

Acute Rheumatic Fever & Rheumatic Heart Disease

‘Diseases of Poverty’

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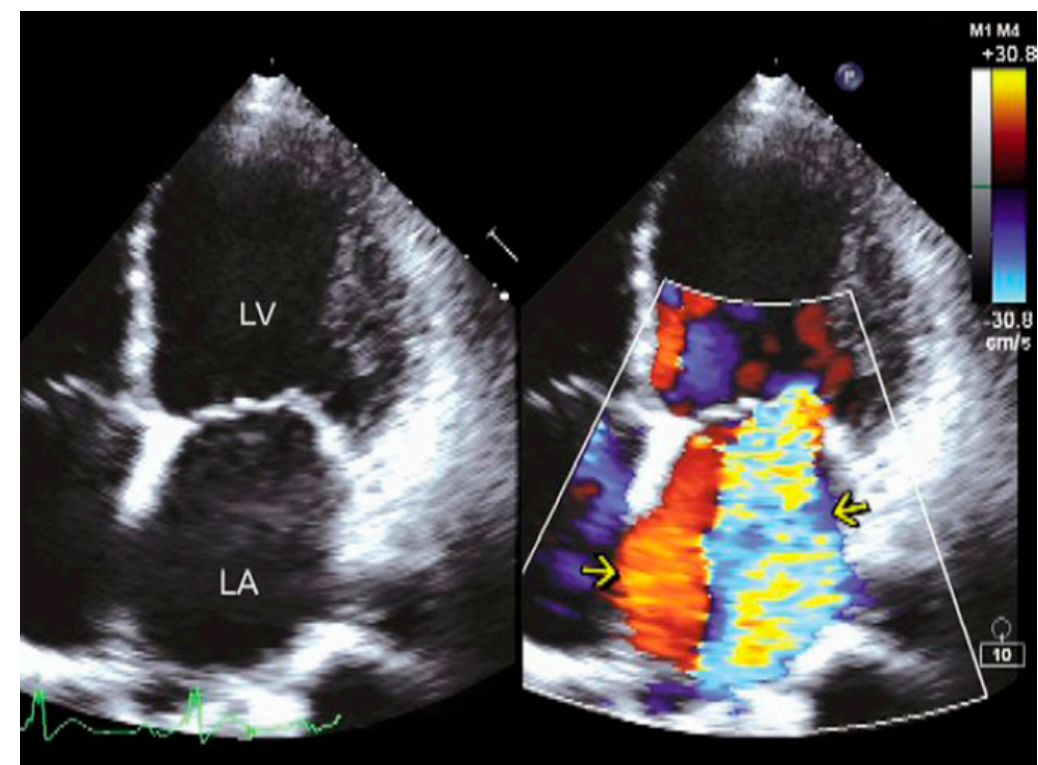
Meet JT!

Case Report

- M/17yo; Grade 10 std @ Jubilee; withdrew from school due to illness
- Referred by NCDPHA TB team from STC
 - ?RHD-MR
 - ?MDRTB
- Bgd: Treated for PTB x2 (2019, 2021) - clinical & CXR
- Now: Sick for >1/12
 - Weight loss, SOBOE, chest pain, easily fatigued, abdominal pain, intermittent fevers
- Cannot recall hx of sore throat; no hx of skin sores or joint pains
- Seen twice at local clinics
- No other significant symptoms

- **O/E:** thin boy, pink, no edema, afebrile, tachypnoeic, tachycardic, Sats 97% RA, BP not taken, no PSIE, bounding & collapsing pulse, JVPNE, active precordium, Lt precordial bulge, AB displaced 7LICS AAL, heave ++, HS-gallop rythm, 3/6 PSM MA-axilla, 3/4 diastolic murmur LSB, liver enlarged 4cm, bibasal crepts
- **Clinical assessment:** MR/AR
- **ECG:** SR, LAD, LVH

- **Echo:** Hugely dilated LV, thickened MV+AV, severe MR & AR, evidence of LV dysfunction
- **Dx:** RHD in HF with LV dysfunction



Learning/Discussion points from JT's case!

