This guideline for the diagnosis, management and secondary prevention of acute rheumatic fever (ARF) and rheumatic heart disease (RHD) was published in 2014. As a result of the 2019 update to the *Group A Streptococcal Sore Throat Management Guideline*, the following medication regimes have changed, but have not been updated in this document.

<table>
<thead>
<tr>
<th>Page ref</th>
<th>Medication</th>
<th>2014 ARF and RHD Guideline</th>
<th>Medication regime change in 2019 GAS guideline update</th>
</tr>
</thead>
<tbody>
<tr>
<td>13</td>
<td>Phenoxymethylpenicillin</td>
<td>Twice daily</td>
<td>2-3 times daily</td>
</tr>
<tr>
<td>13, 29</td>
<td>Amoxicillin</td>
<td>Once daily</td>
<td>1-2 times daily</td>
</tr>
<tr>
<td>26, 29, 36, 70</td>
<td>Erythromycin max daily dose</td>
<td>1000mg</td>
<td>1600mg</td>
</tr>
</tbody>
</table>
New Zealand Guidelines for Rheumatic Fever

Evidence-based, best practice Guidelines on:
3. Proposed Rheumatic Fever Primary Prevention Programme
Endorsed by:

The Cardiac Society of
Australia and New Zealand

Heart Foundation

Heart Foundation

Paediatric Society
New Zealand

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Amendments
The following amendments were made on 5th August 2015:
1. Endorsing organisations logos added above.
2. Endorsing organisations listed (page 8).
3. Table 30: LVESD updated in Point B (page 55).
4. Appendix A: Guideline development process updated to include endorsement process (page 85).
New Zealand Guidelines for Rheumatic Fever

Diagnosis, Management and Secondary Prevention of Acute Rheumatic Fever and Rheumatic Heart Disease: 2014 Update
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2014 Guideline Update – Key Changes

In 2009 the New Zealand government (at the behest of the Māori party) made rheumatic fever a priority health issue. Most of the new funding has been put towards the primary prevention of acute rheumatic fever (ARF). Details are recorded in the 2nd edition of the Group A Streptococcal Sore Throat Management Guideline: 2014 Update.¹

While there has not been large changes in the diagnosis, management and secondary prevention there is a moderate amount of new data of relevance in New Zealand and internationally. The authors felt it was appropriate to update the 2006 Diagnosis, Management and Secondary Prevention Guideline and improve their usefulness.²,³ An entire new section on rheumatic heart disease has been added.

The key changes in the New Zealand Guidelines for Rheumatic Fever: Diagnosis, Management and Secondary Prevention of Acute Rheumatic Fever and Rheumatic Heart Disease: 2014 Update are:

1. Acute rheumatic fever
   - Monoarthritis, whether or not the patient has been on NSAIDs, is now included as a major criterion of ARF (page 15-17)
   - The differences of the New Zealand ARF criteria compared to the American Heart Association⁴ and RHDAustralia criteria⁵ are summarised in Table 4 (page 15)
   - A section on ARF recurrences has been included that clarifies the definition and management of recurrence (page 16)
   - The relevance of indolent carditis is highlighted (page 16 and 23)
   - There is a new summary section called “Discharge planning and long term preventive measures” (page 32)
   - Aspirin is no longer recommended for ARF arthritis because of the risk of Reye’s syndrome.⁶ Naproxen is the evidence-based treatment of choice. However there is no elixir available in New Zealand. Ibuprofen is often used but there is no published evidence (page 26-27). There is no published evidence of Reyes Syndrome being associated with naproxen or ibuprofen. (page 26)

2. The duration of secondary prophylaxis has been clarified. Recommendations for the duration for secondary prophylaxis come in two phases:
   - Firstly, at the time of ARF diagnosis the duration of prophylaxis is recommended
   - Secondly, when at the time potential cessation of prophylaxis: more severe forms of rheumatic heart disease (RHD) at that time require a reevaluation of the length of prophylaxis.

3. A new section on planning for ongoing care following ARF diagnosis has been included (page 32). It has been recognised that without a checklist clinicians can overlook many aspects of what constitutes standard of care for the ARF patient.

4. A new section on rheumatic heart disease (RHD) has been added to highlight the key elements of care for those with chronic significant RHD including the frequency of follow up (page 45). Included features are recommended best practice dental care, anticoagulation for those on warfarin, endocarditis prophylaxis and indications for cardiac surgery. A detailed section of care for the RHD patient undergoing pregnancy and childbirth is included.

