at least two morphological features of RHD of the MV B. MS mean gradient ≥4 mm Hg* C. Pathological AR and at least two morphological features of RHD of the AV, only in individuals aged <35 years‡ D. Pathological AR and at least two morphological features of RHD of the MV

(MR: mitral regurgitation; MS: mitral stenosis; RHD: rheumatic heart disease)

*Congenital MS must be ruled out.

‡Rule out bicuspid AV.

in 4–12% of cases; (3) early diagnosis is a tactical tool for control of RF-RHD as we have a method to control the valvular lesions because SP with BPG has shown emphatic role in prevention of the progression of RHD; (4) frequent echo monitoring may obviate the need of secondary BPG prophylaxis in mild/borderline or suspected but unproven cases; and (5) echo is the best modality to monitor the existing valvular lesions.

The World Heart Federation collected epidemiological data from the concerned countries and published the precise echocardiographic criteria.[30,31] The revised Jones criterion was subsequently published in 2015 by AHA accommodating the echo imaging.[32] AHA also yielded to relax the criteria in endemic areas in line with the previously published Australian guidelines.

Highlights of WHF echo criteria are as follows:

- *Less than 20 years of age:* Prevalence of ambiguity of RF–RHD diagnosis is more in comparison to the patient population >20 years of age.
- WHF echo criteria are divided in twogroups based on age groups.
- These groups are further divided in subgroups **Table 5**.
- WHF preconditioned the image optimization. Accordingly, color Doppler assessment must be done with maximized scale and harmonics must not be used during the evaluation of chordal and valvular thickness. Following pathomorphological features need to present for a diagnosis of RF–RHD:
  - Definition of rheumatic disease of mitral valve: (i) Increased mitral valve thickening ≥3 mm (age-specific); (ii) chordal thickening; (iii) restricted leaflet motion; and (iv) excessive leaflet tip motion during systole.
  - Definition of rheumatic disease of aortic valve—may have following features: (i) irregular or focal thickening; (ii) coaptation defect; (iii) restricted leaflet motion, prolapse.

Revised Jones Criteria 2015:[32] A Course Correction to Drop Down Restriction (Table 6)

Many shortcomings narrated before are now addressed well in AHA revised Jones criteria 2015. Moreover, AHA conceded to the fact that the RF has the global heterogeneity and conventional stringent universal Jones criteria had the potential to miss a diagnosis in the most vulnerable population. Therefore, a definition of low- and high-risk population was accepted as follows:

High- and low-risk population based on prevalence of RF–RHD:

- A population with ARF incidence <2 per 100,000 school-aged children (5–14 years old) per year, or an all-age prevalence of RHD of ≤1 per 1,000 population per year is defined as low risk (Class IIa, Level of Evidence C).
- Depending on their reference population, children not from low-risk population have moderate to high risk (Class I, Level of Evidence C).

Revised criteria conceded that carditis and arthritis are most prevalent major manifestations while chorea, subcutaneous nodule, and erythema marginatum are specific but are less likely to be seen.

Diagnosis of carditis: Revised criteria (2015) have accepted echo imaging as the class I indication for the following:

- For all cases of confirmed and suspected ARF (Level of Evidence B)

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TABLE 6: AHA's (American Heart Association) revised Jones Criteria, 2015.[32]

Evidence of preceding GAS infection (at least one of the following):	
1. Increased or rising anti-streptolysin O titer or other streptococcal antibodies (*anti-DNase B*). A rise in titer is better evidence than a single titer result 2. A positive throat culture for group A β-hemolytic streptococci 3. A positive rapid group A streptococcal carbohydrate antigen test in a child whose clinical presentation suggests a high pre-test probability of streptococcal pharyngitis	
Major criteria:	
Low-risk population (ARF incidence ≤ 2 per 100,000 school-aged children or all-age RHD prevalence of ≤ 1 per 1,000 population year population)	Moderate-/high-risk population (children not clearly from a low-risk population)
Clinical and/or subclinical carditis	Clinical and/or subclinical carditis
Polyarthritis	Monoarthritis, polyarthritis, and/or polyarthralgia
Chorea	Chorea
Erythema marginatum	Erythema marginatum
Subcutaneous nodules	Subcutaneous nodules
Minor criteria:	
Prolonged PR interval	Prolonged PR interval
Polyarthralgia	Monoarthralgia
≥38.5°C	≥38°C
Peak ESR ≥ 60 mm in 1 hour and/or CRP ≥ 3.0 mg/dL	Peak ESR ≥ 30 mm in 1 hour and/or CRP ≥ 3.0 mg/dL
(ARF: acute rheumatic fever; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; RHD: rheumatic heart disease)	

