

# Rheumatic Fever

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This chapter is made up of edited extracts (by Dr Dan Ewald, with permission from the authors and publisher) from Couzos S & Carapetis J 2003, 'Rheumatic Fever', in Aboriginal Primary Health Care: An evidence-based approach, 2nd edition, Oxford University Press, Melbourne. Readers are advised to refer to the full chapter for detailed information on the prevention and management of rheumatic fever, treatment goals and targets, case management, program implementation, data collection, and performance indicators.

## Summary

Rheumatic fever is an autoimmune sequel of infection with group A streptococcus (GAS), characterised by damage to heart valves, brain, joints, and/or skin, and less commonly heart muscle, pericardium, or lungs. The heart valves may be left with permanent damage. This is rheumatic heart disease (RHD), and its prevention is the main aim of all public health efforts for rheumatic fever. RHD remains the most common acquired heart disease of childhood in the world and in Central and Northern Australian Aboriginal people in particular. It is a classic disease of poverty, as overcrowding and difficulties in maintaining community and personal hygiene facilitate transmission of GAS.

Clinicians need to suspect acute rheumatic fever (ARF) to avoid a missed diagnosis and consequently missed secondary prevention of recurrence and RHD.

Secondary prophylaxis of rheumatic fever is the single most important strategy. Benzathine penicillin G is the best prophylactic agent, given every four weeks. A coordinated control program, with rheumatic fever registers, is the best way to improve benzathine penicillin G adherence rates and ensure adequate clinical follow-up, including specialist review and echocardiography.

There are various relevant national and international policy documents.<sup>1,2</sup>

## Background

Rheumatic fever is now rare in Australia with the exception of Aboriginal people in Northern and Central Australia. It is a notifiable disease in the Northern Territory.<sup>3</sup>

The highest confirmed incidence yet reported was 508 per 100 000 children aged 5-14 years in 12 remote Aboriginal communities in northern Australia between 1987 and 1996.<sup>4</sup> The point prevalence of RHD in all ages (as of March 1997) was 11.8 per 1000 in the Top End Aboriginal population, and 22.4 per 1000 in the 12 communities with good ascertainment.<sup>5</sup>

While the incidence of ARF peaked between five and 14 years of age, the prevalence of RHD was greatest in those aged between 20 and 34 years.<sup>4</sup>

Sydenham's chorea features in 28% of ARF presentations in the Top End.<sup>6,7</sup> In one Central Australian community, the annual incidence of ARF was reported as high as 815 per 100 000 persons. The point prevalence for RHD was between 7.9 and 12.3 per 1000 persons.<sup>8</sup> These figures are similar to those observed in the Kimberley region of Western Australia.<sup>9,10,11</sup> The prevalence figures in the north of Australia are over 30 times higher, while the incidence rate for ARF is over 1000 times higher, than those of industrialised nations.<sup>12</sup>

ARF and RHD carry high risks of premature death and considerable morbidity.<sup>13</sup> In the Northern Territory between 1987 and 1996, there were 182 deaths due to ARF or RHD, 94% in Aboriginal people.

**Skin or throat infection as the source**

There has been a long-held view that rheumatic fever only develops following GAS throat infection (not skin) and the American Heart Association restated this in 1992.<sup>14</sup> This is difficult to reconcile with the epidemiology in Aboriginal communities.

The prevalence of throat carriage with GAS is low in Aboriginal children of Northern Australia<sup>15,16</sup>, and presentations with sore throat to clinics in Aboriginal communities may not be common.<sup>17</sup> This raises the possibility that skin infection with GAS may lead to ARF either directly or by skin GAS infecting the throat.

**Case definitions**

The Jones criteria<sup>14</sup> for diagnosis is applicable only to the initial attack of ARF. The diagnosis of ARF recurrences requires special interpretation of the Jones criteria. The diagnosis of chronic RDH is based on clinical and/or echocardiographic features of typical rheumatic heart valve lesions.

**The Jones criteria for guiding the diagnosis of the initial attack of ARF, updated 1992.**

Major manifestations	Minor manifestations
Carditis	Fever
Polyarthrititis	Arthralgia
Chorea	Elevated acute phase
Subcutaneous nodules	Prolonged PR interval
Erythema marginatum	

Plus

**Supporting evidence of a recent group A streptococcal infection**

- Positive throat culture or rapid antigen test OR
- Elevated or increasing streptococcal antibody titre

The presence of two major or one major and two minor manifestations, plus evidence of a preceding GAS infection, indicates a high likelihood of ARF.