Screening for RHD using portable echocardiography did not exist at the time of the 2006 guideline; a summary of knowledge to date is included (page 58).
**Scope and Purpose of Guideline**

This guideline has been developed by the Heart Foundation of New Zealand and the Cardiac Society of Australia and New Zealand. This guideline is complemented by further guidelines on Group A Streptococcal Sore Throat Management Guideline: 2014 Update\(^1\) and Proposed Rheumatic Fever Primary Prevention Programme Guideline 2009.\(^7\)

The objectives of this guideline are:

- To identify and present the evidence for best practice in acute rheumatic fever (ARF) diagnosis
- To identify the standard of care that should be available to all people in New Zealand
- To identify areas where current management strategies may not be in line with available evidence
- To ensure that high-risk populations receive the same standard of care as that available to other New Zealanders.

**About the Guideline**

This guideline was developed by a writing group comprised of experts in rheumatic fever and rheumatic heart disease (RHD). Selected individuals with experience in ARF and relevant stakeholders were also involved. These included a range of general and specialist clinicians, allied health professionals, Māori and Pacific professionals, and lay representative groups.

This guideline has been produced for New Zealand and is endorsed by New Zealand organisations.

In 2006 the co-chairs of the guideline writing committee were involved in the development of a similar document for the Australian population, with the understanding that the Australian guidelines would be adapted for the New Zealand setting. We are grateful for the contribution of our Australian colleagues.

This 2014 2nd edition of the guidelines has been modified based on recent research in New Zealand and elsewhere and has taken account of recent developments in the area of ARF and RHD.

The development processes for the 2006 Guideline and 2014 Update are described in Appendix A.

**Disclaimer**

This document has been produced by the Heart Foundation of New Zealand and the Cardiac Society of Australia and New Zealand for health professionals. The statements and recommendations it contains are, unless labelled as “expert opinion”, based on independent review of the available evidence. Interpretation of this document by those without appropriate health training is not recommended, other than at the request of, or in consultation with, a relevant health professional.

In addition, the recommendations in this guideline are not intended to replace clinical judgment of each individual case. Treatment should take into account comorbidities, drug tolerance, lifestyle, living circumstances, cultural sensibilities and wishes. When prescribing medication, clinicians should observe usual contra-indications, be mindful of potential adverse drug interactions and allergies, monitor responses and ensure regular review.
Outline of Grading Methodology Used

The review includes levels of evidence and accompanying grades of recommendation (Table 1).

Table 1: Levels of Evidence for Clinical Interventions and Grades of Recommendation

<table>
<thead>
<tr>
<th>Level of Evidence</th>
<th>Study Design</th>
<th>Grade of Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Evidence obtained from a systematic review of all relevant randomised controlled trials (RCT)</td>
<td>A</td>
</tr>
<tr>
<td>II</td>
<td>Evidence obtained from at least one properly designed randomised controlled trial</td>
<td>B</td>
</tr>
<tr>
<td>III-I</td>
<td>Evidence obtained from well-designed pseudo-randomised controlled trials (alternate allocation or some other method)</td>
<td>B</td>
</tr>
<tr>
<td>III-2</td>
<td>Evidence obtained from comparative studies with concurrent controls and allocation not randomised (cohort studies), case-control studies, or interrupted time series with a control group</td>
<td>B</td>
</tr>
<tr>
<td>III-3</td>
<td>Evidence obtained from comparative studies with historical control, 2 or more single-arm studies, or interrupted time series with a parallel control group</td>
<td>C</td>
</tr>
<tr>
<td>IV</td>
<td>Evidence obtained from case series, either post-test or pre-test and post-test</td>
<td>C</td>
</tr>
<tr>
<td></td>
<td>Insufficient evidence available – expert opinion or panel consensus judgment</td>
<td>D/1</td>
</tr>
</tbody>
</table>

Note: The levels of evidence and grades of recommendations were originally adapted from the National Heart Foundation of Australia Rheumatic Fever guidelines (2006) and used in the 2006 New Zealand Guidelines for Rheumatic Fever: Diagnosis, Management and Secondary Prevention Guideline.2

The section on Pregnancy and Childbirth (pages 48-53) in this guideline update has been adapted with permission from The Australian Guideline for prevention, diagnosis and management of acute rheumatic fever and rheumatic heart disease (2nd edition). 2012.5

The levels of evidence for clinical interventions and grades of recommendation used in the Pregnancy and Childbirth section are detailed in Table 2.