- Majority of our children with RHD present this way - Severe valvular lesions in heart failure
- JT's case could have been picked up earlier and prevented from progressing to advanced disease
- Highlights importance of:
 - Early referral to major health facility
 - Timely and correct diagnosis of acute rheumatic fever (ARF)
 - Screening for subclinical cases of ARF
 - Appropriate treatment administered
 - Secondary penicillin prophylaxis
 - Education

Differentiating ARF & RHD

- The terms of ARF and RHD are sometimes confused
- **ARF**
 - Short lived autoimmune disease that follows GAS infection;
 - Usually used to describe the initial or acute onset of the disease
- **RHD**
 - long term cardiac sequelae of ARF; chronic form of the disease; persistence of valvular lesions signifying significant damage to valves
 - Many patients lack a history of past ARF, suggesting:
 - ARF frequently missed
 - Initial or recurrent insults may be subclinical or not detected

Epidemiology

ARF/RHD

- Common acquired heart disease in the world affecting children in developing countries *World heart federation rheumatic heart disease information*
 - **Poor socioeconomic status, inadequate access to health care, unchecked exposure to group A streptococcus**
- In wealthier countries, burden of RHD confined to indigenous populations - Aborigine population of Australia, Maori population of New Zealand *Carapetis et al. 2000, 2005*
- Affects school aged children; Peak prevalence 5-15 years age group
- Worldwide conservative estimates: 470,000 new cases of ARF & 275,000 deaths from RHD each year *GBD 2013 Mortality and Causes of Death*

Collaborators, Carapetis et al. 2000, 2005, 2007, Zuhlke et al. 2013

Epidemiology

ARF

- Mean incidence of ARF worldwide: 19 per 100,000 school-aged children *Tibazarwa et al.2008*
- In US: ≤ 2 per 100,000 *Miyake et al.2007*
- Higher in developing countries and indigenous populations; higher numbers attributed to improved recognition & reporting of ARF
 - Aborigines : 153-380 per 100,000 children age 5-14yrs *Parnaby et al.2010*
 - Fiji: 15/100,000 *Kado et al.2011*
 - Tonga: 33.2/100,000 *Fakakoovikaetau et al.2008*
 - Samoa: 31.8/100,000 *Viali et al.2011*

Epidemiology

RHD

- 33 million prevalent cases of RHD world wide causing 275,000 deaths annually *GBD Mortality and causes of Death collaborators.1990-2013*
- Many echocardiographic screening studies put prevalence of RHD at 8-57/1000 children *Zuhlke et al.2013*
- True prevalence closer to 62-78 million individuals worldwide; 1.4 billion deaths each year *Zuhlke et al.2013*

ARF/RHD in PNG

- Burden of disease unknown
- Poor national surveillance system for ARF/RHD - database and follow up essential
- Prospective population based studies required
- Provincial screening 2021 in 10 provinces
 - 16% of new cases referred for echo had ARF/RHD (40/256)
- PMGH echo clinic 2021
 - 33% of new cases referred for echo had ARF/RHD (90/271)

Importance of ARF/RHD

- Endemic in many parts of the developing world where they cause significant morbidity & mortality as well as economic hardship *Carapetis et al. 1997; Carapetis & Currie 1999; Steer et al. 2002*
- ARF can progress to chronic RHD in 80% of cases *Carapetis et al. 2000, 2005*
- Patients with symptomatic chronic RHD face high rates of mortality (16.9% in 2yrs) and morbidity *Zuhlke et al. 2016*
- Morbidity relates to development of complications
 - Heart failure, Atrial fibrillation, Stroke, Recurrent carditis, Infective endocarditis

