2. Diagnosis of acute rheumatic fever

An accurate diagnosis of ARF is important. Overdiagnosis results in unnecessary treatment over a long time, while underdiagnosis leads to further attacks of ARF, cardiac damage and premature death. Diagnosis remains a clinical decision, as there is no specific laboratory test.

This quick reference guide is derived from the *Australian guideline for prevention, diagnosis and management of acute rheumatic fever and rheumatic heart disease* (2nd edn).

What is acute rheumatic fever?

Acute rheumatic fever (ARF) is an illness caused by a reaction to a bacterial infection with group A streptococcus (GAS). It causes an acute, generalised inflammatory response and an illness that targets specific parts of the body, including the heart, joints, brain and skin. Individuals with ARF are often unwell, have significant joint pain and require hospitalisation. Despite the dramatic nature of the acute episode, ARF leaves no lasting damage to the brain, joints or skin, but can cause persisting heart damage, termed 'rheumatic heart disease' (RHD). Recurrences of ARF may cause further cardiac valve damage. Hence, RHD steadily worsens in people who have multiple episodes of ARF.

Who gets ARF?

Although ARF is relatively rare in industrialised countries, in Australia it is a significant illness among Aboriginal people and Torres Strait Islanders, particularly across central and northern Australia.

Problems with diagnosis and management

Several factors contribute to the barriers in diagnosis and management of ARF and RHD in Australia:

- although strategies for preventing RHD have been proven to be simple, cheap and cost-effective, they must be adequately implemented in populations at highest risk of the disease
- because ARF is rare in most metropolitan centres, the majority of clinicians will have seen very few, if any, cases of ARF

- there is great variability in the management of these diseases, with minimal training and experience in the management of ARF and RHD occasionally resulting in inappropriate management
- access to healthcare services by population groups experiencing the highest rates of ARF and RHD is often limited.

Identifying high-risk groups

High-risk groups are those living in communities with high rates of ARF (incidence >30/100,000 per year in 5–14 year olds) or RHD (all-age prevalence >2/1000).

Aboriginal people and Torres Strait Islanders living in rural or remote settings are known to be at high risk.

ARF is predominantly a condition seen in children aged 5–14 years, although people can have recurrent episodes well into their 40s.

Comprehensive data are not available for other populations, but Aboriginal people and Torres Strait Islanders living in urban settings, and potentially immigrants from developing countries, may also be at high risk.

Diagnostic criteria for ARF

An accurate diagnosis of ARF is important, as:

- overdiagnosis will result in the individual receiving treatment unnecessarily
- underdiagnosis may lead to further episodes of ARF, cardiac damage and the need for heart valve surgery and/or premature death.

Currently, there is no diagnostic laboratory test for ARF, so diagnosis remains a clinical decision based on the identification of major and minor manifestations of the illness. The Table below outlines criteria for high- and low-risk populations in Australia.

2012 Updated Australian guidelines for the diagnosis of ARF

	High-risk groups[†]	All other groups
Definite initial episode of ARF	2 major **or** 1 major and 2 minor manifestations **plus** evidence of a preceding GAS infection[‡]	
Definite recurrent episode of ARF in a patient with known past ARF or RHD	2 major **or** 1 major and 1 minor **or** 3 minor manifestations **plus** evidence of a preceding GAS infection[‡]	
Probable ARF (first episode or recurrence)	A clinical presentation that falls short by either one major or one minor manifestation, or the absence of streptococcal serology results, but one in which ARF is considered the most likely diagnosis. Such cases should be further categorised according to the level of confidence with which the diagnosis is made: • highly-suspected ARF • uncertain ARF	
Major manifestations	Carditis (including subclinical evidence of rheumatic valvulitis on echocardiogram) Polyarthritis[††] or aseptic mono-arthritis or polyarthralgia Chorea[§] Erythema marginatum[¶] Subcutaneous nodules	Carditis (excluding subclinical evidence of rheumatic valvulitis on echocardiogram) Polyarthritis[††] Chorea[§] Erythema marginatum[¶] Subcutaneous nodules
Minor manifestations	Monoarthralgia Fever[‡‡] ESR ≥30 mm/h or CRP ≥30 mg/L Prolonged P-R interval on ECG[§§]	Fever[‡‡] Polyarthralgia or aseptic mono-arthritis ESR ≥30 mm/h or CRP ≥30 mg/L Prolonged P-R interval on ECG[§§]

