

DIAGNOSIS OF ACUTE RHEUMATIC FEVER

Quick Reference Guide for Health Professionals



This quick reference guide is derived from 'National Heart Foundation of Australia (NHFA) and the Cardiac Society of Australia and New Zealand (CSANZ) Diagnosis and management of acute rheumatic fever and rheumatic heart disease in Australia — an evidence-based review. 2006'.

What is acute rheumatic fever?

Acute rheumatic fever (ARF) is an auto-immune response to bacterial infection with group A streptococcus (GAS). People with ARF are often in great pain and require hospitalisation. After the acute episode, rheumatic heart disease (RHD) — damage to the heart valves — may remain. People who have had ARF previously are much more likely than the wider community to have subsequent episodes. Recurrences of ARF are likely to cause further valve damage, leading to steady worsening of RHD.

Who gets acute rheumatic fever?

Although ARF is relatively rare in industrialised countries, it is a significant cause of disease among Aboriginal and Torres Strait Islander peoples. Incidence of RHD is also high among these populations, with significant rates of procedures and death among young adults.

Problems with diagnosis and management

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

- although strategies for preventing RHD are proven, simple, cheap and cost-effective, they are not 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 variability in the management of these diseases, with lack of up-to-date training and experience in the management of ARF and RHD occasionally resulting in inappropriate management; and
- access to health care services by population groups experiencing the highest rates of ARF and RHD is limited.

IDENTIFYING HIGH-RISK GROUPS

- High-risk groups are those living in communities with high rates of ARF (incidence >30 per 100,000 per year in 5–14-year-olds) or RHD (all-age prevalence >2 per 1,000).
- Aboriginal and Torres Strait Islander Australians living in rural or remote settings are known to be at high risk.
- Data are not available for other populations, but Aboriginal and Torres Strait Islander Australians living in urban settings and potentially immigrants from developing countries may also be at high risk.
- ARF is predominantly a disease of children aged 5–14 years, although people can have recurrent episodes well into their forties.

DIAGNOSTIC CRITERIA FOR ARF

Accurate diagnosis of ARF is important, as:

- over-diagnosis will result in the individual receiving treatment unnecessarily; and
- under-diagnosis may lead to further attacks of ARF, cardiac damage and 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 disease. The table below outlines diagnostic criteria for high- and low-risk populations in Australia.

2005 AUSTRALIAN GUIDELINES FOR THE DIAGNOSIS OF ARF		
	HIGH-RISK GROUPS	ALL OTHER GROUPS
Initial episode of ARF	2 major or 1 major and 2 minor manifestations plus evidence of a preceding GAS infection [†]	
Recurrent attack of ARF with known past ARF or RHD	2 major or 1 major and 2 minor or 3 minor manifestations plus evidence of a preceding GAS infection [†]	
Major manifestations	Carditis (including subclinical evidence of rheumatic valve disease on echocardiogram) Polyarthritits, aseptic mono-arthritis or polyarthralgia [‡] Chorea [¥] Erythema marginatum [§] Subcutaneous nodules	Carditis (excluding subclinical evidence of rheumatic valve disease on echocardiogram) Polyarthritits [‡] Chorea [¥] Erythema marginatum [§] Subcutaneous nodules
Minor manifestations	Fever [‡] ESR ≥30mm/hr or CRP ≥30mg/L Prolonged P-R interval on ECG [Ⓣ]	Fever [‡] Polyarthralgia or aseptic mono-arthritis [‡] ESR ≥30mm/hr or CRP ≥30mg/L Prolonged P-R interval on ECG [Ⓣ]

Notes: All categories assume that other more likely diagnoses have been excluded (see *Differential diagnosis* table, next page). CRP=C-reactive protein; ECG=electrocardiogram; ESR=erythrocyte sedimentation rate; GAS=group A streptococcus

[†] Elevated or rising anti-streptolysin 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 polyarthritits 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 documented during the current illness.

[Ⓣ] If carditis is present as a major manifestation, prolonged P-R interval cannot be considered an additional minor manifestation.

EVIDENCE OF PRECEDING GROUP A STREPTOCOCCAL INFECTION

- All suspected cases of ARF (except those with chorea or low-grade sub-acute 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 the ULN values below be used for children.
- Patients with suspected ARF should be offered a single dose of benzathine penicillin G at secondary prophylaxis doses and reviewed in 1 month with a repeat echocardiogram to detect the appearance of new lesions.
- If there is evidence of rheumatic valve disease clinically or on echocardiogram, the diagnosis is confirmed, and long-term secondary prophylaxis can be continued.

