

Primary prevention of acute rheumatic fever



CPD 

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Background

Acute rheumatic fever (ARF) is an abnormal immune reaction following *Streptococcus pyogenes* (Strep A) infection of the throat, and likely the skin. Primary prevention is the prompt and appropriate antibiotic treatment of Strep A infection, and it can reduce the risk of developing ARF and subsequent rheumatic heart disease.

Objective

This article explores current recommendations for primary prevention of ARF in Australia.

Discussion

People at increased risk of ARF should be offered empirical antibiotic treatment of Strep A infections to reduce this risk. People at increased ARF risk include young Aboriginal and Torres Strait Islander people in remote Australia as well as those with a personal or family history of ARF and people from migrant communities in urban areas, including Māori and Pacific Island people. Risk-stratified primary prevention can reduce the inequitable burden of ARF and rheumatic heart disease in Australia.

ACUTE RHEUMATIC FEVER (ARF) is an abnormal immune reaction, occurring weeks after *Streptococcus pyogenes* (Strep A) infection in susceptible young people. Susceptibility to ARF is likely to be driven by recurrent Strep A infections in early life, leading to immune priming.¹ This means that children exposed to Strep A early and more frequently – for example, in crowded living environments or with inadequate access to hygiene infrastructure – are at greatest risk of ARF. Aboriginal and Torres Strait Islander people are disproportionately affected by these factors and account for nearly 90% of the approximately 500 ARF diagnoses in Australia each year.² The other 10% of people who develop ARF include non-Indigenous people born in Australia (approximately 7%) and First Nations peoples from other countries and migrants from low- or lower middle-income countries (approximately 3%).² In Australia, the highest burden of ARF is in remote Northern Australia, although confirmed cases occur in all capital cities, and it is important for general practitioners (GPs) to be aware of ARF and the clinical diagnostic features regardless of where they work.^{2,3} Severe or recurrent episodes of ARF lead to the chronic heart valve damage of rheumatic heart disease (RHD), which leads in turn to heart failure and

an increased risk of stroke, arrhythmia, bacterial endocarditis and pregnancy complications. The disease burden experienced by individuals with RHD is substantial but able to be mitigated with high-quality secondary prevention.⁴ This article focuses on the role of GPs and other health professionals in the primary prevention of ARF.

The role of Strep A infections in acute rheumatic fever

The risk of Strep A throat infection precipitating ARF has been recognised since the 1950s.⁵ Without treatment, approximately 3% of people with streptococcal pharyngitis will go on to develop ARF.⁶ There is also growing evidence that Strep A skin infections (impetigo) can precipitate ARF. This hypothesis emerged in Australia with the observation that skin sores are common among Aboriginal and Torres Strait Islander communities with high rates of ARF, whereas reported throat infections are relatively rare.⁷ Similar epidemiological patterns have been described internationally, and a well-described case report from New Zealand has provided new evidence that Strep A skin infection can lead to ARF.^{8,9} This is important because skin infections

are common; half of all children in remote communities have skin infections at any one time, primarily caused by Strep A.^{10,11} Skin problems, including skin sores, are also common presentations in regional and urban general practice.¹²

Primary prevention of acute rheumatic fever

Primary prevention involves the identification of Strep A infections and delivery of appropriate antibiotic treatment to prevent ARF (as distinct from antibiotic treatment to shorten the duration of infection, heal the sores or provide symptomatic relief). The evidence that treatment of Strep A throat infections can prevent ARF is strong, albeit based on historic studies.¹³ Prompt treatment with oral penicillin is reported to reduce the attack rate of ARF following Strep A throat infection by approximately 70%, increasing to 80% if a single intramuscular injection of benzathine benzylpenicillin G (BPG) is given. Benefit has been reported within nine days of symptom onset, although lowest risk is likely to be achieved with earlier commencement of effective antibiotics.^{14,15} There is no empirical evidence that antibiotic treatment of Strep A skin infections has the same effect in reducing ARF risk.

However, it is biologically plausible that timely treatment of skin infection would limit the immune response, immune priming and molecular mimicry that underpin the pathophysiology of ARF. Additionally, treatment of skin sores is important to limit spread to other sites or transmission to other people, and reduce direct complications (skin infection including cellulitis, sepsis and bone infections) and indirect complications (glomerulonephritis). Australian public health guidelines require patients to receive an effective antibiotic for 24 hours prior to return to school, to limit onward transmission.¹⁶

Acute rheumatic fever risk assessment and treatment choices

Sore throat

Approximately 70% of young people presenting to general practice with a sore throat have a viral infection and should not receive antibiotics.¹⁷ A number of antimicrobial stewardship studies and programs have contributed to appropriately discouraging antibiotic prescriptions for tonsillitis in Australia.^{18,19} However, these efforts should not preclude antibiotic prescriptions for primary prevention of ARF among young people who are at higher risk of immune-mediated

consequences. A diagnosis of ARF or RHD has lifelong medical and social effects.²⁰ The devastating consequences of RHD can be prevented by primary prevention for people at greatest risk of ARF.