[†]High-risk groups are those living in communities with high rates of ARF (incidence >30/100,000 per year in 5–14 year olds) or RHD (all-age prevalence >2/1000). Aboriginal people and Torres Strait Islanders living in rural or remote settings are known to be at high risk. Data are not available for other populations, but Aboriginal people and Torres Strait Islanders living in urban settings, Maoris and Pacific Islanders, and potentially immigrants from developing countries, may also be at high risk. [‡]Elevated or rising antistreptolysin O or other streptococcal antibody, or a positive throat culture or rapid antigen test for GAS. [††]A definite history of arthritis is sufficient to satisfy this manifestation. Note that if polyarthritis is present as a major manifestation, polyarthralgia or aseptic mono-arthritis cannot be considered an additional minor manifestation in the same person. [§]Chorea does not require other manifestations or evidence of preceding GAS infection, provided other causes of chorea are excluded. [¶]Care should be taken not to label other rashes, particularly non-specific viral exanthemas, as erythema marginatum. [‡‡]Oral, tympanic or rectal temperature ≥38°C on admission, or a reliably reported fever documented during the current illness. [§§]If carditis is present as a major manifestation, a prolonged P-R interval cannot be considered an additional minor manifestation.

CRP, C-reactive protein; ECG, electrocardiogram; ESR, erythrocyte sedimentation rate.

Evidence of preceding group A streptococcal infection

All suspected cases of ARF (except those with chorea or low-grade subacute carditis) should have elevated serum streptococcal serology demonstrated.

If the initial titre is below the upper limit of normal (ULN) for age, repeat testing after 10–14 days.

In the absence of local data, it is recommended that ULN values in the following Table be used.

Upper limit of normal for serum streptococcal antibody titres

Age group	ULN (U/mL)	
(years)	ASO titre	Anti-DNase B titre
1-4	170	366
5-14	276	499
15-24	238	473
25-34	177	390
≥35	127	265

Anti-DNase, antideoxyribonuclease B; ASO, antistreptolysin O; ULN, upper limit of normal.

Manifestations of ARF

Major manifestations	
Carditis	Usually presents clinically as an apical holosystolic murmur, with or without a mid-diastolic flow murmur, or an early diastolic murmur at the base of the heart or left sternal edge
Polyarthritis	Extremely painful, affecting the large joints, especially the ankles and knees, is usually asymmetrical and migratory, but can be additive Usually responds within 3 days of starting NSAID therapy
Aseptic mono-arthritis or polyarthralgia	A major manifestation in high-risk group but a minor manifestation in other groups. Arthralgia that is migratory and asymmetrical, affecting large joints, is most indicative of ARF
Sydenham's chorea	Consists of jerky, uncoordinated movements, especially affecting the hands, feet, tongue and face, disappears during sleep Echocardiography is essential for all patients with chorea
Erythema marginatum	Extremely rare, as well as difficult to detect in Aboriginal people, but highly specific for ARF Occurs as circular patterns of bright pink macules or papules on the trunk and proximal extremities
Subcutaneous nodules	Rare, but-highly specific manifestations of ARF and strongly associated with carditis Present as crops of small, round, painless nodules over the elbows, wrists, knees, ankles, Achilles tendon, occiput and posterior spinal processes of vertebrae
Minor manifestations	
Fever	Most manifestations of ARF are accompanied by fever A reported recent history of fever or presenting fever of ≥38°C
Elevated acute phase reactants	Serum CRP level of ≥30 mg/L or ESR of ≥30 mm/h meets this diagnostic criterion
Prolonged P-R interval	If a prolonged P-R interval is detected, ECG should be repeated after 1–2 months. If it has returned to normal, ARF becomes a more likely diagnosis

CRP, C-reactive protein; ECG, electrocardiogram; ESR, erythrocyte sedimentation rate; NSAID, non-steroidal anti-inflammatory drug.