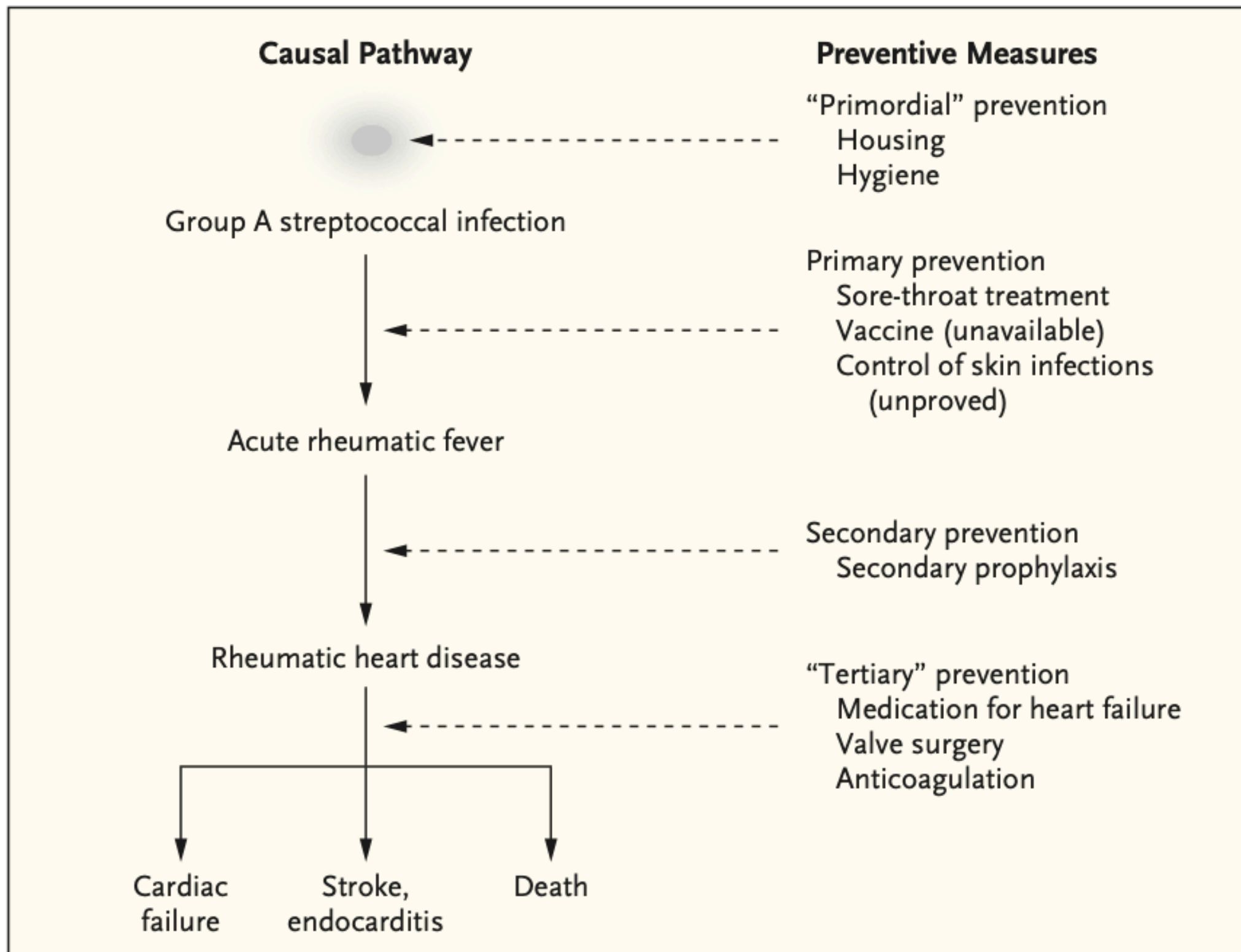
- Morbidity also exacerbated by limited resource allocation to operate on such patients
- In resource limited settings like ours, prevention and control of ARF & RHD may be a cost effective way to reduce morbidity and mortality of chronic RHD

Prevention & Control of ARF & RHD

Identified by the WHO Expert Report on RHD

Undertaken at number of levels

1. **Primordial prevention** - improvement of environmental, social & economic conditions of populations at risk of RF & RHD
2. **Primary prevention** - Refers to treatment of acute streptococcal pharyngitis with antibiotics to reduce incidence of ARF
3. **Secondary prevention** - use of antibiotic prophylaxis to reduce recurrence of ARF & development or progression of RHD
4. **Tertiary prevention** - medical & surgical treatment of the complications of ARF/RHD



Potential Preventive Measures for Rheumatic Fever and Rheumatic Heart Disease.

"Sore-throat treatment" refers to primary prophylaxis — that is, diagnosis and treatment of group A streptococcal pharyngitis.

Primordial Prevention

Improvement of environmental, social & economic conditions of populations at risk of RF & RHD

- Involves prophylactic strategies to avoid GAS infection
- GAS transmission facilitated by close contact between people
- Living conditions
- Knowledge regarding importance of sore throat caused by GAS
- Understanding of the mechanisms of transmission
- Important for public and health professionals to know

Primary Prevention

Refers to treatment of acute streptococcal pharyngitis with antibiotics to reduce incidence of ARF

- Accomplished by prompt diagnosis & ABx treatment of GAS tonsillopharyngitis; GAS skin infection also implicated in ARF pathogenesis
- Appropriate ABx treatment prevents ARF in most cases
- However, at least one-third of ARF episodes occur in the setting of subclinical streptococcal infection
- ABx options: Penicillins preferred - oral Pen V or amoxcil for 10days
- Alternatives for allergy to penicillin: Cephalexin, Azithromycin

