# Acute rheumatic fever and rheumatic heart disease in resource-limited settings

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**ABSTRACT**

Poststreptococcal complications, such as acute rheumatic fever (ARF) and rheumatic heart disease (RHD), are common in resource-limited settings, with RHD recognised as the most common cause of paediatric heart disease worldwide. Managing these conditions in resource-limited settings can be challenging. We review the investigation and treatment options for ARF and RHD and, most importantly, prevention methods in an African setting.

## INTRODUCTION

Infections caused by Group A streptococcus (GAS) were identified as the ninth leading cause of global mortality from an individual pathogen in the 2004 World Health Report.[1] The WHO reported 18.1 million people living with serious GAS disease (acute rheumatic fever (ARF), rheumatic heart disease (RHD), RHD-related stroke or infective endocarditis and invasive GAS diseases (iGAS)) and 5 170 000 deaths in 2005. The majority of deaths were attributable to RHD complications, iGAS or acute poststreptococcal glomerular nephritis (APSGN). Close living conditions, overcrowding and poor hygiene promote transmission, while poor public health infrastructure prevents early recognition, prompt treatment and appropriate prevention measures.[2] While ARF is debilitating, it is the long-term sequelae of RHD that are the most devastating; young children and adolescents presenting with limited exercise capacity and young women presenting in pregnancy or post childbirth in congestive cardiac failure (CCF). Data from the paediatric cardiac clinic at the Medical Research Council Gambia Unit have demonstrated a median age of presentation with symptomatic RHD of 11 years (work in preparation, Watson *et al*). A systematic review by Carapetis *et al*[3] of GAS diseases estimated 1.88 million existing cases of ARF globally and 180 000 new cases annually.

RHD is the most common cause of paediatric heart disease worldwide.[4] The estimated prevalence among 5 year olds to 14 year olds in Sub-Saharan Africa is 5.7/1000 compared with 0.3/1000 in developed countries.[3] More recent echocardiographic (ECHO) screening programmes in Mozambique and Uganda have shown prevalence rates of RHD in schoolchildren of 30.4/1000 and 14.8/1000, respectively.[5 6] With RHD accounting for 5.9 million disability-adjusted life-years lost in 2002, this poses a significant medical and socioeconomic burden on populations.[1] In this article, we review the cardiac complications of iGAS disease, the challenges faced by the clinician working in resource-limited settings in their diagnosis and management, and approaches for overcoming some of these difficulties.

## ACUTE RHEUMATIC FEVER

### Case vignette

A 12-year-old Gambian girl presented to a health centre complaining of lethargy, arthralgia and intermittent fever. She was diagnosed with clinical malaria and treated accordingly.

Four months later she presented to clinic with similar symptoms. On examination she looked acutely unwell with a soft systolic murmur in the mitral area. Blood tests showed leukocytosis and a raised erythrocyte sedimentation rate (ESR) of 130 mm/h. Chest radiograph (CXR) showed cardiomegaly (figure 1A). ECG showed prolonged PR interval, and ECHO demonstrated a moderately dilated left ventricle and left atrium with moderate mitral regurgitation (see figure 1B and online supplementary video). A throat swab grew GAS. She was diagnosed with ARF and admitted for inpatient treatment; bed rest with mobilisation as symptoms allowed, intramuscular benzathine penicillin 900 mg, aspirin 50 mg/kg/day in five divided doses, lisinopril 10 mg once daily and frusemide 40 mg twice daily. Her symptoms improved, and she was discharged 7 days later on monthly intramuscular benzathine penicillin, regular frusemide, lisinopril and 3 months of aspirin. Outpatient follow-up was arranged 2 weeks later for repeat ESR and to monitor progress.

She missed her initial follow-up appointment due to financial constraints, but presented 2 months later complaining of worsening exercise tolerance since her medications finished. On examination she had a raised jugular venous pressure, pedal oedema, hepatomegaly of 6 cm and bilateral basal crackles on chest auscultation. Repeat ECHO revealed worsening mitral regurgitation. She was diagnosed with RHD with CCF and admitted for treatment with intravenous frusemide 1 mg/kg twice a day, lisinopril 10 mg once daily, intramuscular benzathine penicillin 900 mg and restarted on aspirin 50 mg/kg/day in five dived doses. Her symptoms gradually improved, and she was discharged to home 6 days later on her previous medications and the importance of regular outpatient follow-up emphasised.

