Therapeutics for rheumatic fever and rheumatic heart disease

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SUMMARY

The goals of acute rheumatic fever therapy are to relieve symptoms, mitigate cardiac valve damage and eradicate streptococcal infection. Preventing future recurrences requires long-term secondary antibiotic prophylaxis and ongoing prevention of *Streptococcus pyogenes* (group A streptococcus) infections.

The recommended regimen for secondary prophylaxis comprises benzathine benzylpenicillin G intramuscular injections every four weeks. For patients with non-severe or immediate penicillin hypersensitivity, use erythromycin orally twice daily.

The goals of therapy for rheumatic heart disease are to prevent progression and optimise cardiac function. Secondary antibiotic prophylaxis can reduce the long-term severity of rheumatic heart disease.

Patients with rheumatic heart disease, including those receiving benzathine benzylpenicillin G prophylaxis, should receive amoxicillin prophylaxis before undergoing high-risk dental or surgical procedures. If they have recently been treated with a course of penicillin or amoxicillin, or have immediate penicillin hypersensitivity, clindamycin is recommended.

Introduction

At least 8000 people in Australia currently have acute rheumatic fever or rheumatic heart disease. The conditions are notifiable in the Northern Territory, Western Australia, Queensland, South Australia and New South Wales. The Rheumatic Heart Disease Control Programs in these jurisdictions are important sources of support for healthcare providers.[1] Nationally, Rheumatic Heart Disease Australia provides educational resources for providers, patients and families.

Important changes were made to the therapeutic recommendations in the 2020 Australian Guideline for Prevention, Diagnosis and Management of Acute Rheumatic Fever and Rheumatic Heart Disease.[2,3] The duration of secondary prophylaxis after a diagnosis of acute rheumatic fever or rheumatic heart disease is now shorter for some people without cardiac involvement. Non-steroidal anti-inflammatory drugs (NSAIDs) such as naproxen or ibuprofen are now the recommended first-line drugs for arthritis instead of aspirin. Lidocaine (lignocaine) is no longer contraindicated with intramuscular injections of benzathine benzylpenicillin G. Endocarditis prophylaxis is now recommended for all patients with rheumatic heart disease, not just for Aboriginal and Torres Strait Islander people.

What is rheumatic fever and who gets it?

In less than 10% of the population, infection with *Streptococcus pyogenes* (group A streptococcus) can trigger autoimmune conditions including acute rheumatic fever or acute post-streptococcal glomerulonephritis days to months after the initial infection.[4] Acute rheumatic fever is not a homogenous condition and shows high immunological[5] and clinical[2] diversity. It can also be subtle and mimic other conditions. There is no dedicated diagnostic test, and instead it is diagnosed using the Jones criteria.[6] These factors make the diagnosis highly challenging. In up to 75% of people with rheumatic heart disease, previous acute rheumatic fever was unrecognised.[7]

The abnormal immune responses characterising acute rheumatic fever chiefly occur in immature immune systems, with the peak incidence occurring at 5–14 years of age. The risk increases with repeated exposure to streptococci.[8] Most cases occur when the exposure risk is high, such as in crowded living conditions or when there is inadequate access to sanitation facilities and health care.[9,10]

Acute rheumatic fever also affects adults. Approximately 7% of notifications in Australia are in 35–44 year olds.[11] In Australia, nearly 90% of acute rheumatic fever cases and 70% of rheumatic heart disease diagnoses

are in Aboriginal and Torres Strait Islander people.[11] Migrants or second-generation Australians from regions with a high streptococcal burden and low-income countries, especially Maori and Pacific Islander populations, also have an elevated risk (Box).[2]

Diagnosis

The diagnosis of acute rheumatic fever requires actively excluding alternative diagnoses, followed by applying the Jones criteria,[6] which can be facilitated using the ARF RHD Guideline mobile phone app. The role of echocardiography in diagnosis and follow-up has become increasingly emphasised.