- Challenges:
 - Determining whether the tonsillopharyngitis is due to GAS or other organisms
 - Readily available testing for GAS
- Other general measure - Hand hygiene

Secondary Prevention

Use of antibiotic prophylaxis to prevent recurrence of ARF and development or progression of RHD

- The importance of secondary penicillin prophylaxis for prevention of recurrent ARF and progressive RHD cannot be overemphasised
- This strategy has been proven in RCTs to prevent recurrence of ARF
- Remains the single most important step of management of ARF
- There is strong evidence that secondary prophylaxis reduces severity of RHD by preventing progression

Carapetis et al, 2016

ARF

- Timely and correct diagnosis of ARF & RHD important
- ARF diagnosed using the Jones criteria
- Many patients with RHD lack a history of past ARF; initial or recurrent insults may have been subclinical or not detected
 - Leads to delayed diagnosis and onset of secondary prophylaxis
- Presence of carditis on initial diagnosis of ARF will also determine duration of secondary prophylaxis

- Carditis in ARF
 - classically considered pancarditis
 - But predominant manifestation is involvement of endocarditis presenting as valvulitis
 - Mitral valve and aortic valve mostly affected
- Presence of valvulitis established by auscultatory findings + echo evidence of mitral or aortic regurgitation (MR/AR)
- If valvulitis severe, acute heart failure may occur

Revised Jones criteria

A. For all patient populations with evidence of preceding GAS infection	
Diagnosis: initial ARF	2 Major manifestations or 1 major plus 2 minor manifestations
Diagnosis: recurrent ARF	2 Major or 1 major and 2 minor or 3 minor
B. Major criteria	
Low-risk populations*	Moderate- and high-risk populations
Carditis [¶]	Carditis
<ul style="list-style-type: none"> Clinical and/or subclinical 	<ul style="list-style-type: none"> Clinical and/or subclinical
Arthritis	Arthritis
<ul style="list-style-type: none"> Polyarthrititis only 	<ul style="list-style-type: none"> Monoarthrititis or polyarthrititis Polyarthralgia^Δ
Chorea	Chorea
Erythema marginatum	Erythema marginatum
Subcutaneous nodules	Subcutaneous nodules
C. Minor criteria	
Low-risk populations*	Moderate- and high-risk populations
Polyarthralgia	Monoarthralgia
Fever ($\geq 38.5^{\circ}\text{C}$)	Fever ($\geq 38^{\circ}\text{C}$)
ESR ≥ 60 mm in the first hour and/or CRP ≥ 3.0 mg/dL [◇]	ESR ≥ 30 mm/h and/or CRP ≥ 3.0 mg/dL [◇]
Prolonged PR interval, after accounting for age variability (unless carditis is a major criterion)	Prolonged PR interval, after accounting for age variability (unless carditis is a major criterion)

Evidence of preceding GAS infection is required for both populations.

Treatment of ARF - 4 major goals

- Symptomatic relief of acute disease manifestations
- Eradication of group of GAS
- Prophylaxis against future GAS infection to prevent progression of cardiac disease
- Provision of education for the patient and patient's caregivers

Box 3 | **Priorities in management of ARF**

Key management priorities in acute rheumatic fever (ARF) and the main actions used to address them include:

Diagnosis

- Hospitalization for assessment and investigations, including echocardiography, acute phase reactants, streptococcal serology and tests for other differential diagnoses

Eradication of group A *Streptococcus* from the throat

- Single dose benzathine penicillin G

Symptomatic treatment of joint involvement and fever

- Nonsteroidal anti-inflammatory drugs (paracetamol may be used until diagnosis has been confirmed)

Management of heart failure

- Bed rest, fluid restriction and cardiac medications
- Corticosteroids may be considered for severe heart failure
- Deferral of surgery, if possible, until acute inflammation has subsided

Management of chorea

- Rest and calm environment
- For severe or refractory cases, administration of valproic acid, carbamazepine or corticosteroids may be considered

Commencement of long-term care

- Education and registration for long-term care
- First dose of benzathine penicillin G (to eradicate group A *Streptococcus* from the throat)

RHD

- RHD with chronic valvular lesions is a transition from rheumatic carditis that evolve over years after ≥ 1 episode of ARF
- Mitral valve more commonly involved than aortic valve
- MR most common finding of RHD
- Progression to mitral stenosis occurs over several years due to fibrosis and calcification as a result of repeated insults of ARF
- Diagnosis of RHD generally confirmed by echo - assessment of valve morphology & severity of valve dysfunction
- The World Heart Federation criteria used for echo diagnosis of RHD