### Diagnosing acute rheumatic fever: are the Jones criteria appropriate for high-prevalence settings?

ARF is a short-lived, multisystem, autoimmune disease that progresses to RHD in up to 80% of

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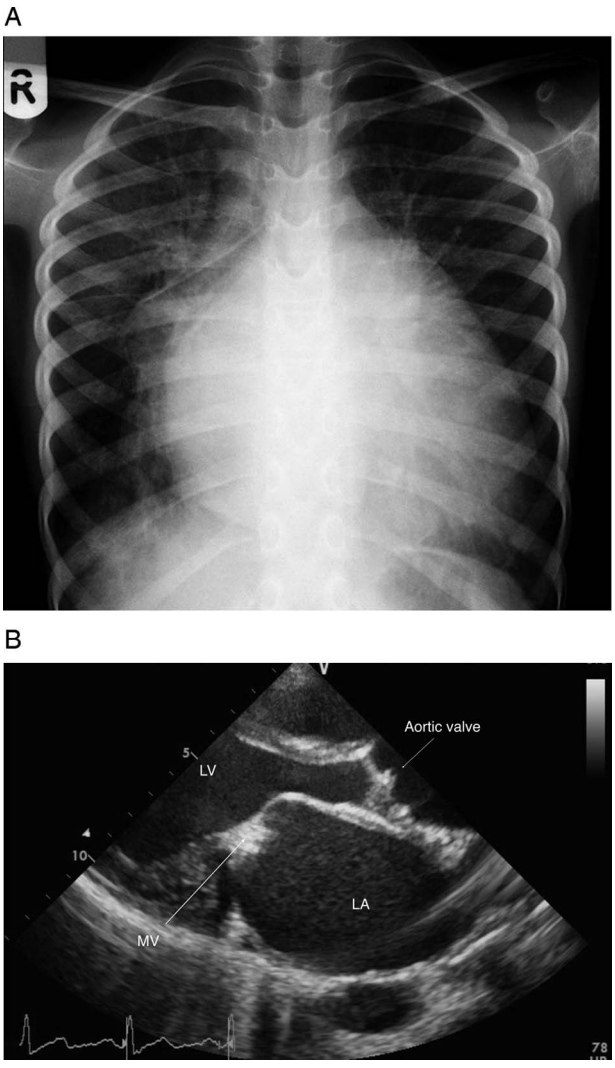


**Figure 1** (A) A plain chest radiograph demonstrating an enlarged cardiothoracic ratio due to cardiomegaly. The carina is also splayed due to the marked enlargement of the left atrium (LA). There is coexisting evidence of pulmonary congestion. (B) A parasternal long-axis echocardiographic view demonstrating a markedly dilated LA. The mitral valve (MV) leaflets appear thickened and have restricted movement with a typical 'hockey stick' appearance of the anterior MV leaflet. This view is shown as a moving image in online supplementary video. LV, left ventricle.

cases. There is no specific laboratory test for ARF and diagnosis remains a clinical one, based on major and minor criteria first outlined by Jones in 1944. Changes have been made to increase specificity at the expense of sensitivity, primarily for resource-rich countries. However, in areas where the risk of underdiagnosis may outweigh that of overdiagnosis, as in many resource-limited regions, the Jones criteria may be too insensitive. Recent Australian guidelines for high-prevalence communities (Aboriginal people and Torre Straits Islanders), defined as an ARF incidence >30/100 000 per year in 5 year olds to 14 year olds (or RHD all age prevalence >2/1000), are designed to increase diagnostic sensitivity particularly for patients who may have an atypical or delayed presentation, or where diagnostics such as C-reactive protein, ESR, antistreptolysin O titre and ECG are not routinely available.[7]

Table 1 illustrates the changes in ARF diagnostic criteria.