In Australia, approximately 50% of cases involve a fever with joint pain.[12] Joint pain associated with rheumatic fever may be subtle (no heat, effusion or erythema of the joints; only pain and limping) or florid with classical migratory polyarthritis, predominantly affecting large joints. Carditis with arthritis is the next most common manifestation, followed in decreasing order by chorea, carditis alone or other combinations of these 'major' Jones criteria. Erythema marginatum and subcutaneous nodules are reported in less than 1% of local cases.[12]

Carditis alone may comprise only fever with evidence of valve disease, such as mitral valve thickening and mild regurgitation on echocardiography. It may manifest with or without a murmur and with or without a conduction abnormality seen on electrocardiography, such as first-degree heart block. Acute rheumatic fever should therefore be considered in a child with a high risk of streptococcal exposure presenting with unexplained fever. Electrocardiography, measurements of inflammatory markers (C-reactive protein concentrations, erythrocyte sedimentation rate), streptococcal serologic tests and echocardiography may all be indicated for investigation, as fever can be the only sign that the child has acute rheumatic fever.

Sydenham chorea is a neuropsychiatric manifestation of acute rheumatic fever characterised by chorea, decreased muscle tone and sometimes psychiatric and behavioural symptoms. It may occur weeks to months after the onset of streptococcal infection depending on the history of disease recurrence and time of diagnosis, and thus fever, elevated concentrations of inflammatory markers and elevated streptococcal serology may be absent.

Management of acute rheumatic fever

Symptom management is critical to reduce morbidity and return children home and to school. The goals of acute rheumatic fever therapy are to:

- relieve symptoms
- mitigate cardiac damage
- eradicate the inciting streptococcal infection
- prevent future recurrences.

Hospitalisation for rheumatic fever is recommended to confirm the diagnosis and facilitate prompt access to an echocardiogram. A variety of doctors (paediatricians, physicians, cardiologists, GPs) with

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Box   **Groups at risk of acute rheumatic fever and rheumatic heart disease**

At high risk

- People living in an acute rheumatic fever-endemic setting*
- Aboriginal and Torres Strait Islander people living in rural or remote areas
- Aboriginal and Torres Strait Islander people and Maori and Pacific Islander people living in metropolitan households affected by crowding or low socioeconomic status
- Patients with a personal history of acute rheumatic fever or rheumatic heart disease and <40 years of age

May be at high risk

- Family or household recent history of acute rheumatic fever or rheumatic heart disease
- People with household overcrowding (>2 people/bedroom) or low socioeconomic status
- Migrants or refugees from low- or middle-income countries and their children

Additional factors that increase risk

- Previous residence in a high-risk setting
- Frequent or recent travel to a high-risk setting
- Age 5–20 years (peak years for developing acute rheumatic fever)

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* This refers to communities where the rates of acute rheumatic fever and rheumatic heart disease are high (for example, an acute rheumatic fever incidence higher than 30/100,000 per year in those aged 5–14 years and a rheumatic heart disease all-age prevalence higher than 2/1000).

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experience in endemic settings may have specialty knowledge of rheumatic fever, which should be sought to guide diagnosis and management.

Arthritis

Naproxen and ibuprofen are the recommended first-line anti-inflammatory analgesics for rheumatic arthritis (Table 1). Aspirin is now used second line due to its less favourable safety profile. Initial high-dose NSAID therapy, weaned after 1–2 weeks, is usual. Proton pump inhibitor therapy for gastric protection can be considered for patients requiring prolonged anti-inflammatory treatment.

The duration of treatment is guided by the disease severity, clinical response and concentrations of inflammatory markers (C-reactive protein, erythrocyte sedimentation rate). Most episodes of acute rheumatic fever resolve within six weeks and 90% resolve within 12 weeks. A rebound in inflammatory symptoms can occur on ceasing treatment, requiring the drugs to be re-introduced.[2,13]

