

### Note 4

#### Investigations in Suspected ARF

##### RECOMMENDED FOR ALL CASES

- White blood cell count
- Erythrocyte sedimentation rate (repeat weekly once diagnosis confirmed)
- C-reactive protein
- Blood cultures if febrile
- Electrocardiogram (repeat as necessary if conduction abnormality more than first degree)
- Chest x-ray if clinical or echocardiographic evidence of carditis
- Echocardiogram (repeat as necessary in 2-4 weeks if equivocal, or if serious carditis)
- 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

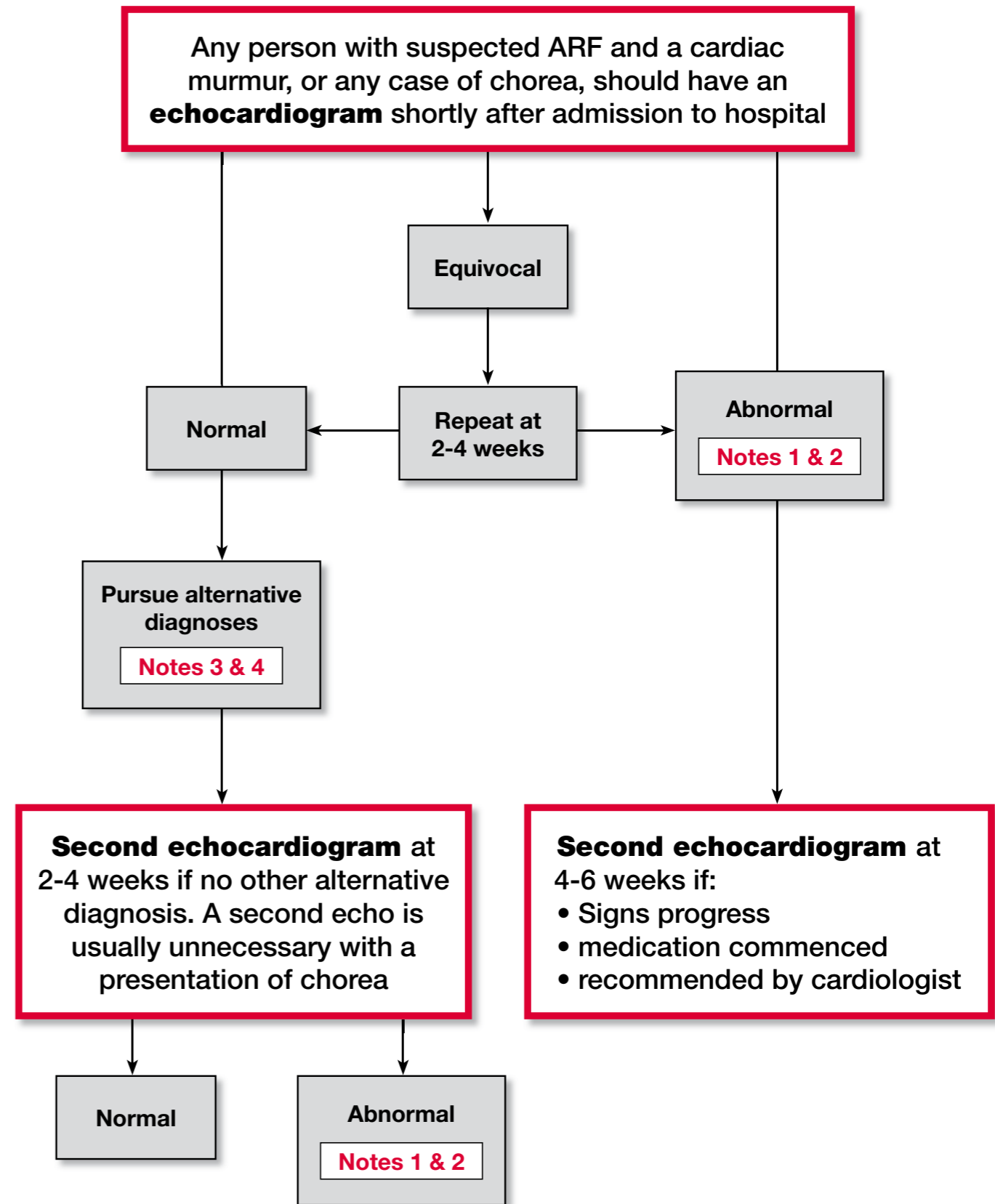
- Repeated blood cultures if possible endocarditis or septic arthritis
- Joint aspirate (microscopy and culture) for possible septic arthritis\*
- Joint X-ray
- Copper, caeruloplasmin, anti-nuclear antibody, drug screen, and consider CT/MRI head for choreiform movements\*\*
- Serology and auto-immune markers for auto-immune or reactive arthritis (including ANA - Anti Nuclear Antibody).