AGE GROUP	UPPER LIMIT OF NORMAL (IU/ML)	
(years)	ASO titre	Anti-DNase B titre
4–5	120	100
6–9	480	400
10–14	320	380

Notes: ASO=anti-streptolysin; anti-DNase=anti-deoxyribonuclease B

MANIFESTATIONS OF ARF

MAJOR MANIFESTATIONS

Carditis	<ul style="list-style-type: none"> 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
Polyarthritis	<ul style="list-style-type: none"> Extremely painful, affecting the large joints — especially the ankles and knees; usually asymmetrical and migratory, but can be additive Usually responds within 3 days of starting NSAID therapy
Sydenham's chorea	<ul style="list-style-type: none"> Consists of jerky, uncoordinated movements, especially affecting the hands, feet, tongue and face Echocardiography is essential for all patients with chorea
Erythema marginatum	<ul style="list-style-type: none"> Extremely rare as well as difficult to detect in Aboriginal Australians, but highly specific for ARF Occurs as circular patterns of bright pink macules or papules on the trunk and proximal extremities
Subcutaneous nodules	<ul style="list-style-type: none"> Rare but highly specific manifestations of ARF, 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 the vertebrae

MINOR MANIFESTATIONS

Aseptic mono-arthritis or polyarthralgia	<ul style="list-style-type: none"> A major manifestation in high-risk groups and may suggest ARF in other groups if the arthralgia is migratory, asymmetrical, affecting large joints
Fever	<ul style="list-style-type: none"> Most manifestations of ARF are accompanied by fever
Elevated acute-phase reactants	<ul style="list-style-type: none"> Serum CRP level of $\geq 30\text{mg/L}$ or ESR of $\geq 30\text{mm/hr}$ meets this diagnostic criterion
Prolonged P-R interval	<ul style="list-style-type: none"> 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

Notes: CRP=C-reactive protein; ECG=electrocardiogram; ESR=erythrocyte sedimentation rate; NSAID=non-steroidal anti-inflammatory drug

DIFFERENTIAL DIAGNOSES OF COMMON MAJOR PRESENTATIONS OF ARF

- 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.
- Some post-streptococcal syndromes may be confused with ARF and these diagnoses should rarely, if ever, be made in high-risk populations.

	PRESENTATION		
	POLYARTHRITIS AND FEVER	CARDITIS	CHOREA
Differential diagnoses	<ul style="list-style-type: none"> Septic arthritis (including gonococcal) Connective tissue and other auto-immune disease* Viral arthropathy† Reactive arthropathy‡ Lyme disease¥ Sickle-cell anaemia Infective endocarditis Leukaemia or lymphoma Gout and pseudogout 	<ul style="list-style-type: none"> Innocent murmur Mitral valve prolapse Congenital heart disease Infective endocarditis Hypertrophic cardiomyopathy Myocarditis — viral or idiopathic Pericarditis — viral or idiopathic 	<ul style="list-style-type: none"> Systemic lupus erythematosus Drug intoxication Wilson's disease Tic disorder‡ Choreoathetoid cerebral palsy Encephalitis Familial chorea (including Huntington's) Intracranial tumour Lyme disease¥ Hormonal§

Notes:

- * Includes rheumatoid arthritis, juvenile chronic arthritis, inflammatory bowel disease, systemic lupus erythematosus, systemic vasculitis and sarcoidosis, among others.
- † *Mycoplasma*, cytomegalovirus, Epstein–Barr virus, parvovirus, hepatitis, rubella vaccination, *Yersinia* spp and other gastrointestinal pathogens.
- ‡ Possibly including PANDAS (paediatric auto-immune neuropsychiatric disorder associated with streptococcal infection).
- ¥ Lyme disease has not been confirmed in Australia or New Zealand.
- § Includes oral contraceptives, pregnancy (chorea gravidarum), hyperthyroidism, hypoparathyroidism.

INVESTIGATIONS IN SUSPECTED ACUTE RHEUMATIC FEVER

- 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
- C-reactive protein
- Blood cultures if febrile
- Electrocardiogram (repeat in 2 weeks, then 2 months if prolonged P-R interval or other rhythm abnormality)
- 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
- Anti-streptococcal serology: both anti-streptolysin O 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, anti-nuclear antibody, drug screen for choreiform movements
- Serology and auto-immune markers for arboviral, auto-immune or reactive arthritis

FURTHER INFORMATION

The full evidence-based review from which this quick reference guide is derived provides detailed information on the diagnosis and management of ARF, secondary prevention and RHD control programs, and diagnosis and management of RHD.

Other quick reference guides are:

- *Management of Acute Rheumatic Fever*
- *Secondary Prevention of Acute Rheumatic Fever*
- *Rheumatic Heart Disease Control Programs*
- *Management of Rheumatic Heart Disease.*



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