**Two important exceptions to the Jones criteria**

Sydenham's chorea commonly occurs without other manifestations of ARF and following a prolonged latent period after GAS infection (after serological markers have returned to normal), so isolated chorea of itself is

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sufficient to fulfil the criteria if other causes of chorea have been excluded.

The finding of a sub-acute or chronic carditis (usually manifest by a murmur and raised ESR) is also an exception.<sup>14</sup>

Recurrent attacks can be diagnosed with few of the criteria (one major or more than one minor), provided there is evidence of a recent GAS infection,<sup>18</sup> and other diagnoses have been excluded.<sup>19-22</sup>

### **Making a diagnosis**

The diagnosis of rheumatic fever may be easily missed; in the Northern Territory nearly half of all patients diagnosed with RDH had no recognised history of ARF.<sup>6</sup> It is likely that many cases were missed through low awareness of the staff, and some were subclinical or mild.

### **Throat culture for GAS**

Many infections would have cleared before ARF developed, and throat culture can have poor sensitivity.<sup>12,23</sup> Of Top End Aboriginal patients with ARF who had throat swabs, only 4% were positive for GAS.<sup>22</sup>

### **Rapid antigen detection kits**

Rapid antigen detection kits for GAS diagnosis have been used in the USA for many years and were found to be cost effective in the primary health care setting.<sup>24</sup> These are not recommended for CARPA regions where rheumatic fever is still common. (See Sore Throat chapter).

### **Diagnosing tonsillitis**

Making the clinical diagnosis of bacterial tonsillitis or pharyngitis can be difficult. Clinical prediction rules and screening tests for GAS are not recommended for Aboriginal children because of the lack of validation for their use in this group. (See chapter on Sore Throat)

### **Streptococcal antibody testing**

Either the ASOT (anti-streptolysin O titre) or anti-DNase B (anti-deoxyribonuclease B) titre can be used to confirm a recent GAS infection for the purposes of rheumatic fever diagnosis. Both the ASOT and anti-DNase B titres are elevated following GAS pharyngitis but, by contrast, skin infection with GAS leads to a strong anti-DNase B but a relatively weak ASOT response.<sup>25,26,27</sup>

An elevated ASOT occurs in more than 80% of patients after GAS tonsillitis, and adding the anti-DNase B titre improves the sensitivity of diagnosis to approximately 95%.<sup>14</sup> A twofold rise in ASOT is usually accepted as confirmation of a recent GAS infection. However, streptococci other than GAS can cause an elevated ASOT and elevation may not occur if antibiotics are given early in the infection.<sup>28</sup> In many communities, most children will have had a recent GAS infection and background serology titres may be high.<sup>29</sup> Therefore, a single ASOT result must be interpreted with caution in the diagnosis of recent GAS infection.<sup>28</sup>

In a Northern Territory study of 293 cases of confirmed non-chorea ARF, both titres were elevated in 82% of cases, the ASOT was the only elevated test in 1% of cases, whereas the anti-DNase B titre was the only elevated test in 17%.<sup>22</sup>

## **Prevention: Primary prevention**

### **Decreasing GAS infections**

Acute rheumatic fever is still common in developing countries, probably because overcrowding and inadequate community sanitation increase the exposure of susceptible children to GAS.<sup>30,31</sup> This is likely to be important in the Aboriginal health setting.<sup>32</sup>

### **Mass antibiotic prophylaxis to prevent initial episodes**

There have been numerous outbreaks of rheumatic fever in United States military training camps. Benzathine penicillin prophylaxis given at the start of training decreased occurrences, and has been continued since 1953.<sup>33</sup> This is partly based on prevented cellulitis and pharyngitis as well as decreased ARF. This approach (for limited duration) is not recommended for Aboriginal communities.

### **Targeted screening and antibiotic prophylaxis**

A 1993 Australian primary prevention trial concluded that rheumatic fever could be prevented.<sup>34</sup> However, there are limitations (design) to how this study can influence policy.