There are at least seven clinical guidelines for management of sore throat in Australia, with variable guidance on ARF risk stratification.^{21,22} The most recent is *The 2020 Australian guideline for prevention, diagnosis and management of acute rheumatic fever and rheumatic heart disease*, 3rd edition.²³ This guideline recommends a risk stratification approach for ARF to identify those at highest risk of ARF and hence increase the likelihood of prescribing antibiotics to treat Strep A infections to prevent ARF (Table 1).

This approach to ARF risk stratification is the most appropriate driver of antibiotic therapy decisions in the Australian setting. Clinical scoring tools, including the Centor score, have been developed to help assess the likelihood of Strep A sore throat relative to other causes. However, positive and negative predictive values are relatively low, and scores focus on diagnostic probability rather than the risk of autoimmune sequelae from untreated infection.^{23,24}

People who may be at high risk of ARF require primary prevention antibiotic treatment for sore throat (Figure 1).

Table 1. Risk groups for primary prevention of ARF²³

At high risk	Living in an ARF-endemic setting* Aboriginal and/or Torres Strait Islander peoples living in rural or remote settings Aboriginal and/or Torres Strait Islander peoples, and Māori and/or Pacific Islander peoples living in metropolitan households affected by crowding and/or lower socioeconomic status Personal history of ARF/RHD and aged <40 years
May be at high risk	Family or household recent history of ARF/RHD Household overcrowding (>2 people per bedroom) or low socioeconomic status Migrant or refugee from low- or middle-income country and their children
Additional considerations that increase risk	Prior residence in a high ARF risk setting Frequent or recent travel to a high ARF risk setting Aged 5–20 years (the peak years for ARF)

*This refers to populations where community ARF/RHD rates are known to be high, eg ARF incidence >30/100,000 per year in 5–14-year-olds or RHD all-age prevalence >2/1000

ARF, acute rheumatic fever; RHD, rheumatic heart disease

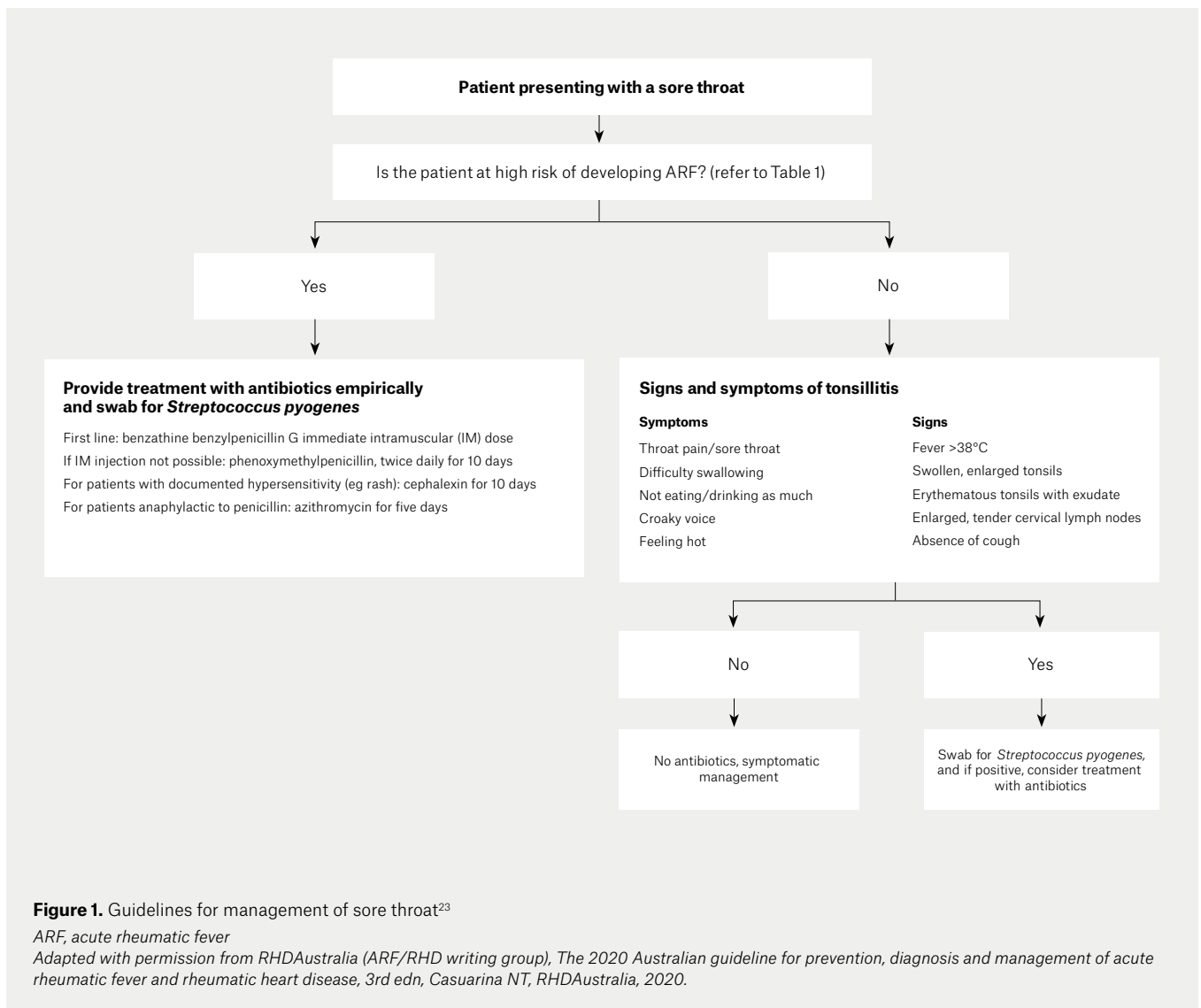
Reproduced with permission from RHD Australia (ARF/RHD writing group), *The 2020 Australian guideline for prevention, diagnosis and management of acute rheumatic fever and rheumatic heart disease*, 3rd edn, Casuarina NT, RHD Australia, 2020.