Carditis

There is no targeted drug therapy available for cardiac valve damage during the acute inflammatory stage. Hydroxychloroquine has been used as a targeted disease-modifying agent[14] based on promising in vitro findings,[15] but clinical trial data are not yet available. For severe carditis, corticosteroids are recommended (Table 1). However, meta-analyses have suggested their lack of benefit in preventing subsequent rheumatic heart disease,[16,17] although the studies were mostly performed before the availability of echocardiography. Expert opinion recommends corticosteroids for carditis associated with heart failure.[2] If NSAIDs have been prescribed for pericarditis or arthritis, these can be discontinued when corticosteroids are started, as corticosteroids provide effective relief of the manifestations of acute rheumatic fever. Proton pump inhibitor therapy can be considered for gastric protection in patients requiring prolonged corticosteroid treatment. Screening for and the management of latent infections (e.g. hepatitis B, strongyloidiasis, tuberculosis) are required before or on starting immunosuppressive corticosteroid doses.[2]

Chorea

Pharmacotherapy is not needed for mild chorea. For more severe cases, carbamazepine is recommended as first-line treatment due to its safety profile, followed by sodium valproate (Table 1). A treatment response may not be observed for 1–2 weeks, and drugs may only reduce, not eliminate, chorea. Treatment should be continued for 2–4 weeks after chorea has subsided, and then be withdrawn.

Corticosteroids have reported benefits for severe or refractory chorea and are therefore recommended if the response to carbamazepine or sodium valproate is insufficient (Table 1).[18] Intravenous immunoglobulin and plasmapheresis might be beneficial experimental immunotherapies for Sydenham chorea.[2]

Antibiotics

As rheumatic fever is associated with group A streptococci, antibiotics play a key therapeutic role. S. pyogenes remains susceptible to penicillin, as it is unable to genetically express resistance to penicillin.[19]

Treatment and prevention of streptococcal infection

The inciting streptococcal infection can be treated with the first dose of benzathine benzylpenicillin G administered for ongoing secondary prophylaxis. Other options are presented in Table 1.

Secondary antibiotic prophylaxis is the mainstay of treatment for acute rheumatic fever and rheumatic heart disease globally to prevent recurrences of rheumatic fever and thereby prevent cumulative valve damage with the development or progression of rheumatic heart disease.[20] The recommended regimen is intramuscular injections of benzathine benzylpenicillin G every four weeks for a minimum of five years (if there is no cardiac involvement) or 10 years (if there is cardiac involvement) after the last acute rheumatic fever episode or until 21 years of age, whichever is longer (Table 2).[21] The recurrence rates of acute rheumatic fever are significantly reduced by this regimen compared to a placebo[22] or oral penicillin.[23] Increasing adherence to benzathine benzylpenicillin G is associated with improved rheumatic fever outcomes.[24] Regular oral penicillin is not as effective as benzathine benzylpenicillin G.[25] This is potentially due to the serum penicillin concentrations achieved and problems with adherence.

Non-beta-lactam antibiotic options

An estimated 3.2% of people have an allergic reaction to penicillin and 0.2% have anaphylactic reactions.[2,26] These people require alternative antibiotics.

Macrolide antibiotics (erythromycin, roxithromycin, azithromycin and clarithromycin) are favoured alternatives in people with adverse reactions to beta-lactams due to their tolerability and dosing regimen. They cover approximately 88% of S. pyogenes isolates (Northern Territory Top End antibiogram data) due to the development of class resistance to macrolides and clindamycin in some isolates. The proportion of S. pyogenes resistant to macrolides in any region is related to local prescribing practices.[4] As long as most S. pyogenes isolates remain susceptible, macrolides are an acceptable second-line option.