### What investigations are required to diagnose ARF?

All patients should be admitted ensuring appropriate investigations, management and education. Box 1 outlines the investigations recommended—these may have to be adapted depending on diagnostic facilities available. In particular, absence of cardiologists, appropriate ultrasound equipment or staff skilled in completing and interpreting findings may make cardiac ECHO unfeasible.

### How do you manage a patient with ARF?

Patients with carditis and heart failure should be put on bed rest. The initial use of salicylates, corticosteroids or non-steroidal anti-inflammatories should be avoided until clinical diagnosis is established as diagnostic symptoms can be masked.[8]

Table 2 illustrates treatment options summarised from the WHO and Australian guidelines for the management of ARF.

## RHEUMATIC HEART DISEASE

### Composite case vignette

A 15-year-old boy presented to our clinic with fever, cough, leg swelling and poor exercise tolerance for 4 months. On examination he was wasted, weight of 35 kg, short of breath at rest, had a soft systolic murmur and an irregular heart rate. He was admitted for investigation and treatment. CXR showed massive cardiomegaly and pulmonary plethora. ECHO demonstrated significantly thickened and regurgitant aortic and mitral valves (MV) resulting in a hugely dilated left atrium and ventricle. The tricuspid valve was similarly affected. Ventricular function was preserved, with an ejection fraction of 70%. He had an ESR of 50 mm/h without lymphocytosis and three negative blood cultures. Throat swab showed no growth. He was diagnosed with multivalvular RHD and CCF and managed with intravenous frusemide, lisinopril, penicillin prophylaxis and discharged 6 days later.

In the following year, he had eight further admissions with decompensated heart failure. Given the limited medical and surgical resources for patients with RHD in The Gambia, definitive surgical treatment (mitral and tricuspid annuloplasty and mechanical aortic valve (AV) replacement) was performed overseas, funded by a charitable organisation. He made a rapid postoperative recovery and is currently managed on intramuscular Benzathine Penicillin, lisinopril, bisoprolol and warfarin adjusted according to monthly international normalised ratio (INR) measurements. He has good exercise tolerance and significantly improved nutritional status.

### How do you diagnose RHD in low-resource settings?

ECHO is the most sensitive and specific diagnostic tool for RHD,[9] and standardised ECHO criteria for diagnosing asymptomatic RHD exist.[10] The most commonly affected valves are the MV and AV. Morphological features of MV disease in RHD include anterior MV leaflet thickening, chordal thickening, restricted leaflet motion and excessive leaflet tip motion in systole. Morphological features of AV in RHD include irregular or focal valve thickening, coaptation defect, restricted leaflet motion and prolapse.[10]

In countries with an effective ARF register and RHD screening programmes, early detection of RHD and secondary prophylaxis with regular penicillin offers the best possible outcome for patients.[10] However, in the absence of ECHO, auscultation has low sensitivity for the detection of subclinical RHD and disease is more often diagnosed when patients present with features of heart failure. Simplified screening

**Table 1** Evolution of diagnostic criteria for acute rheumatic fever since 1992

| Manifestation | AHA 1992 | WHO 2003 | Australia 2006 | | Australia 2012 | |
|---|---|---|---|---|---|---|
| | | | High risk | Low risk | High risk | Low risk |
| Carditis | Major | Major | Major | | Major | |
| Subclinical carditis | n/a | n/a | Major | | Major | n/a |
| Prolonged PR interval | Minor | Minor | Minor | | Minor | |
| Polyarthritis | Major | Major | Major | | Major | |
| Polyarthralgia | Minor | Minor | Major | Minor | Major | Minor |
| Aseptic mono-arthritis | | | Major | Minor | Major | Minor |
| Monoarthralgia | | | n/a | n/a | Minor | n/a |
| Subcutaneous nodules | Major | Major | Major | | Major | |
| Sydenham's chorea | Major | Major | Major | | Major | |
| Erythema marginatum | Major | Major | Major | | Major | |
| Fever | Minor | Minor | Minor | | Minor | |
| Inflammatory markers | Minor | Minor | Minor | | Minor | |
| Evidence of streptococcal infection | Required | Required | Required | | Required | |