First-line treatment is a single immediate dose of intramuscular BPG delivered according to evidence-based guidance to minimise the pain of injection delivery.^{21,23} When intramuscular injection is declined or unavailable, a 10-day course of phenoxymethylpenicillin can be provided.²³ Although no other antibiotic regimen has shown efficacy in primary prevention risk reduction, clinical guidelines provide second-line options for patients with documented penicillin hypersensitivity or allergy (usually a cephalosporin or macrolide antibiotic).²³ Supportive therapy including analgesia should be offered.

Skin sores

There is also a range of guidelines for treatment of Strep A skin infection, including the *National healthy skin guideline: For the prevention, treatment and public health control of impetigo, scabies, crusted scabies and tinea for Indigenous populations and communities in Australia*.²⁵ Skin infections are generally not caused by viruses, and the decision to initiate antibiotics for skin infection is usually clearer than for sore throat. This decision-making process is outlined in Figure 2. The evidence for topical treatment, such as mupirocin ointment for people with few sores, is well established and derives from

studies in non-endemic, urban settings.²⁶ Systemic treatment with oral cotrimoxazole is more appropriate as primary prevention for people at risk of ARF.^{27,28} A three-day course of twice-daily trimethoprim/sulfamethoxazole should be offered; where injectable therapy is preferred, a single dose of BPG may be given.²⁵ A limited number of other oral alternatives are also available. Topical treatment is not recommended in settings with a high burden of skin disease because of rapid development of resistance.²⁵ People with skin sores should also be offered examination for scabies infestation, tinea or head lice, which predispose to skin damage and subsequent



Strep A infection. Sores should be covered with a watertight dressing and antibiotic therapy commenced before returning to school.²⁵ Daily handwashing has been shown to reduce incidence of impetigo internationally.²⁹ Where services exist, referral to discuss environmental health and housing infrastructure issues may be appropriate to support health hygiene practices.

Strep A. A throat swab should be taken in the case of sore throat, and oral antibiotics can be ceased if the swab result is negative for Strep A.²³ Molecular point-of-care testing (PoCT) for Strep A sore throat may support decision making regarding antibiotic use, but emerging PoCT guidance has not yet been incorporated into clinical guidelines.²⁴ Wound swabs are generally not indicated for skin sores unless there has been treatment failure.²⁵

to acceptable healthcare for primary prevention. These inequities mean the burden of ARF is concentrated among – but not exclusive to – Aboriginal and Torres Strait Islander peoples. Development of ARF can be prevented by early detection and appropriate antibiotic treatment of sore throats and skin sores for higher-risk groups. Clinical guidelines that assess treatment needs in the context of population risk are important tools to reduce recognised underlying health disparities. Primary care has a critical role in encouraging, validating and providing best practice care for young people attending with these common and potentially serious infections.