Table 1 **Drugs used for rheumatic fever**

Indication	Drug options listed in order of preference	Comment
Eradication of inciting streptococcal infection	1. Benzathine benzylpenicillin G 1,200,000 units (child <20 kg: 600,000 units, ≥20 kg: 1,200,000 units) intramuscularly, single dose OR	Streptococcal infection may not be evident by the time acute rheumatic fever manifests (e.g. cultures often negative), but eradication therapy for possible persisting streptococci is recommended. Intramuscular penicillin is preferred as streptococcal eradication therapy due to better adherence and its subsequent ongoing use in secondary prophylaxis.
	2. Phenoxymethylpenicillin 500 mg (child: 15 mg/kg up to 500 mg) orally, every 12 hours for 10 days OR	
	3. For patients with penicillin hypersensitivity (non-severe): cefalexin 1 g (child: 25 mg/kg up to 1 g) orally, every 12 hours for 10 days OR	Between 3% and 30% of group A streptococcus isolates internationally are resistant to macrolide antibiotics (e.g. azithromycin).
	4. For patients with immediate penicillin hypersensitivity: azithromycin 500 mg (child: 12 mg/kg up to 500 mg) orally, daily for 5 days	
Initial analgesia while awaiting diagnostic confirmation: • mild to moderate pain • severe pain	Paracetamol 1000 mg (in children: 15 mg/kg) orally, every four hours as needed up to a maximum of 60 mg/kg/day or 4000 mg/day	Initial analgesia is preferred during diagnostic uncertainty to avoid the masking effect that anti-inflammatory use can have on migratory joint symptoms, fever and concentrations of inflammatory markers.
	Tramadol immediate-release 50–100 mg (in children: 1–2 mg/kg) orally, every four hours as needed up to a maximum of 400 mg/day	Tramadol (or codeine) is usually avoided in children <12 years of age due to variable metabolism. Use only when strong analgesia is essential and cautious monitoring is available.
Symptomatic management of arthritis/arthralgia after confirmation of acute rheumatic fever diagnosis	1. Naproxen immediate-release 250–500 mg (in children: 10–20 mg/kg/day) orally twice daily, up to a maximum of 1250 mg daily OR	Naproxen may be safer than aspirin and convenient due to twice-daily dosing and the availability of oral suspension. Ibuprofen is well tolerated and readily available, but there are less data and experience with its use for acute rheumatic fever than those associated with naproxen. The dose of NSAIDs needed for acute rheumatic fever is generally higher than the dose recommended for other conditions; therefore, it may be appropriate to start at the higher dose range. Due to the rare possibility of Reye's syndrome in children, aspirin may need to be discontinued during intercurrent acute viral illness; thus, influenza vaccination is strongly recommended to reduce the likelihood of this case.
	2. Ibuprofen 200–400 mg (in children: 5–10 mg/kg) orally three times daily, up to a maximum of 2400 mg daily OR	
	3. Aspirin 50–60 mg/kg/day orally, in 4–5 divided doses in adults and children. Dose can be escalated up to a maximum of 80–100 mg/kg/day in 4–5 divided doses	
Symptomatic management of moderate to severe chorea	1. Carbamazepine 3.5–10 mg/kg per dose orally twice daily	Treatment of Sydenham chorea should be considered if movements interfere substantially with normal activities.
	2. Sodium valproate 7.5–10 mg/kg per dose orally twice daily	
Symptomatic management of very severe chorea or chorea paralytica	In addition to an anticonvulsant drug, consider adding a corticosteroid: • Prednisolone 1–2 mg/kg up to a maximum of 80 mg orally once daily	

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Table 1 **Drugs used for rheumatic fever *(continued)***