- Serial echo screening would be justified in suspected or diagnosed patients of RF with no evidence of carditis to begin with (Level of Evidence C).
- Echocardiography/Doppler testing should be performed to assess whether carditis is present even in the absence of auscultatory findings, particularly in moderate- to high-risk populations and when ARF is considered likely (Level of Evidence B).
- Specific criteria for valvulitis incriminated are as follows:
  - *Mitral regurgitation (MR)*—seen in ≥2 views, jet length ≥2 cm, peak velocity >3 m/s, pansystolic
  - *Aortic regurgitation (all four)*—seen in ≥2 views, jet length ≥1 cm, peak velocity >3 m/s, pandiastolic

Diagnosis of joint involvement: In high-risk population, any of following—monopoly arthritis or polyarthritis, or polyarthralgia, is accepted as the major and monoarthralgia as the minor criteria. For low-risk population, only polyarthritis has to be considered as the major and polyarthralgia as the minor criteria.

Other minor criteria: Besides the joint involvement, following criteria were included as minor criteria—fever (≥38.5°F), sedimentation rate ≥30 mm and/or C-reactive protein (CRP) ≥3.0 mg/dL, and prolonged PR interval (unless carditis is a major criterion).

Revised criteria 2015 now take a cut-off erythrocyte sedimentation rate (ESR) as 60 mm/1st hour for low risk and 30 mm/1st hour in high-risk population.

Evidence of preceding Streptococcal infection:

Any one of the following can serve as Class I level indication of preceding infection:

- *Raised anti-streptolysin O titer or anti-DNase B*: A rising titer is better indicator (Level of Evidence B)
- Throat swab culture positive for group A β-hemolytic *Streptococci* (Level of Evidence B)
- Rapid group A *Streptococcal* carbohydrate antigen test positive in a child who have high probability of *Streptococcal* sore throat (Level of Evidence B).

ARF diagnosis in high-risk population: First episode of RF is diagnosed by presence of two major or one major + two minor criteria; Now, polyarthralgia and monoarthritis are included as major criteria for high-risk population..

Subsequent episode: Patients with a history of ARF or RHD are at high risk for recurrent attacks if re-infected with group A *Streptococci*. In cases with past history of RF or established RHD, if GABHS infection has been documented, two major, one major and two minor, or three minor manifestations may be sufficient for a presumptive diagnosis. In the cases where none of the major criteria is present, a meticulous effort to be made to rule out the other possible diagnosis.

Rheumatic chorea and insidious onset rheumatic carditis: No requirement of other major manifestations or supportive evidence of streptococcal sore throat infection.

Chronic valve lesions of RHD (patient presenting with pure MS or MS/MR with or without aortic valve disease): Do not require any other criteria to diagnose as RHD.

With publication of AHA guidelines and new Australian guidelines, a tremendous hope has been generated and now India and other countries are in better position to have an early diagnosis, better monitoring, and discretion to implement an effective epidemiological control program of RF-RHD.

FUTURE OF CONTROL PROGRAM: ROLE OF PRIMORDIAL, PRIMARY, AND SECONDARY PREVENTION

Vaccines[19,20-23,42-45] (Table 7)

"A safe, globally effective and affordable GAS vaccine is needed to prevent and potentially eliminate acute GAS infections (pharyngitis, skin infections, cellulitis, and invasive disease) and associated antibiotic use, immune-mediated sequelae (kidney disease, RF and RHD) and associated mortality."

—WHO, Vision statement 2018[43]

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TABLE 7: Vaccines against the Group A β-hemolyticus Streptococci.*

Antigen	*Comments*
Non-M protein vaccine:	
Group A carbohydrate GAC	*Preclinical stage*: Ag conserved in species of *Streptococcus* pyogenes
C5a peptidase	*Preclinical stage*: Potentially, high emm type coverage and cross-protection against other streptococcal pathogens
Type-specific M protein vaccines: N-terminus based:	
Hexavalent tandem Antigen	Clinical trial phase II, protective in humans but low emm coverage
26-valent combination of tandem antigens (StreptAvax™)	Clinical trial stage II completed. Protective but low emm coverage
30-valent combination of tandem antigens	Preclinical. Increased emm coverage
M protein vaccines—conserved C-repeat based:	
C-terminal protective epitope StreptInCor	Preclinical, capable of inducing cellular and humoral responses, mucosal IgA and systemic IgG production in mice
P145 and derivatives J8 and J14	Preclinical stage; human antibodies against P145 cross-react with different emm types
Multivalent J14	Preclinical; broader emm coverage

*Adapted from reference 44

Primordial and primary prevention of RF is highly desirable but hardly feasible as if now. An effective vaccine is expected to be an asset to the world and India as it would reduce the cost for diagnostic procedures, antibiotics, and eventually interventional management for valvular heart diseases. We must appreciate that polyarthritis and chorea are benign and inconsequential in long term, but they cause significant transient disability to the affected person.