Microbial testing

Empirical antibiotic treatment for people at high risk of ARF should be started for sore throat and skin sores without waiting for microbiological confirmation of

Conclusion

There is a persistently high incidence of ARF in Australia driven by inequities in environmental health and access

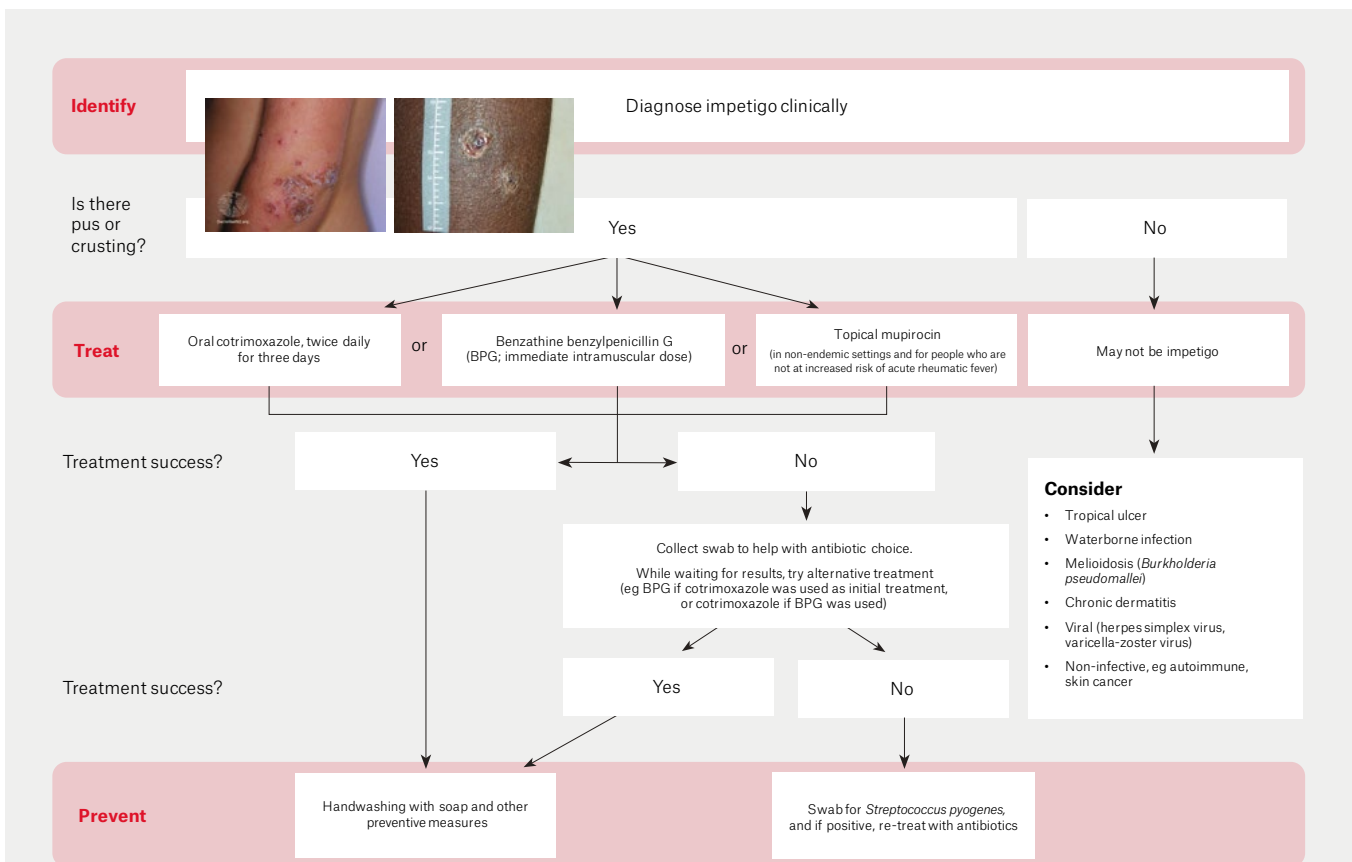


Figure 2. Guidelines for management of skin sores²⁵

Adapted with permission from The Australian Healthy Skin Consortium, National healthy skin guideline: For the prevention, treatment and public health control of impetigo, scabies, crusted scabies and tinea for Indigenous populations and communities in Australia, 1st edn, Nedlands, WA: Telehealth Kids Institute, 2018. Clinical images from National healthy skin guideline: For the prevention, treatment and public health control of impetigo, scabies, crusted scabies and tinea for Indigenous populations and communities in Australia, 1st edn and DermNet NZ (Creative Commons Attribution-NonCommercial-NoDerivs 3.0 (New Zealand) at <https://creativecommons.org/licenses/by-nc-nd/3.0/nz/legalcode>).

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