Table 2. Recommended Durations of Secondary Prophylaxis According to International Guidelines

Guideline	Secondary Prophylaxis Duration Recommended
American (AHA 2009) ⁶⁰	ARF with carditis and residual heart disease: until age 40 y or for 10 y after last ARF (whichever is longer); lifetime prophylaxis may be needed
	ARF with carditis but no residual heart disease: until age 21 y or for 10 y after last ARF (whichever is longer)
	ARF without carditis: until age 21 y or for 5 y after last ARF (whichever is longer)
WHO Expert Consultation Geneva (2004) ⁶³	Lifelong if severe valvular disease or after valve surgery
	For 10 y after last ARF or until age 25 y in patients with previous diagnosis of carditis
	For 5 y after last ARF or until age 18 y in patients without proven carditis
Indian (2008) ⁶⁴	Lifelong in severe disease or postintervention patients; may opt for secondary prophylaxis until age 40 y
	ARF with healed, mild, or moderate carditis: until age 25 y or for 10 y after last ARF (whichever is longer)
	ARF without carditis: until age 18 y or for 5 y after last ARF (whichever is longer)
New Zealand (2014) ⁶⁵	After definite/probable ARF, continue prophylaxis for at least 10 y; consider 5 y of prophylaxis after ARF in patients with mild or no carditis >21 y of age or in patients with ARF classified as “possible”
	Severe RHD generally until age 40 y, with review at age 30 y
	Moderate RHD until age 30 y
	Mild RHD or ARF without RHD diagnosis, until age 21 y or for 10 y after last ARF (whichever is longer)
Australian (2020) ⁶²	Possible ARF: 12 mo
	Probable or definite ARF without carditis: minimum of 5 y or until age 21 y (whichever is longer)
	Borderline RHD: not usually recommended but can be considered for 1–3 y based on risk factors
	Mild RHD: If documented history of ARF, then a minimum of 10 y after the most recent episode of ARF or until age 21 y (whichever is longer) If no documented history of ARF and aged <35 y, then a minimum of 5 y after diagnosis of RHD or until age 21 y (whichever is longer)
	Moderate RHD: If documented history of ARF, then a minimum of 10 y after the most recent episode of ARF or until age 35 y (whichever is longer) If no documented history of ARF and aged <35 y, then a minimum of 5 y after diagnosis of RHD or until age 35 y (whichever is longer)
	Severe RHD: If documented history of ARF, then a minimum of 10 y after the most recent episode of ARF or until age 40 y (whichever is longer) If no documented history of ARF, then a minimum of 5 y after diagnosis of RHD or until age 40 y (whichever is longer)

AHA indicates American Heart Association; ARF, acute rheumatic fever; RHD, rheumatic heart disease; and WHO, World Health Organization.

Secondary prophylaxis for rheumatic fever - Duration of therapy

Category	Duration after last attack
Rheumatic fever with carditis and residual heart disease (persistent valvular disease*)	10 years or until 40 years of age (whichever is longer) Sometimes lifelong prophylaxis (refer to UpToDate topics on treatment and prevention of acute rheumatic fever and management and prevention of rheumatic heart disease)
Rheumatic fever with carditis but no residual heart disease (no valvular disease*)	10 years or until 21 years of age (whichever is longer)
Rheumatic fever without carditis	5 years or until 21 years of age (whichever is longer)

* Clinical or echocardiographic evidence.

Modified with permission from: Gerber MA, Baltimore RS, Eaton CB, et al. Prevention of Rheumatic Fever and Diagnosis and Treatment of Acute Streptococcal Pharyngitis: A Scientific Statement From the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee of the Council on Cardiovascular Disease in the Young, the Interdisciplinary Council on Functional Genomics and Translational Biology, and the Interdisciplinary Council on Quality of Care and Outcomes Research. Circulation 2009; 119(11):1541-51. Copyright © 2009 Lippincott Williams & Wilkins.

Secondary prophylaxis for rheumatic fever - Selection of therapy

	Continuous regimen	
	Children >27 kg and adults	Children ≤27 kg
Penicillin G benzathine intramuscular (Bicillin LA, benzathine benzympenicillin)*	1.2 million units every 21 to 28 days [¶]	600,000 units every 21 to 28 days [¶]
Penicillin V oral*	250 mg orally twice daily	250 mg orally twice daily

Parenteral penicillin by deep intramuscular injection is preferred for all patients receiving secondary prophylaxis. Oral medication is considered second line.