Reproduced with kind permission from the Australian Guidelines[8] (http://www.rhdaustralia.org.au/resources/arf-rhd-guideline).
AHA, American Heart Association.

protocols using pocket-sized ECHO machines have been recently evaluated, and training non-physicians in their use holds promise for improved surveillance and implementation of effective secondary prophylaxis.[11 12]

## What is the progression of GAS disease to RHD and how can this be prevented?

GAS is a Gram-positive bacterium transmitted via droplet spread from people with pharyngeal colonisation or carriage. Pharyngitis and skin infection are the most common infection caused by GAS. ARF is a delayed autoimmune response to the GAS infection. Recurrent episodes of ARF lead to cardiac valvular damage and RHD. Prevention can be at four different stages as described in table 3 and figure 2.

### Primordial prevention

Primordial prevention has been successfully achieved in most developed countries, almost eradicating ARF in this setting, with associated loss of rheumatogenic GAS strains from the population.[13]

## What is the purpose of primary prevention?

When GAS colonises the oropharynx causing a superficial infection, an immune response is initiated, and ARF may present 2–3 weeks later. Primary prevention aims to identify those at greatest risk of developing ARF, typically children aged 5–14 years with a symptomatic GAS infection, and treat them with penicillin to eradicate the infection before the immune-mediated disease has taken hold. The role of GAS skin disease in the aetiology of ARF is still unclear, although growing evidence suggests the link between GAS skin disease, scabies and RHD may have been overlooked, particularly in tropical settings.[14]

Ideally patients presenting with fever and sore throat should be investigated with a throat swab and, if GAS positive, treated with appropriate antibiotic therapy. Treatment should be started within 9 days of onset of symptoms for effective primary prevention; see table 4 for WHO-recommended treatment. While penicillins are widely recommended for both primary and secondary prevention of GAS disease, there are reports of resistance in the literature.[15]

Unfortunately in many resource-limited settings, widespread use of penicillin for primary prevention is not routinely practised. Lack of awareness of the importance of treating pharyngitis to prevent ARF and RHD among both the population and health practitioners, and the tendency to consult traditional healers are likely contributing factors. However, a recent meta-analysis from South Africa has shown primary prevention to be highly cost effective; treatment of suspected GAS pharyngitis with a single, intramuscular benzathine penicillin had an estimated marginal cost of $46 in preventing one case of ARF.[16]

**Box 1 Investigations in acute rheumatic fever:[7]**

- Bloods—white blood cell, erythrocyte sedimentation rate or C-reactive protein
- Blood cultures (if febrile)
- ECG—if prolonged PR interval repeat in 2 weeks then at 2 months
- Chest radiograph if evidence of carditis (clinically or on echocardiography (ECHO))
- ECHO
- Throat swab for bacterial culture—before starting antibiotics
- Antistreptococcal serology—ASO and anti-DNase B titres (unavailable in many low-resource settings)

### Secondary prevention

Secondary prophylaxis is the only preventable measure that has proven both cost effective and practical in resource-limited settings, and has been recommended by WHO for the last 20 years.[8] Efficacy, however, requires accurate case detection and delivery of prophylaxis in the context of a formal, register-based, ARF and RHD control programme.[17]

Following discharge from hospital, all patients with ARF should commence penicillin prophylaxis and receive appropriate health education with regard to recurrent infection. Options for prophylaxis are monthly intramuscular benzathine penicillin 450 mg for weight <20 kg, 900 mg for weights >20 kg (or 600 000 units and 1 200 000 units, respectively), or penicillin V 250 mg twice daily for children <35 kg weight or 500 mg for ≥35 kg or, for patients with known penicillin allergies, oral erythromycin 250 or 500 mg twice daily. Prophylaxis should be sustained for a minimum of