Indication	Drug options listed in order of preference	Comment
Symptomatic management of carditis	Paediatric dosing: • Furosemide (frusemide) 1–2 mg/kg orally as a single dose, then 0.5–1 mg/kg (to a maximum of 6 mg/kg) orally every 6–24 hours • Spironolactone 1–3 mg/kg (initially) up to 100 mg orally in 1–3 divided doses daily. Round dose to a multiple of 6.25 mg (a quarter of a 25-mg tablet)	Treatment of heart failure may be required for severe, acute carditis. Seek advice from a specialist cardiologist.
	• Enalapril 0.1 mg/kg orally in 1 or 2 divided doses daily, increased gradually over 2 weeks to a maximum of 1 mg/kg orally in 1 or 2 divided doses daily. Alternative ACE inhibitors: captopril, lisinopril	The choice of ACE inhibitor will vary depending on the clinical situation. Seek advice from a specialist cardiologist.
	Adult dosing: • Furosemide (frusemide) 20–40 mg orally or intravenously as a single dose followed by 20–40 mg orally or intravenously every 8–12 hours. Ongoing dose adjustment is based on clinical progression and renal function. • Spironolactone may be added for patients with limited or no response to loop diuretic; 12.5–200 mg orally once daily with dose escalation based on clinical and electrolyte responses. • Nitrate therapy may be added for patients with limited or no response to diuretic therapy and systolic blood pressure greater than 90 mmHg. Intravenous or topical glyceryl trinitrate may be used. • ACE inhibitor therapy with perindopril or ramipril is recommended in patients with moderate or severe left ventricular systolic dysfunction, unless contraindicated.	The management of acute carditis follows the same principles as those for the management of acute heart failure. This table provides a guide to the initial management of acute heart failure due to acute carditis in adults. Seeking advice from a specialist cardiologist early is strongly recommended.
	Digoxin 15 micrograms/kg orally as a single dose, then 5 micrograms/kg after 6 hours, then 3–5 micrograms/kg (in adults: 125–250 micrograms) orally, daily	Digoxin is rarely used for the treatment of acute carditis. Seek advice from a specialist cardiologist.
Disease-modifying (immunomodulatory) treatments	Prednisolone 1–2 mg/kg up to a maximum of 80 mg orally, once daily	Considered for use in selected cases of severe carditis, despite meta-analyses in which the overall benefit was not evident.
Secondary prophylaxis	1. Benzathine benzylpenicillin G by deep intramuscular injection 1,200,000 units (≥20 kg) or 600,000 units (<20 kg) * OR	Every 28 days. † Every 21 days for selected groups. ‡
	2. Phenoxymethylpenicillin (penicillin V) 250 mg orally twice daily OR	Intramuscular penicillin is preferred due to greater effectiveness in head-to-head trial and better adherence.
	3. For patients with penicillin hypersensitivity (non-severe) or immediate penicillin hypersensitivity: erythromycin 250 mg orally twice daily	

NSAID non-steroidal anti-inflammatory drug

* For children weighing less than 10 kg, a dose of 600,000 units is still generally recommended, but seek paediatric advice for careful planning of the secondary prophylaxis regimen.

† Patients on 28-day regimens can be recalled from 21 days to help ensure that injections are given by day 28.

‡ Benzathine benzylpenicillin G given every 21 days may be considered for:
  • patients who have breakthrough acute rheumatic fever despite complete adherence to a 28-day regimen
  • patients who are at a high risk of adverse consequences if acute rheumatic fever occurs (have severe rheumatic heart disease or a history of heart valve surgery).

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Table 2   **Recommended duration of secondary prophylaxis**

Diagnosis	Definition	Duration of prophylaxis	Conditions for ceasing prophylaxis*	Timing of echocardiography after cessation†
Possible acute rheumatic fever (without cardiac involvement)	Incomplete features of acute rheumatic fever with a normal echocardiogram and normal ECG‡ throughout acute rheumatic fever episodes	12 months (then reassess)	No signs and symptoms of acute rheumatic fever within the previous 12 months Normal echocardiogram	At 1 year
Probable acute rheumatic fever (without cardiac involvement)	Highly suspected acute rheumatic fever with a normal echocardiogram	Minimum of 5 years after the most recent episode of probable acute rheumatic fever, or until 21 years of age (whichever is longer)	No probable or definite acute rheumatic fever within the previous 5 years Normal echocardiogram	At 1, 3 and 5 years
Definite acute rheumatic fever (without cardiac involvement)	Acute rheumatic fever with a normal echocardiogram and normal ECG‡ throughout acute rheumatic fever episodes	Minimum of 5 years after the most recent episode of acute rheumatic fever, or until 21 years of age (whichever is longer)	No probable or definite acute rheumatic fever within the previous 5 years Normal echocardiogram	At 1, 3 and 5 years
Definite acute rheumatic fever (with cardiac involvement)	Acute rheumatic fever with carditis or rheumatic heart disease on echocardiography, or with atrioventricular conduction abnormality on ECG‡ during acute rheumatic fever episodes	According to the severity of rheumatic heart disease (borderline, mild, moderate, severe)		
Borderline rheumatic heart disease (in people ≤20 years of age only)	Borderline rheumatic heart disease on echocardiography without a documented history of acute rheumatic fever	In a high-risk setting: minimum of 2 years following the diagnosis of borderline rheumatic heart disease If borderline rheumatic heart disease is still present at 2 years, continue for another 2 years and reassess. Seek specialist input§	No probable or definite acute rheumatic fever within the previous 10 years Normalisation of echocardiogram after a minimum of 2 years of follow-up	Medical review and repeat echocardiogram at 1–2 years after diagnosis, and 1–2 years after stopping secondary prophylaxis
Mild rheumatic heart disease #	Mild rheumatic heart disease on echocardiography or atrioventricular conduction abnormality on ECG‡ during acute rheumatic fever episodes	If there is a documented history of acute rheumatic fever: minimum of 10 years after the most recent episode of acute rheumatic fever, or until 21 years of age (whichever is longer) If there is NO documented history of acute rheumatic fever and age is <35 years:¶ minimum of 5 years following the diagnosis of rheumatic heart disease or until 21 years of age (whichever is longer)	No probable or definite acute rheumatic fever within the previous 10 years and no progression of rheumatic heart disease Stable echocardiographic features for 2 years	At 1, 3 and 5 years