\* Typically, the synovial fluid in joints affected by ARF contains 10,000 to 100,000 white blood cells/mm<sup>3</sup> (predominantly neutrophils). The protein concentration is approximately 4g/dL, glucose levels are normal, gram stain negative and a good mucin clot is present<sup>7</sup>

\*\* The chorea of ARF can be readily diagnosed on the basis of history, physical examination and laboratory evaluation. Neuroimaging is not necessary and should be reserved for patients who have an atypical presentation, such as hemichorea.<sup>8</sup>

### References

1. Vasan RS et al. Echocardiographic evaluation of patients with acute rheumatic fever and rheumatic carditis. *Circulation*. 1996; 94: 73-82.
2. Wilson NJ & Neutze JM. Echocardiographic diagnosis of subclinical carditis in acute rheumatic fever. *Int J Cardiol*. 1995; 50: 1-6.
3. World Health Organisation. WHO workshop for the development of standard definitions and methods for epidemiological studies and vaccine trials for group A streptococcus, 22-24 September 2005, Cairns, Australia.
4. Voss LM et al. Intravenous immunoglobulin in acute rheumatic fever: a randomized control trial. *Circulation*. 2001; 103: 401-406.
5. Lennon D. Acute rheumatic fever in children: recognition and treatment. *Pediatric Drugs*. 2004; 6: 363-373.
6. Carapetis J et al. Seminar: acute rheumatic fever. *Lancet*. 2005; 366: 155-168.
7. Homer C, Shulman ST. Clinical aspects of acute rheumatic fever. *J. Rheumatol*. 1991; 18 (Suppl. 29): 2-13.
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## Note 1

### Minimal Echocardiographic Criteria to Allow a Diagnosis of Pathological Valvular Regurgitation

#### AORTIC REGURGITATION

- Colour: Substantial colour jet seen in 2 planes extending greater than or equal to 1 cm beyond the valve leaflets
- Continuous wave or pulsed Doppler: Holodiastolic with well-defined high velocity spectral envelope

#### MITRAL REGURGITATION

- Colour: Substantial colour jet seen in 2 planes extending greater than or equal to 2 cm beyond the valve leaflets
- Continuous wave or pulsed Doppler: Holosystolic with well-defined high velocity spectral envelope

If the aetiology of aortic or mitral regurgitation on Doppler echocardiography is not clear, the following features support a diagnosis of rheumatic valve damage:

- Both mitral and aortic valves have pathological regurgitation
- The mitral regurgitant jet is directed posteriorly, as anterior mitral valve prolapse is more common than posterior valve prolapse
- Multiple jets of mitral regurgitation
- The presence of morphological or anatomical changes consistent with RHD (see guideline), but excluding slight thickening of valve leaflets:
  - definite thickening of mitral valve leaflets, indicative of chronic RHD\*
  - elbow or dog leg deformity\*\* of anterior mitral valve leaflets

\* Echocardiography allows the operator to comment on the appearance of valves that are affected by rheumatic inflammation. The degree of thickening gives some insight into the duration of valvulitis, no significant thickening occurring in the first weeks of acute rheumatic carditis (**Level IV** evidence - see guideline)

\*\* Only after several months is immobility of the subchordal apparatus and posterior leaflet observed. Several other findings have also been reported, including acute nodules, seen as a beaded appearance of the mitral valve leaflets.<sup>1</sup> Although none of these morphological features are unique to ARF, the experienced echocardiographic operator can use their presence as supportive evidence of a rheumatic aetiology of valvulitis.

Source: Adapted with permission from Wilson, N.J. & Neutze, J.M.<sup>2</sup> These criteria further evolved as part of the development of the Heart Foundation of Australia's guideline on rheumatic fever diagnosis (see guideline for writing group), and the WHO working groups on echocardiography.<sup>3</sup>

## Note 2

### Severity of ARF Carditis

#### MILD CARDITIS\*

- Mild mitral or aortic regurgitation clinically and/or on echo (fulfilling the minimal echo standards in **Note 1**) with no clinical evidence of heart failure and no evidence of cardiac chamber enlargement on CXR, ECG or echocardiography