* Macrolides are acceptable alternatives for patients who cannot take penicillins. Optimal drug selection and dosing for prophylaxis is not known. Some experts use azithromycin dosed at 6 mg/kg orally once daily (up to 250 mg/day).

¶ The shorter interval (21 days) is recommended in high-risk situations (eg, a patient has had an episode of recurrent acute rheumatic fever despite adherence to once every 28-day regimen). Refer to UpToDate topic on treatment and prevention of acute rheumatic fever.

Role of active case detection & screening in secondary prevention

- Reality today
 - Many patients living with RHD are unaware of their diagnosis & the sore throat/ARF preceding RHD
 - Many RHD-endemic areas, majority of patients seek help once severe RHD develops & present with complication
 - Access to life-saving surgical or catheter-based interventions often limited or cost prohibited
- The cumulative nature of repetitive cases of ARF that lead to RHD means there is typically a latent period between the initial ARF episode & the development of advanced cardiac disease
- Screening or active case finding aims to identify individuals with RHD during this latent period and commence secondary prophylaxis

Table 1. Proposed RHD Definitions

Latent RHD	All cases of RHD diagnosed through echocardiographic screening, to include previously unrecognized clinical RHD and subclinical RHD
Clinical RHD	All cases of RHD that have clinical signs or symptoms including pathological heart murmur* diagnosed either through echocardiographic screening or clinical evaluation. Clinical RHD is typically more advanced than subclinical RHD.
Subclinical RHD	All cases of RHD that do not have clinical signs or symptoms including heart murmur.* Subclinical RHD is only diagnosed by echocardiography and is typically less advanced than clinical RHD.

RHD indicates rheumatic heart disease.

*Detection of a pathological heart murmur without echocardiography has been shown to be poorly sensitive and specific in echocardiographic screening studies for RHD.

- The WHO recommends school-based screening for RHD in high prevalence regions and populations
- Studies in 3 countries -Mozambique, Cambodia & Tonga -have shown that echocardiography as a primary screening tool for RHD is extremely sensitive; up to 13x more sensitive than auscultation
- To date, screening & active case finding have been almost exclusively performed in the research arena & focused predominantly on school-aged children
 - Key focus has been to:
 - Establish disease burden, thereby demonstrating need for active case finding
 - Use prevalence data for regional & global advocacy
 - Ascertain the short and medium term outcomes of echo detected latent RHD, thereby demonstrating its clinical significance
 - Develop models to make echocardiographic screening practical and affordable in resource poor settings, by evaluating task-shifting and the use of cheaper handheld machines

Tertiary Prevention

Medical & surgical treatment of the complications of ARF/RHD

Medical care

- Optimal medical care critical to minimise morbidity and mortality related to RHD
- Sequelae of RHD - Heart failure, atrial fibrillation, stroke, infective endocarditis
- Availability of WHO-listed essential cardiac medications including diuretics, ACE inhibitors & β -blockers effective in clinical care
- Optimal medical care also requires access to basic diagnostic modalities - ECG, Echo, biochemical & microbiological blood test

Medical care

- Heart failure
 - Pharmacological management only option in resource limited settings for symptomatic improvement; Surgical or catheter-based treatment unavailable
 - Symptomatic Mx of moderate - severe MR
 - Diuretics - Loop & spironolactone
 - Afterload reduction with vasodilator - ACE inhibitor
 - Digoxin may be considered
 - MS - proven effective treatment is catheter or surgical intervention; Diuretics indicated to reduce preload
 - AR - treatment targeted at symptom relief & treatment of underlying LV dysfunction & HF - ACE inhibitors

Surgical care

- Indicated when there is severe valvular dysfunction, especially if patient is symptomatic
- Exception for isolated severe MS for which balloon mitral valvuloplasty may be procedure of choice