Recently, we have seen quick evolution of multiple vaccines in short duration, against the COVID-19 [Severe Acute Respiratory Syndrome Corona Virus (SARS-COV-2)].

Whereas, development of the streptococcal vaccine remained an elusive project despite of catching attention of many laboratories worldwide, but no interest has been shown by the corporates. The reason for this probably lies in the inability to find out a promising project for the profit-seeking industry, with the conclusively proven streptococcal molecules responsible for the cardiac cross-reactive antibodies found in the patients with RF. Besides, there is no ideal cost-effective animal model other than nonhuman primates. Research laboratories have very limited access to the monkey model for various reasons, which includes tremendous cost escalation. Finally, selection of a safe and effective delivery system/adjuvant is also a challenging task. Besides these technical issues, it can also be argued that lack of initiatives from developed nations is a root cause for lack of enthusiasm and prevailing ignorance towards the potential of an effective vaccine against the GABHS.

Nonetheless, there are multiple antigenic components of streptococci speculated to be good candidate for vaccine. Moreover, use of technical "reverse vaccinology" (use of genome, transcriptome, and proteome data) for identification of vaccine antigens may shorten the time in picking up candidate antigen.[45]

Presently, expectation of addition of vaccines in the armor of RF–RHD program is a far-fetched dream though any such efforts may be a big gift to the vulnerable population.

Secondary Prophylaxis with Antibiotics: Glittering Gold or Else?

Long-acting BPG is the backbone of RF prevention program. Addition of benzathine counterion to the penicillin sodium creates a compound, which has low solubility in water. Intramuscular administration of BPG has tendency to be released slowly over the time of 3–4 weeks and, therefore, maintaining the blood levels sufficient to kill GABHS acquired during this period.[46] Long-acting BPG provides opportunity to supervised injection at 3–4 weeks interval and with good adherence (>80%) recurrence of RF can be prevented and RHD related morbidity and morbidity can be reduced drastically. BPG prophylaxis is the Grade 1A indication (AHA guidelines 2010).[19,20,32,37,46]

However, in a recent publication, none of children had benzylpenicillin concentrations >0.02 mg/L for the full time between doses.[47] This observation has shown a major knowledge gap relating to pharmacokinetic/pharmacodynamic relationships between BPG and clinical outcomes. BPG was included in WHO list of essential drugs in 2011.[39] Oral penicillin is not equally effective.[46] Oral erythromycin is prescribed to the patients allergic to the penicillin. There are studies to suggest that erythromycin- and tetracycline-resistant strains are emerging.[48] However, following issues related to the BPG must be debated and resolved:

- *Role of liquid penicillin*: BPG salt had poor water solubility. It may block the needle during the intramuscular injection. To overcome that liquid (prediluted), penicillin was introduced. This development led to shortage of regular BPG in India and many other countries. Furthermore, it was costlier and required cold chain. IAP took up this matter to the central ministry and subsequently BPG (0.6 million IU and 1.2 million IU doses) was included in the list of essential drugs (2011 edition) in India. Year 2000 onwards, penicillin supply was erratic. Recently, WHO has taken responsibility to maintain supply of BPG consistent.
- *BPG sensitivity test* has also problem. It is not advised in many countries but India sensitivity testing is recommended. Being a lipid-soluble agent and poor water solubility, it cannot be diluted to the lowest strength

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required for skin sensitivity test and being a long-acting agent, it may not reflect response in stipulated time.[37]

- *Safety of BPG injections* need to be established. Respective reported incidence of allergic reaction and anaphylactic reaction is 3.2% and 0.2%. It is advisable that first injection must be administered in a hospital set-up. However, emerging data suggests that anaphylaxis may not be as common as it was thought to be and many other factors may be responsible for the life-threatening events.[48] Fear for anaphylaxis has led to ban on BPG in few of the Indian states (Kerala and Tamil Nadu).[49]
- *Mitigation of pain during the intramuscular injection:* BPG injection is painful and may cause decompensation of cardiac status in few patients causing life-threatening events.[46] The possibility exists that inadequate dose gets administered.
- *Reformulation of drug:* To improve the solubility, emulsifying agents are often added to the BPG, which may include substance such as soy lecithin, responsible for allergic reaction.