#### MODERATE CARDITIS

- Any valve lesion of moderate severity clinically (e.g. mild or moderate cardiomegaly), **or**
- Any echocardiographic evidence of cardiac chamber enlargement or any moderate severity valve lesion on echo\*\*:
  - Mitral regurgitation is considered moderate if there is a broad high-intensity proximal jet filling half the left atrium or a lesser volume high-intensity jet producing prominent blunting of pulmonary venous inflow<sup>4</sup>
  - Aortic regurgitation is considered moderate if the diameter of the regurgitant jet is 15% to 30% of the diameter of the left ventricular outflow tract with flow reversal in upper descending aorta<sup>4</sup>

#### SEVERE

- Any impending or previous cardiac surgery for RHD, **or**
- Any severe valve lesion clinically (significant cardiomegaly expected, and/or heart failure), **or**
- Any severe valve lesion on echo:
  - Abnormal regurgitant colour and Doppler flow patterns in pulmonary veins are a prerequisite for severe mitral regurgitation<sup>4</sup>
  - Doppler reversal in lower descending aorta is required for severe aortic regurgitation.<sup>4</sup>

### Notes:

\* Valvular regurgitation is usually relatively mild in the absence of pre-existing disease; in first episodes of ARF, severe mitral and aortic regurgitation occurred in less than 10% of patients in New Zealand<sup>4</sup>

\*\* When there is both mitral and aortic regurgitation, one of them must be moderate by echo criteria in order for the carditis to be classified of moderate severity

Tricuspid and pulmonary regurgitation graded mild or greater may be seen in people with normal hearts who have fever, volume overload or pulmonary hypertension. For this reason a diagnosis of carditis should not be based on right-side regurgitation alone. Although pulmonary and tricuspid regurgitation are often seen in association with left-sided lesions in ARF, pressure and volume overload must be excluded before attributing even moderate tricuspid regurgitation to valvulitis. If both left and right-sided lesions coexist in ARF carditis, then the predominant influence for diagnosis is the severity of the left-sided lesion.

## Note 3

### Differential Diagnoses of Common Major Manifestations of ARF<sup>5,6</sup>

|                               | POLYARTHRITIS AND FEVER  | CARDITIS   | PRESENTATION | CHOREA  |
|-------------------------------|--|--|--------------|---|
| <b>Differential diagnoses</b> | <ul style="list-style-type: none"><li>• Other infections* (including gonococcal)</li><li>• Connective tissue and other auto-immune disease**</li><li>• Reactive arthropathy</li><li>• Sickle cell anaemia</li><li>• Infective endocarditis</li><li>• Leukaemia or lymphoma</li><li>• Gout and pseudogout</li><li>• Henoch-Schonlein purpura</li><li>• Post-streptococcal reactive arthritis***</li><li>• Other, e.g. HIV/AIDS, leukaemia</li></ul> | <ul style="list-style-type: none"><li>• Innocent murmur</li><li>• Mitral valve prolapse</li><li>• Congenital heart disease</li><li>• Infective endocarditis</li><li>• Hypertrophic cardiomyopathy</li><li>• Myocarditis — viral or idiopathic</li><li>• Pericarditis — viral or idiopathic</li></ul> |              | <ul style="list-style-type: none"><li>• Systemic lupus erythematosus</li><li>• Drug ingestion (extrapyramidal syndrome)#</li><li>• Wilson's disease (usually adult onset)</li><li>• Tic disorder (see guideline)</li><li>• Congenital, e.g. hyperbilirubinaemia</li><li>• Choreoathetoid cerebral palsy</li><li>• Encephalitis</li><li>• Familial chorea (including Huntington's)</li><li>• Intracranial tumour</li><li>• Hormonal§</li><li>• Metabolic, e.g. Lesch-Nyhan, hyperalanaemia, ataxia, telangiectasia</li><li>• Antiphospholipid antibody</li></ul> |

\* Includes bacterial arthritis, influenza B, cytomegalovirus, Epstein-Barr Virus, mycoplasma, rubella (also post-vaccination), hepatitis B, parvovirus, Yersinia spp and other gastrointestinal pathogens

\*\* Includes rheumatoid arthritis, juvenile chronic arthritis, inflammatory bowel disease, systemic lupus erythematosus, systemic vasculitis and sarcoidosis, among others

\*\*\* In these cases the arthritis may affect joints that are not commonly affected in ARF (such as the small joints of the hand), and is less responsive to anti-inflammatory treatment. It is recommended that the diagnosis of post-streptococcal reactive arthritis should rarely, if ever, be made in high-risk populations and with caution in low-risk populations (**Grade C** evidence - see guideline)

# Drugs and toxins include anticonvulsants, antidepressants, lithium, scopolamine, calcium channel blockers, methylphenidate, theophylline and antihistamines

§ Includes oral contraceptives, pregnancy (chorea gravidarum), hyperthyroidism and hypoparathyroidism.