A review of primary prophylaxis did not support the treatment of family contacts of those with GAS pharyngitis. There was some evidence that primary prophylaxis could reduce GAS infections but did not prevent non-suppurative sequelae.<sup>35</sup>

Asymptomatic GAS carriage is not believed to pose a threat to rheumatic fever control.

### **Primary chemoprophylaxis**

#### **Treatment of symptomatic bacterial tonsillitis/ pharyngitis (also see the Sore Throat chapter for more detail).**

GAS tonsillitis can be treated with oral, or better with intramuscular (IM), antibiotics and this strategy prevents development of ARF.<sup>36,37,30,38</sup>

A systematic review suggested that the routine use of antibiotics for sore throat when the prevalence of pharyngeal GAS is high (>20%) is justified, and that there is evidence of a benefit in a reduction of rheumatic fever.<sup>39</sup> Given the high incidence of ARF and difficulty in confirming GAS infection, there should be a low threshold for antibiotic treatment of throat infections in Aboriginal children.

The chance of developing rheumatic fever following throat infection is usually very low (up to 3% in epidemic conditions). In those who have already suffered an attack, the risk of recurrence is much higher and can be up to 50% following another streptococcal infection.<sup>31</sup> This is because host susceptibility is an important factor.

## **Secondary prevention**

### **Regular antibiotics to prevent recurrent episodes**

This is the single most cost-effective strategy in rheumatic fever and RDH control.

In the Northern Territory over the period 1987-96, nearly 40% of episodes of ARF were recurrences. These cases probably reflect poor adherence to secondary prophylaxis regimens.<sup>5</sup> The incidence of recurrent episodes is greatest in the first five years after the most recent attack of ARF. The prevention of recurrent attacks of rheumatic fever in these patients is crucial and justifies active intervention programs.

A New Zealand study showed that secondary prophylaxis of rheumatic fever in those with RDH is cost-effective, with the bulk of the savings in the management of established RDH.<sup>40</sup>

Prophylactic benzathine penicillin or oral phenoxymethyl penicillin are both recommended to prevent recurrences of ARF.<sup>41</sup> All patients diagnosed with ARF with or without carditis should receive subsequent antibiotic chemoprophylaxis (see 'Duration of prophylactic therapy').<sup>45,18</sup>

### **Benzathine penicillin**

Many randomised controlled trials, prospective studies<sup>42</sup> and retrospective studies<sup>43</sup> show that benzathine penicillin is the best choice in prophylactic therapy for rheumatic fever. The World Health Organization (WHO) recommends benzathine penicillin as the prophylactic drug of choice, to be given 4-weekly.<sup>18</sup>

The current recommended dose for secondary prophylaxis is 2.0 ml (900 mg or 1.2 million units) given every four weeks, regardless of age or weight.<sup>37,45</sup> The Australian antibiotic guidelines recommends that benzathine penicillin be administered monthly (rather than four-weekly) for convenience.<sup>44</sup>

In those who have a recurrence while on 4-weekly benzathine penicillin, three-weekly benzathine penicillin may be considered.<sup>45</sup> This is supported by a RCT in Taiwan.<sup>45,46</sup>

An international prospective study involving 1790 rheumatic fever patients showed that the rate of allergic reactions with long-term penicillin was no different from short-term therapy for sexually transmitted diseases.<sup>48</sup>

Skin testing for hypersensitivity is recommended in those with suspected penicillin allergy.<sup>48</sup> Truly penicillin-allergic patients may be offered penicillin desensitisation.

### **Oral phenoxymethyl penicillin**

The recommended oral phenoxymethyl penicillin dose is 250 mg twice daily for all ages.<sup>37</sup> However, compliance is a significant issue. Erythromycin is recommended as first-line oral prophylactic therapy in those allergic to penicillin.<sup>37</sup>

### **Duration of prophylactic treatment**

Existing guidelines agree on the duration of therapy, which depends on the age at which the most recent episode of ARF occurred, and the presence and severity of RDH.<sup>37,18</sup> A reasonably simple recommendation for Aboriginal people is that anyone with ARF or RHD should receive secondary prophylaxis for a minimum of five years or until age 21 years, whichever is longer. If at that time there is evidence of persistent cardiac valve damage (usually a persistent heart murmur with or without evidence of heart failure), prophylaxis should be continued until age 35 years. Severe cardiac disease or cardiac surgery warrants lifelong prophylaxis.