  Few studies came out with innovative suggestions for reformulation of the BPG, which include microemulsions, nanoparticles, and implantable drug monoliths.[50] Finally, global efforts are on, to develop a safe, quality assured BPG, which is critical to establish an RF control program.
- *Duration of SP:* Recent publications advocate duration of SP up to 21 years or 10 years from the day of first diagnosis, whichever is longer, if there are no established valvular lesions. There is no unanimity about duration of SP (35 or 40 years or lifelong) for patients with established valvular lesions.[13-23,37]
- *Dose of BPG and body weight criteria:*[13-23,37] Though there is uniformity about the doses of BPG (1.2 million IU or 900 mg for adults and 0.6 million IU or 450 mg for children) but cut-off value of body weight has variation as follows: Australian–New Zealand guidelines—20 kg, Indian, AHA guidelines—27 kg, and WHO guidelines—30 kg. Indian guidelines proposed 2 weeks interval between two injections for children who are receiving low (0.6 million IU) doses. The BPG levels may be suboptimal in many patients predisposing them to the recurrent GABHS infection. A serious discussion is warranted to establish the right cut-off values for body weight and duration of SP.[47]
- *Compulsory training of paramedic for administration of BPG:* It is important, therefore, a training program and guidelines for the paramedics that how to administer BPG and how to take care of anaphylactic reaction. It is important to give first injection in hospital setting where prefilled syringes with adrenaline and steroids are available.

CONCLUSION

With the available statistical data, we can say that there has been a conscientious effort to fill-up the gaps and overcome barriers in the healthcare delivery system, which has allowed us to create a better preventive strategy in India. However, more aggressive approach is needed to access remote area and to get a more realistic epidemiological picture of the problem. Although introduction of a suitable cost-effective vaccine is the best preventive armor, it is not expected in recent future due to varied reasons. It is difficult to envisage that agent (GABHS) can be eradicated or environment can be modulated drastically in India. Yet, with the help of community outreach and adherence to SP program, India can achieve the major epidemiological breakthrough to decrease mortality and morbidity associated with RHD. Securing and providing the good-quality BPG is a task, which must be prioritized on all the fronts. Utility, efficacy, and cost of liquid BPG need to be titrated in a balance of cost and benefits. Finally, sensitivity testing of BPG, dosing schedule, and dose interval need a consensus across the board to keep BPG SP effective and fruitful.

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Acute Rheumatic Fever and Chronic Rheumatic Heart Disease

The purpose of this monogram is to describe the whole gamut of acute rheumatic fever (ARF) and chronic rheumatic heart disease (RHD) and give the methods of management. This book, both in its concept and design, is aimed at giving a comprehensive and complete knowledge about ARF and RHD, to the pediatricians, physicians, cardiologists, and the medical students dealing with health problems of ARF and RHD in the socioeconomically poor community. This book helps the clinicians to approach the diagnostic problems presented by children with ARF and RHD; through proper assessment and integration of the history, physical examination, investigations, especially the modern tool, the echocardiography and learn about the prevention of the disease and its complications. The modern tool, echocardiogaraphy, plays an important role in the precise and early diagnosis, hence two chapters on, ECHO in ARF and RHD have been written. The access to videos of ECHOs in patients with carditis and RHD are available with QR code inside the book. The influence of this is likely to be truly spectacular and special, as this will help in bringing many patients, into the net of penicillin prophylaxis and may assist in changing the epidemiological face of the disease. This book with a galaxy of distinguished contributors, will surely be a valuable reference resource for the years to come.

IB Vijayalakshmi MD (Gold Medalist) DM DSc FICC FIAMS FIAE FICP FCSI FNAMS FISH FRCP (London), Professor Emeritus, is a skilled Interventionalist and Pioneer in Pediatric Cardiology. She is a Professor and Head, Department of Pediatric Cardiology at Super Specialty Hospital, Bengaluru, Karnataka, India. She has also worked as a Professor of Pediatric Cardiology at Sri Jayadeva Institute of Cardiovascular Sciences and Research, Bengaluru, Karnataka, India. She has had a brilliant academic career, secured 38 gold medals, 2 silver medals, delivered 27 prestigious orations, 82 publications, 155 research papers (42 international), delivered 456 scientific lectures, and 850 public lectures. She has authored Step-by-Step to Echo in Congenital Heart Disease and edited Second Edition of Monogram on Acute Rheumatic Fever and Rheumatic Heart Diseases. She has proposed Vijaya's Echo criteria for the early and precise diagnosis of carditis in ARF and got First Prize for outstanding scientific presentation at World Congress of Echocardiography. She received the Best Presentation Award for My Nightmare Case at PICS at Chicago and in Boston. She has also received more than 60 prestigious awards including Rajyotsava Award and Life-time Achievement Award from Past Presidents of India, Bharat Ratna Shri APJ Abdul Kalam ji and Her Excellency Smt Pratibha Devisingh Patil. Now, she is the President Elect of Indian Academy of Echocardiography and Vice President of Indian Institute of World Culture. She has the distinction of being a member of the prestigious World Heart Federation group for standardizing Echocardiography in Rheumatic Heart Disease, which is widely cited all over the world.

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