**Table 2** Doses, regimens and indications for medications used in ARF[7 8]

| | Dose | Route | Duration |
|---|---|---|---|
| All patients should receive one of the following antibiotic regimens: | | | |
| Benzathine penicillin | 450 mg <20 kg<br>900 mg ≥20 kg | Intramuscularly | Single dose |
| Or | | | |
| Penicillin V | 250 mg twice daily (child)<br>500 mg twice daily (adolescent/adult) | Orally | 10 days |
| Or | | | |
| Erythromycin (if penicillin allergic) | 12.5 mg/kg up to 500 mg twice daily (child)<br>500 mg twice daily (adult) | Orally | 10 days |
| For symptom control of fever and arthritis while awaiting confirmed diagnosis: | | | |
| Paracetamol | 60 mg/kg/day given in four divided doses (max 4 g/day) | Orally | While symptomatic and before NSAIDs started |
| ± | | | |
| Codeine | 0.5–1 mg/kg/dose 4–6 hourly | Orally | While symptomatic and before NSAIDs started |
| For symptom control of fever and arthritis with confirmed ARF diagnosis: | | | |
| Aspirin | 50–60 mg/kg/day, increase if required to 80–100 mg/kg/day in 4–5 divided doses (If higher doses have been required, wean to 50–60 mg/kg/day when symptoms improve.) | Orally | While symptomatic<br>Stop when symptom free for 1–2 weeks |
| ± | | | |
| Ibuprofen | 30 mg/kg/day three times a day (max 1600 mg) | Orally | While symptomatic |
| Or | | | |
| Naproxen | 10–20 mg/kg/day twice daily (max 1250 mg) | Orally | While symptomatic |
| If no response to treatment, severe carditis, heart failure or pericarditis: | | | |
| Prednisolone | 1–2 mg/kg/day once daily (max 80 mg) | Orally | 1–3 weeks (case dependent) |

ARF, acute rheumatic fever; NSAIDs, non-steroidal anti-inflammatory drugs.

10 years after the last episode of ARF or until 21 years of age, whichever the longest. For severe valvular disease, penicillin treatment should be life-long. While the effectiveness of secondary prevention is proven, achieving effective delivery and uptake is often difficult. Oral antibiotics are inferior in effect to benzathine penicillin which has the advantage of monthly, low-cost injections. However, the need for painful injections and poor clinic attendance limit efficacy. While methods have been devised to minimise pain associated with intramuscular injection,[7] new strategies are urgently needed for prophylaxis regimens that are more convenient, less painful and longer acting.[18]

## Tertiary prevention

### Medical management

The aim of long-term RHD management is to prevent recurrent episodes of ARF, halting the progression of RHD and, in some cases, leading to resolution of valvular lesions.

In addition to penicillin prophylaxis, symptomatic patients with mitral or combined mitral and aortic regurgitation should be started on diuretics and an angiotensin-converting enzyme (ACE) inhibitor. Afterload reduction may aid reduction of the regurgitant fraction and improve forward flow, preserving myocardial function. Patients with predominantly mitral stenosis and symptomatic pulmonary venous congestion or pulmonary oedema should be managed with diuretics. Patients with severe mitral stenosis are at risk of atrial fibrillation and development of left atrial thrombus and systemic emboli, and benefit from ventricular rate control with β-blockers or digoxin and anticoagulation with warfarin. However, where warfarin and INR measurements are unavailable, aspirin is used. In patients with mitral stenosis, ACE inhibitors are not beneficial as they only serve to reduce systemic afterload where the left ventricular preload is limited by the mitral stenosis. Rheumatic tricuspid valve disease is not usually seen in isolation, and these patients are usually already on diuretics ±ACE inhibitors, depending on the dominant valve lesion present.

Preventing complications such as infective endocarditis also requires education on the benefits of maintaining good dental hygiene and for girls and young women the avoidance of earrings and other piercings.

**Table 3** Stages and methods of GAS prevention[13]

| Stage of prevention | Methods of prevention |
|---|---|
| Primordial | Improving social determinants of health |
| Primary | Treatment of initial GAS infections and future vaccinations |
| Secondary | Antibiotic prophylaxis for patients following ARF |
| Tertiary | Medical and surgical management of RHD |

ARF, acute rheumatic fever; GAS, Group A streptococcus; RHD, rheumatic heart disease.