Table 3 | **Indications for cardiac surgery in RHD**

Condition	Patient group	Criteria
Severe mitral regurgitation	Adults	<ul style="list-style-type: none"> • Severe mitral regurgitation with symptoms (NYHA class 2–4) and an LVEF of >30% • Asymptomatic mitral regurgitation and one of the following: LVESD of ≥40 mm, impaired left ventricular function with an LVEF of >30% and <60%, pulmonary hypertension of >50 mmHg or new onset atrial fibrillation • Moderate to severe mitral regurgitation with an LVEF of >60% and an LVESD of <40 mm, and only if the valve is judged to have a high likelihood of repair
	Children	<ul style="list-style-type: none"> • Severe mitral regurgitation with symptoms of breathlessness • Asymptomatic mitral regurgitation and one of the following: impaired left ventricular function of <60%, an LVESD z-score of ≥2.5 mm or pulmonary hypertension of >50 mmHg
Mitral stenosis*	Adults and children	<ul style="list-style-type: none"> • Severe mitral stenosis with symptoms (NYHA class 2–4) • Asymptomatic severe mitral stenosis and one of the following: paroxysmal atrial fibrillation, a mitral valve area of <1.5 cm², pulmonary hypertension of >50 mmHg or thromboembolism
Severe aortic regurgitation	Adults	<ul style="list-style-type: none"> • Symptoms NYHA class 2–4 • Asymptomatic severe aortic regurgitation and one of the following: an LVESD of ≥50 mm, impaired left ventricular function with an LVEF of <50% or a LVEDD of >65 mm
	Children	<ul style="list-style-type: none"> • Symptoms • Asymptomatic severe aortic regurgitation with an LVESV z-score of >4 and impaired left ventricular function with an LVEF of <50%

LVEDD, left ventricular end-diastolic dimension; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic dimension; LVESV, left ventricular end-systolic volume; NYHA, New York Heart Association; RHD, rheumatic heart disease.

*Mitral valvuloplasty or cardiac surgery is recommended.

Way forward for us!

Establish true burden of RHD in PNG

- A fundamental prerequisite for developing an objective, quantified argument for policy change & prioritisation of RHD in limited resource environments
 - Establishment of high quality, regularly maintained ARF/RHD registries - vital component of primary data collection
 - Making ARF & RHD notifiable diseases seems to help increase case detection & establish disease burden
 - National Surveillance system
 - Prospective population based study
 - Screening in school aged children

Rheumatic Fever / Rheumatic Heart Disease Case Report Form

Province: _____ Hospital: _____

Examiners Name: _____ Date of Report: dd / mm/ yy

Patient Identification

Patient's Name: _____	Patient's Sex: Male Female
Mother's Name: _____	Patient's date of birth: dd / mm/ yy
Father's Name: _____	Patient's age: years ____ months ____
Permanent Address (to find child for follow-up): _____	Parent's mobile telephone number: _____
Admission ID # _____	

Examination for Rheumatic Fever and Rheumatic Heart Disease

Date of examination: dd / mm/ yy

Date of onset of symptoms: dd / mm/ yy

Acute rheumatic fever is diagnosed clinically (Jones criteria): Two major criteria OR 1 major *and* 2 minor criteria**Major criteria**

Previous rheumatic fever or rheumatic heart disease:	Y N U	If yes, date previously diagnosed: dd / mm/ yy
Recent sore throat	Y N U	
New heart murmur	Y N U	
Polyarthritis (swelling and pain of ≥ 1 joints)	Y N U	
Subcutaneous nodules (raised swellings in skin)	Y N U	
Erythema marginatum (red rash without other cause)	Y N U	
Chorea	Y N U	

Minor criteria

Fever	Y N U
ESR >30 mm/Hr	Y N U
Prolonged PR interval on ECG	Y N U
Polyarthralgia or aseptic monoarthritis	Y N U

Rheumatic Heart Disease complications

Heart failure	Y N
Atrial fibrillation	Y N
Infective endocarditis	Y N
Stroke	Y N

All children need ongoing antibiotic prophylaxis

Give monthly benzathine penicillin: weight 20kg or less: 600,000 IU (450mg) weight >20kg: 1,200,000 IU (900mg)

Date commenced penicillin prophylaxis (date commenced): dd / mm/ yy

Book every 4 weeks for follow-up appointment**ENTER PATIENT'S DETAILS IN WARD CARDIAC REGISTER BOOK****Treatment received (see PNG Standard Treatment Manual for guidance on treatment for RHD)**

Aspirin	Y N U	Oxygen	Y N U
Prednisolone	Y N U	Blood transfusion	Y N U
Fruzemide	Y N U		

Date of discharge: dd / mm/ yySend completed form to **Dr Cornelia Kilalang**, Paediatric Department, Port Moresby General Hospital, Fax: 3250342. Email: ckilalang@yahoo.com

Screening programs

- The use of echocardiography for screening programs for case detection and institution of secondary prophylaxis; identify burden of disease
- Will require trained health workers in the use of the echo machine
- Will require portable echo machines
- Hand held machines now available

Echocardiography training

- Paediatricians in all provinces should have some basic echo training to diagnose RHD/ARF
- Attachments at PMGH with cardiology team