Differential diagnoses of common major presentations of ARF

The diagnosis of ARF is based on the assumption that other likely diagnoses have been excluded.

Many of the clinical features of ARF are non-specific, so a wide range of differential diagnoses should be considered.

Post-streptococcal syndromes such as PANDAS and post-streptococcal reactive arthritis may be confused with ARF, and these diagnoses should rarely, if ever, be made in high-risk populations.

Upper limits of normal of P-R interval

Age group (years)	Sec
3–12	0.16
12–16	0.18
17+	0.20

Source: Adapted from Park MK, *Pediatric cardiology for practitioners*, 2nd edn. Chicago: Year Book Medical; 1998.

Presentation		
Polyarthritis and fever	**Carditis**	**Chorea**
Septic arthritis (including disseminated gonococcal infection)[†]	Innocent murmur	Systemic lupus erythematosus
Connective tissue and other autoimmune disease[††]	Mitral valve prolapse	Drug intoxication
Viral arthropathy[¥]	Congenital heart disease	Wilson's disease
Reactive arthropathy[¥]	Infective endocarditis	Tic disorder[‡]
Lyme disease[≠]	Hypertrophic cardiomyopathy	Choreoathetoid cerebral palsy
Sickle cell anaemia	Myocarditis: viral or idiopathic	Encephalitis
Infective endocarditis	Pericarditis: viral or idiopathic	Familial chorea (including Huntington's)
Leukaemia or lymphoma		Intracranial tumour
Gout and pseudogout		Lyme disease[≠]
		Hormonal[§]

[†]Gonorrhoea should be actively sought in all sexually-active cases. Tests for gonorrhoea include polymerase chain reaction (PCR) of joint aspirate, endocervical PCR (gonococcal and chlamydia) and microscopy, culture and sensitivity, or urine/self-collected vaginal swabs in cases where endocervical PCR is not possible. [††]Includes rheumatoid arthritis, juvenile chronic arthritis, inflammatory bowel disease, systemic lupus erythematosus, systemic vasculitis and sarcoidosis. [¥]Mycoplasma, cytomegalovirus, Epstein–Barr virus, parvovirus, hepatitis, rubella vaccination, and *Yersinia* spp and other gastrointestinal pathogens. [≠]Lyme disease has not been confirmed in Australia or New Zealand. [‡]Possibly including PANDAS (paediatric autoimmune neuropsychiatric disorder associated with streptococcal infection). [§]Includes oral contraceptives, pregnancy (chorea gravidarum), hyperthyroidism and hypoparathyroidism.

Investigations in suspected ARF

All patients with suspected or confirmed ARF should undergo echocardiography to confirm or refute the diagnosis of rheumatic carditis.

Other investigations are listed below.

Recommended for all cases

White blood cell count

Erythrocyte sedimentation rate (ESR)

C-reactive protein (CRP)

Blood cultures, if febrile

Electrocardiogram (if prolonged P-R interval or other rhythm abnormality, repeat in 2 weeks and again at 2 months, if still abnormal

Chest X-ray, if clinical or echocardiographic evidence of carditis

Echocardiogram (consider repeating after 1 month, if negative)

Throat swab (preferably before giving antibiotics): culture for group A streptococcus

Antistreptococcal serology: both ASO and anti-DNase B titres, if available (repeat 10–14 days later if first test not confirmatory)

Tests for alternative diagnoses, depending on clinical features

Repeated blood cultures, if possible endocarditis

Joint aspirate (microscopy and culture) for possible septic arthritis

Copper, ceruloplasmin, antinuclear antibody, drug screen for choreiform movements

Serology and autoimmune markers for arboviral, autoimmune or reactive arthritis

RHD Australia

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The Australian guideline for prevention, diagnosis and management of acute rheumatic fever and rheumatic heart disease (2nd edition)

Quick reference guides include:

- Primary prevention of ARF
- Diagnosis of ARF
- Management of ARF
- Secondary prevention of ARF
- Management of RHD
- RHD in pregnancy
- RHD control programs

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