### Surgical intervention

The late detection of RHD in low-income to middle-income countries leads to increased disease severity with a greater likelihood surgical intervention. Guidelines exist for the selection of patients for surgical intervention.[8] However, any symptomatic patient with valvular RHD and New York Heart Association class 2 or more should be considered for surgery. Selection criteria should take into account any comorbidity, long-term compliance with medication and access to follow-up. Finucane *et al* recently published selection criteria for surgical intervention in valvular RHD and excluded patients with severe ventricular dysfunction because of poor recovery.[19]

## What are the issues surrounding surgical intervention and long-term postoperative management in low-resource settings?

Patients with severe RHD die without cardiac surgery, and for most, access to surgical intervention is limited. Africa has just 1% of the world's cardiothoracic surgeons.[20]

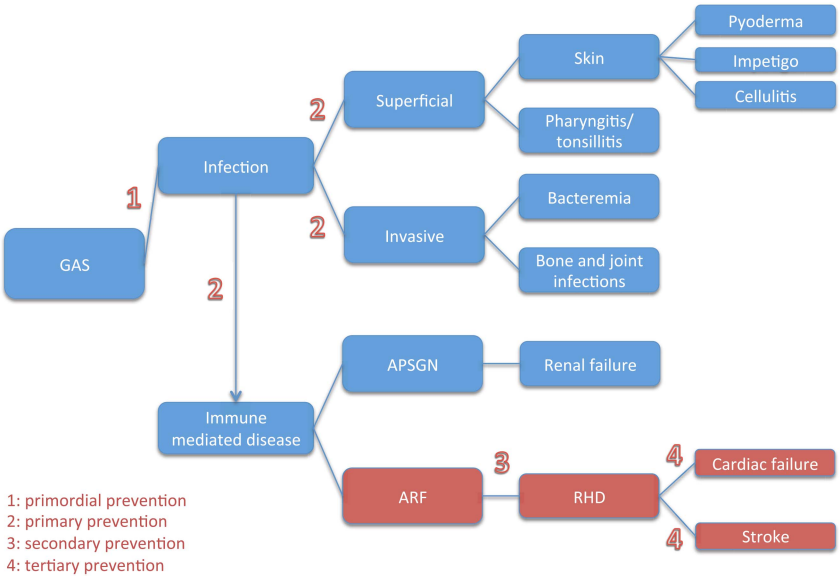


**Figure 2** Flow chart showing progression of Group A streptococcus (GAS) diseases and stages of prevention. APSGN, acute poststreptococcal glomerular nephritis; ARF, acute rheumatic fever; RHD, rheumatic heart disease.

Surgical outcomes depend on severity of disease, left ventricular function, nutritional status of the patient and long-term postoperative management. Patients with chronic RHD with poor ventricular function and cardiac failure may be too late for effective surgical intervention. The best outcomes will be in patients with preserved ventricular function and those in whom valve repair, rather than replacement, is viable, thus avoiding the need for warfarinisation.

The patterns of valve disease may also vary in some regions, and surgical expertise should be pooled in specialist centres to improve the outcome of valve repair for those patients. Increasingly, there is a positive move to develop regional cardiac surgical centres through international collaboration such as those in Egypt, Sudan and Ethiopia.[21]

Mechanical valve replacement in particular poses many potential complications with increased risk of thromboembolic events, prosthetic endocarditis and need for life-long anticoagulation. Finucane *et al* have highlighted the poor outcomes associated with mechanical valves and anticoagulation in patients with RHD from resource-limited settings.[19] Another study reported significant survival advantages in patients undergoing MV repair compared with replacement. Fifty per cent of patients with an MV replacement were found to have a significant haemorrhagic or thromboembolic event within 11 years of operation.[22]

Anticoagulation in resource-limited settings raises numerous issues. Availability of warfarin and reagents for regular INR checks may not be reliable. Poor adherence in adolescent patients is a serious concern, particularly where health education is limited. Regular attendance at clinic for review and anticoagulation status may become a significant and unexpected long-term financial burden.