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Table 2 **Recommended duration of secondary prophylaxis (continued)**

Diagnosis	Definition	Duration of prophylaxis	Conditions for ceasing prophylaxis*	Timing of echocardiography after cessation†
Moderate rheumatic heart disease#**	Moderate rheumatic heart disease on echocardiography	If there is a documented history of acute rheumatic fever: minimum of 10 years after the most recent episode of acute rheumatic fever or until 35 years of age (whichever is longer) If there is no documented history of acute rheumatic fever and age is <35 years:¶ minimum of 5 years following the diagnosis of rheumatic heart disease or until 35 years of age (whichever is longer)	No probable or definite acute rheumatic fever within the previous 10 years Stable echocardiographic features for 2 years	Initially every 12 months
Severe rheumatic heart disease**††	Severe rheumatic heart disease on echocardiography OR Previous valve repair or prosthetic valve replacement	If there is a documented history of acute rheumatic fever: minimum of 10 years after the most recent episode of acute rheumatic fever or until 40 years of age (whichever is longer) If there is no documented history of acute rheumatic fever:‡‡ minimum of 5 years following the diagnosis of rheumatic heart disease or until 40 years of age (whichever is longer)	Stable valvular disease/cardiac function on serial echocardiography for 3 years OR Patient or family preference to cease due to advancing age or end-of-life care	Initially every 6 months

* All people receiving secondary prophylaxis require a comprehensive clinical assessment and echocardiogram before cessation. Risk factors including future exposure to environments with a high burden of group A streptococcus must be considered.

† Echocardiography may be more frequently performed based on the clinical status and specialist review.

‡ 'Normal ECG' indicates that there is no atrioventricular conduction abnormality during the acute rheumatic fever episode, including first-degree heart block, second-degree heart block, third-degree (complete) heart block or an accelerated junctional rhythm.

§ An update in March 2022 recommends secondary prophylaxis for people ≤20 years of age living in high-risk settings without a documented history of acute rheumatic fever but who have an echocardiogram showing borderline rheumatic heart disease.[21]

Prophylaxis may be considered for longer in women considering pregnancy who live in high-risk circumstances for acute rheumatic fever.

¶ If diagnosed with mild or moderate rheumatic heart disease and aged ≥35 years (without acute rheumatic fever), secondary prophylaxis is not required.

** Rarely, moderate or severe rheumatic heart disease may improve on echocardiography without valve surgery. In these cases, the conditions for ceasing prophylaxis can change to follow the most recent severity category. For instance, if moderate rheumatic heart disease improves to mild on echocardiography, recommendations for mild rheumatic heart disease can then be followed.

†† The risk of acute rheumatic fever recurrence is low in people ≥40 years of age; however, lifelong secondary prophylaxis is usually recommended for patients who have had, or are likely to need, heart valve surgery.