People who have had rheumatic fever with carditis should also receive prophylactic antibiotics (usually clindamycin) for certain invasive diagnostic or surgical procedures for the prevention of bacterial endocarditis.<sup>37</sup>

### **Reducing failure of secondary prophylaxis**

In the Northern Territory, it was shown that nearly 40% of all episodes of ARF were recurrences.<sup>5</sup> The most likely reason for failure of prophylaxis is

that patients did not receive it. This is more likely than failure secondary to dose or dosing interval.<sup>49</sup>

### **Community programs and registers**

Coordinated approaches to controlling ARF and RHD should include local service provision and coordination at a central level. A register of cases maintains staff awareness of the disease in spite of high staff turnover and is the best way to ensure timely clinical reviews and chemoprophylaxis. Education or health promotion strategies for those who are likely to be non-adherent can also be facilitated.

There are coordinated rheumatic fever and RHD control programs in the Top End of the Northern Territory and Central Australia. Early reductions in the incidence of recurrent cases suggest that secondary prophylaxis delivery may be improving.<sup>50,51</sup>

### **Clinical recognition and management of acute cases**

The WHO and Northern Territory experts recommend hospital admission for all patients suspected of having ARF.<sup>18,49</sup> This is for clinical assessment, diagnostic tests, patient's education and developing a long-term management plan.

### **Important clinical aspects of ARF**

The clinical features of ARF in the Aboriginal population are similar to those in classic descriptions.<sup>52,53,7,22</sup> However, there are a number of particular issues of note in this population:

#### **Sydenham's chorea**

'Purposeless, involuntary, rapid movements of the trunk and/or extremities often associated with muscle weakness' are characteristic of Sydenham's chorea.<sup>14</sup> The movements can be unilateral, making diagnosis difficult.

Sydenham's chorea is a common manifestation of ARF in Northern Australia (28% of cases). Almost half of all NT people with chorea will develop RHD.<sup>5</sup>

Haloperidol, sodium valproate and carbamazepine have been reported to be effective agents in the treatment of the chorea.<sup>54-56</sup> [Editor: See discussion of the potential long term sequela of haloperidol use in the Psychosis chapter.]

#### **Arthritis**

Polyarthritis of ARF is usually migratory (can be atypical) and does not result in permanent joint deformity. Improvement with aspirin is so dramatic that observing this greatly helps confirm or refute the diagnosis.

In Northern Territory Aboriginal people, arthritis affecting only one joint was present in 17% of non-chorea cases.<sup>22</sup> Therefore, although other causes of mono-arthritis (including septic arthritis) should be excluded, mono-arthritis should be considered a major manifestation of rheumatic fever in Aboriginal people.

#### **Fever**

Low-grade fevers (>37.5°C) were common in confirmed cases in Northern Territory Aboriginal people<sup>22</sup> and should be considered a minor manifestation, for diagnostic purposes.

## Treatment

There are no interventions in ARF that can alter the likelihood or severity of long-term valvular disease. Aspirin is only useful for limiting the symptoms of pain and fever, and should be withheld if the diagnosis is not clear and pain can be controlled with other medications.

## Rheumatic heart disease (RHD)

Carditis associated with ARF is almost always associated with a murmur due to inflammation of the heart valves. In the absence of a murmur, other causes of myocarditis or pericarditis should be sought.<sup>14</sup> The mitral valve (incompetence) is most commonly affected, followed by the aortic valve (incompetence).

Severe or recurrent episodes of valve inflammation leads to scarring, contracture and stenosis of the valves. Of Aboriginal people in the Northern Territory with RHD, 48% have two or more valves involved.<sup>5</sup>

Echocardiography with Doppler is accurate for assessing and managing suspected carditis and RHD.<sup>19</sup> This has become more important with the advent of valvular repair surgery (rather than valve replacement); a technique best performed before valve damage becomes severe, and which is associated with reduced complications due to infection or problems with anticoagulation.<sup>57</sup> Mitral valve repair rather than replacement is the surgical procedure of choice<sup>58,59,60</sup>, and early referral for consideration of this treatment should be in management plans.

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