Warfarinisation in adolescent women raises further concerns. Warfarin is teratogenic in the first trimester of pregnancy, and alternative anticoagulation is required both preconception and throughout the first trimester. However, subcutaneous low-molecular-weight heparin is either unavailable or unaffordable in many low-resource settings. Pregnancy is therefore not an option for the majority of young women with mechanical valves, contributing to social and cultural exclusion. Reproductive health is of strong psychological importance for women in low-resource countries; the ability to have and raise a child establishes social status for both the mother and the father. Coleman *et al* found a significant association between depression and infertility in Gambian women of childbearing age.[23] Therefore, long-term, accessible, acceptable and reliable contraception must be considered for all warfarinised women of childbearing age.

## What progress is being made in the development of a GAS vaccine?

The development of a safe, effective and affordable GAS vaccine will be the most cost-effective method for primary prevention of both ARF and RHD. Several vaccine candidates are

**Table 4** WHO-recommended treatment options for Group A streptococcus pharyngitis[1]

| Antibiotic | Dose | Route | Duration |
|---|---|---|---|
| Benzathine penicillin | 450 mg <20 kg<br>900 mg ≥20 kg | Intramuscularly | Single injection |
| Or | | | |
| Penicillin V | 250 mg twice daily–four times a day (child)<br>500 mg twice daily–four times a day (adolescent) | Orally | 10 days |
| Or | | | |
| Amoxicillin | 25–50 mg/kg/day three times a day | Orally | 10 days |
| Or | | | |
| Erythromycin (for penicillin-allergic patients) | 12.5 mg/kg twice daily (up to 500 mg) | Orally | 10 days |

in the early stages of development. However, progress with GAS vaccines has been hampered for a number of reasons, including lack of data on the molecular epidemiology of GAS strains; the theoretical risk that vaccines may induce ARF or APSGN through molecular mimicry or other autoimmune mechanisms (concerns that have been allayed by subsequent studies); immune correlates of protection against GAS required for vaccine evaluation are not clearly identified and the limited data on the global burden of disease associated with ARF, RHD, APSGN and iGAS.[24 25] Even with the development of an effective vaccine, issues of cost and accessibility to areas most in need may hinder availability.

## CONCLUSION

Although nearly eradicated in well-resourced countries, ARF and RHD are prevalent in resource-limited settings. Investigation and management can be challenging with limited resources and lack of specific expertise, and international guidelines may not be best suited for all settings.

The socioeconomic burden of RHD on society and public health services is considerable, with no effective prevention strategy in place in many countries, while surgical management is not a feasible long-term goal for the majority. Primary prevention is the best approach for the future, through primary prophylaxis and hopefully, an effective vaccine. To achieve this, a better understanding of the burden of disease in low-resource countries is required, including knowledge of the most prevalent GAS strains to aid future vaccine research, and establishment of good health systems for the effective delivery of preventative measures.

With ever-increasing migration into western Europe, there is potential for the re-emergence of ARF and RHD within developed countries, highlighting the importance of continued education and vigilance by healthcare workers to recognise the GAS diseases.