Community awareness

- Public awareness on GAS pharyngitis and ARF/RHD
- Posters, pamphlets, radio and TV talks

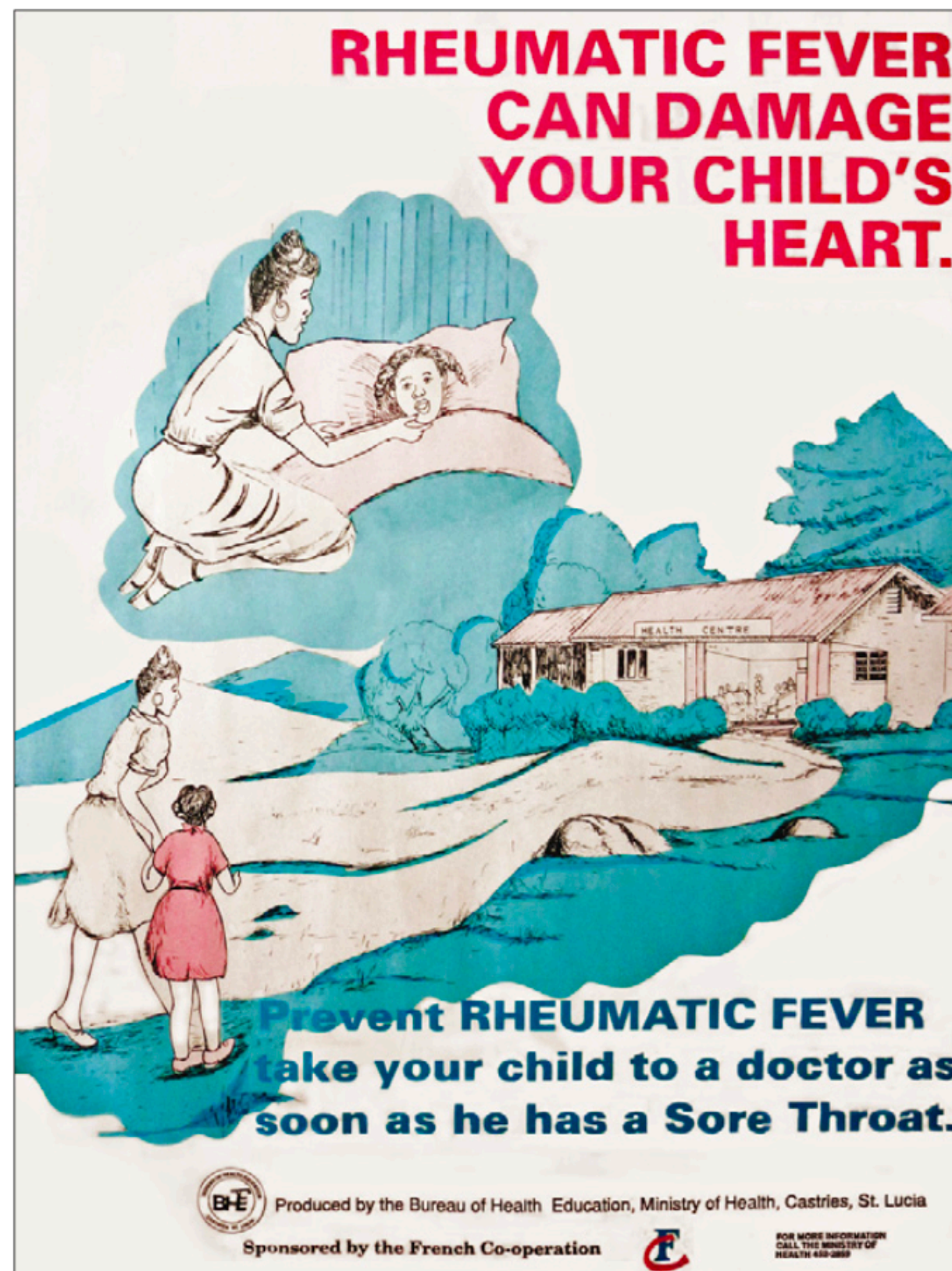


Figure 3: Poster to raise awareness of rheumatic fever in the low-income Caribbean island of Santa Lucia

Health authorities achieved success by redistributing part of the budget for rheumatic heart disease, taking some away from cardiac surgery and putting it towards a control programme for acute rheumatic fever and rheumatic heart disease, which included primary and secondary prophylaxis. Image courtesy of Xavier Jouven, Hôpital Européen Georges Pompidou.

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Thankyou!