‡‡ If a person is diagnosed with severe rheumatic heart disease at ≥40 years of age (without acute rheumatic fever), specialist input is required to determine the need for secondary prophylaxis.

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For non-severe penicillin hypersensitivity, use cefalexin to treat the inciting streptococcal infection and erythromycin for secondary prophylaxis. For immediate penicillin hypersensitivity, use azithromycin to treat the inciting streptococcal infection and erythromycin for secondary prophylaxis (Table 1).

Management of rheumatic heart disease

Secondary antibiotic prophylaxis is the only treatment confirmed to be associated with a long-term reduction in the severity of rheumatic heart disease. Patients with moderate to severe rheumatic heart disease require cardiology services and regular echocardiographic follow-up.[2] Women with rheumatic heart disease who are pregnant or of childbearing age require pre-conception counselling and specialist care. Comprehensive guidance on medical and surgical management is detailed in the 2020 Australian Guideline for Acute Rheumatic Fever and Rheumatic Heart Disease.[2]

Prevention of infective endocarditis

Rheumatic heart disease poses a risk for infective endocarditis. Certain dental and other invasive surgical procedures can cause transient bacteraemia, leading to infection of damaged or prosthetic valves. Guidelines have oscillated on antibiotic prophylaxis for infective endocarditis. The weight of evidence now favours antibiotic use for infective endocarditis prophylaxis in all patients with rheumatic heart disease undergoing high-risk dental or other surgical procedures.[1,27] These procedures are listed in Therapeutic Guidelines: Antibiotic.[28]

Amoxicillin is the recommended first-line drug for endocarditis prophylaxis for certain dental procedures in patients with specified cardiac conditions including rheumatic heart disease, even in those receiving benzathine benzylpenicillin G for secondary prophylaxis (Table 3). However, if a patient has recently had a course of treatment with penicillin, amoxicillin or another beta-lactam (providing higher antibiotic concentrations than prophylactic doses), clindamycin is the recommended first-line drug. This is because the treatment course may have reduced the amoxicillin susceptibility of viridans streptococci, which are commensal oral organisms that can be mobilised into the bloodstream following dental procedures.

Conclusion

Practitioners in Australia might encounter cases of acute rheumatic fever and rheumatic heart disease. Those practising in high-burden settings, especially remote Aboriginal and Torres Strait Islander communities, need a low threshold for suspecting these conditions and familiarity with guidelines and resources. Rheumatic Heart Disease Control Programs and Rheumatic Heart Disease Australia can assist practitioners, address clinical queries and provide resources. ◄

Table 3 **Oral prophylactic antibiotics for infective endocarditis in certain dental procedures***

Indication	Drug	Time before the procedure
For endocarditis prophylaxis	Amoxicillin 2 g (in children: 50 mg/kg up to 2 g)	60 minutes
For patients with **delayed non-severe** hypersensitivity to penicillins, cefalexin can be used in most cases	Cefalexin 2 g (in children: 50 mg/kg up to 2 g)	60 minutes
For patients with **immediate (severe or non-severe)** or **delayed severe** hypersensitivity to penicillins	Clindamycin[‡] 600 mg (in children: 20 mg/kg up to 600 mg)	60–120 minutes
For patients who have recently received a treatment-dose course of a beta-lactam antibiotic	Clindamycin[‡] 600 mg (in children: 20 mg/kg up to 600 mg)	60–120 minutes

* See Therapeutic Guidelines: Antibiotic, Box 2.13 'Procedures for which endocarditis prophylaxis is recommended for patients with a cardiac condition'[28] for a list of the dental procedures for which endocarditis prophylaxis is recommended in patients with rheumatic heart disease. For endocarditis prophylaxis for other procedures, see eTG[28]

† See Therapeutic Guidelines: 'Endocarditis prophylaxis regimens for dental procedures' for details on intramuscular or intravenous options[28]

‡ There is some evidence to suggest that moxifloxacin may be used as an alternative to clindamycin in patients with immediate (severe) or non-severe or delayed hypersensitivity to penicillins, but this has not been validated.

Source: modified with permission from reference 2, which includes intravenous and intramuscular options.

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