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## REFERENCES

1 World Health Organisation. The World Health Report, 2004: changing history. World Health Organization, 2004.
2 World Health Organisation. *The current evidence for the burden of group A streptococcal diseases*. Discussion papers on Child Health. Department of Child and Adolescent Health and Development. World Health Organisation, 2005.
3 Carapetis JR, Steer AC, Mulholland EK, *et al*. The global burden of group A streptococcal diseases. *Lancet Infect Dis* 2005;5:685–94.
4 Carapetis JR. Rheumatic heart disease in developing countries. *N Engl J Med* 2007;5:439–41.
5 Marijon E, Ou P, Celermajer DS, *et al*. Prevalence of rheumatic heart disease detected by echocardiographic screening. *N Engl J Med* 2007;5:470–6.
6 Beaton A, Okello E, Lwabi P, *et al*. Echocardiography screening for rheumatic heart disease in Ugandan schoolchildren. *Circulation* 2012;25:3127–32.
7 RHDAustralia (ARF/RHD writing group), National Heart Foundation of Australia and the Cardiac Society of Australia and New Zealand. Australian guideline for prevention, diagnosis and management of acute rheumatic fever and rheumatic heart disease (2nd edition). *Quick reference guides* 2012.
8 World Health Organisation. *Rheumatic fever and rheumatic heart disease: report of a WHO Expert Consultation. Geneva, 29 October–1 November 2001*. Geneva: World Health Organization, 2004.
9 Marijon E, Celermajer DS, Tafflet M, *et al*. Rheumatic heart disease screening by echocardiography the inadequacy of World Health Organization criteria for optimizing the diagnosis of subclinical disease. *Circulation* 2009;8:663–8.
10 Reményi B, Wilson N, Steer A, *et al*. World Heart Federation criteria for echocardiographic diagnosis of rheumatic heart disease—an evidence-based guideline. *Nat Rev Cardiol* 2012;9:297–309.
11 Beaton A, Lu JC, Aliku T, *et al*. The utility of handheld echocardiography for early rheumatic heart disease diagnosis: a field study. *Eur Heart J Cardiovasc Imaging* 2015. [Epub ahead of print 5 Jan 2015].
12 Mirabel M, Bacquelin R, Tafflet M, *et al*. Screening for rheumatic heart disease: evaluation of a focused cardiac ultrasound approach. *Circ Cardiovasc Imaging* 2015;8:1.
13 Ralph AP, Carapetis JR. Group a streptococcal diseases and their global burden. *Curr Top Microbiol Immunol* 2013;368:1–27.
14 Parks T, Smeesters PR, Steer AC. Streptococcal skin infection and rheumatic heart disease. *Curr Opin Infect Dis* 2012;25:145–53.
15 Passàli D, Lauriello M, Passali GC, *et al*. Group A streptococcus and its antibiotic resistance. *Acta Otorhinolaryngol Ital* 2007;27:27–32.
16 Robertson KA, Volmink JA, and Mayosi BM. Antibiotics for the primary prevention of acute rheumatic fever: a meta-analysis. *BMC Cardiovasc Disord* 2005;5:11.
17 Carapetis JR, McDonald M, Wilson NJ. Acute rheumatic fever. *Lancet* 2005;366:155–68.
18 Rémond MG, Wheaton GR, Walsh WF, *et al*. Acute rheumatic fever and rheumatic heart disease--priorities in prevention, diagnosis and management. A report of the CSANZ Indigenous Cardiovascular Health Conference, Alice Springs 2011. *Heart Lung Circ* 2012;21:632–8.
19 Finucane K and Wilson N. Priorities in cardiac surgery for rheumatic heart disease. *Global Heart* 2013;8:213–20.
20 Turina MI. European association for cardio-thoracic surgery: carrying the torch. *Eur J Cardiothorac Surg* 2002;22:857–63.
21 Swain JD, Mucumbisti J, Rusingiza E, *et al*. Cardiac surgery for advanced rheumatic heart disease in Rwanda. *Lancet Glob Health* 2014;2:141–2.
22 Remenyi B, Webb R, Gentles T, *et al*. Improved long-term survival for rheumatic mitral valve repair compared to replacement in the young. *World J Pediatr Congenit Heart Surg* 2013;4:155–64.
23 Coleman R, Morison L, Paine K, *et al*. Women's reproductive health and depression, a community survery in the Gambia, West Africa. *Soc Psychiatry Psychiatr Epidemiol* 2006;41:720–7.
24 Steer AC, Dale JB, Carapetis JR. Progress toward a global group a streptococcal vaccine. *Pediatr Infect Dis J* 2013;32:180–2.
25 Dale JB, Fischetti VA, Carapetis JR, *et al*. Group A streptococcal vaccines: paving a path for accelerated development. *Vaccine* 2013;31:B216–22.

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