Table 2: Levels of Evidence for Clinical Interventions and Grades of Recommendation Used in the Pregnancy and Childbirth Section

<table>
<thead>
<tr>
<th>Level of Evidence</th>
<th>Study Design</th>
<th>Grade of Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Evidence obtained from a systematic review of all relevant RCT</td>
<td>A Rich body of high quality RCT data</td>
</tr>
<tr>
<td>II</td>
<td>Evidence obtained from at least one properly-designed RCT</td>
<td>B Limited body of RCT data or high-quality non-RCT data</td>
</tr>
<tr>
<td>III-I</td>
<td>Evidence obtained from well-designed pseudo RCT (alternate allocation or some other method)</td>
<td>C Limited evidence</td>
</tr>
<tr>
<td>III-2</td>
<td>Evidence obtained from comparative studies, with concurrent controls and allocation not randomised (cohort studies), case-control studies, or interrupted time series with a control group</td>
<td>D No evidence available; panel consensus judgement</td>
</tr>
<tr>
<td>III-3</td>
<td>Evidence obtained from comparative studies with historical control, 2 or more single-arm studies, or interrupted time series with a parallel control group</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>Evidence obtained from case series, either post-test or pre-test and post-test</td>
<td></td>
</tr>
</tbody>
</table>

Note: The levels of evidence and grades of recommendations are adapted from the National Health and Medical Research Council levels of evidence for clinical interventions and the US National Institutes of Health clinical guidelines (details can be found at www.nhlbi.nih.gov/guidelines/obesity/ob_home.htm).

RCT, randomised, controlled trial.

2014 Guideline Update

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Endorsing Organisations for 2006 Guideline
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- Te Hotu Manawa Māori
- Pacific Islands Heartbeat
- Paediatric Society of New Zealand
- The Rheumatic Fever Trust.

Organisations Consulted for 2006 Guideline
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- Australasian Faculty of Public Health Medicine
- National Heart Foundation of Australia
- New Zealand Nurses Organisation
- New Zealand Ministry of Health
- Pasifika Medical Association of New Zealand
- Royal Australasian College of Physicians
- Te Ohu Rata o Aotearoa - Māori Medical Practitioners Association.

Declaration
No conflicts of interest were involved in the development of this guideline. Rachel Liddel who coordinated the writing of this guideline was funded by the Heart Foundation of New Zealand and the Australasian Faculty of Public Health Medicine.
Introduction

Key Points

- Acute rheumatic fever (ARF), an auto-immune response to group A streptococcus (GAS) infection of the upper respiratory tract, may result in carditis or inflammation of the mitral and/or aortic valves. When the inflammation leads to permanent damage of the valves the individual has rheumatic heart disease (RHD). Recurrences of rheumatic fever are likely in the absence of preventative measures and may cause further cardiac valve and muscle damage, leading to heart failure, strokes and premature death. Bacterial endocarditis is also a complication.

- Although ARF is now rare in industrialised countries, it is a significant cause of disease among Māori and Pacific children in New Zealand. The prevalence of RHD is also high among these populations, with significant morbidity and mortality among young and middle aged adults.

- Appropriate treatment of sore throats in high risk populations will eliminate GAS in most cases, and prevent individual cases of ARF.

- Prevention of recurrence (and secondary prevention), with intramuscular benzathine penicillin is both effective and a highly cost-effective means of reducing the burden of RHD.

- Primary prevention concerns the prevention of ARF and is the subject of separate guidelines (Group A streptococcal sore throat management guideline update 2014, Proposed rheumatic fever primary prevention plan guideline 2009).

- Primordial prevention concerns the social and environmental risk factors that could be altered to decrease the intensity and effect of GAS infection on the population. These factors include overcrowding, poor living conditions, and perhaps other effects of poverty.

Acute rheumatic fever (ARF) is thought to be an auto-immune consequence of infection with the bacterium group A streptococcus (GAS). It causes an acute generalised inflammatory response and an illness that affects only certain parts of the body, mainly the heart, joints, brain and skin. Individuals with ARF are often severely unwell, in great pain and require hospitalisation. Despite the dramatic nature of the acute episode, ARF leaves no lasting damage to the brain, joints or skin. However, the damage to the heart, or more specifically the mitral and/or aortic valves, may remain once the acute episode has resolved. These long term changes are RHD. People who have had ARF previously are much more likely than the wider community to have subsequent episodes. These recurrences of ARF may cause further cardiac valve damage. Hence RHD steadily worsens in people who have multiple episodes of ARF.

Because of its high prevalence in developing countries, RHD is the most common form of paediatric heart disease globally. In many countries it is the most common cause of cardiac mortality in children and adults aged less than 40 years.

Pathogenesis

ARF has been shown to develop in approximately one to three percent of those in an epidemic situation of untreated exudative pharyngitis and/or a culture positive for GAS. In a New Zealand study of primary prevention the attack rate after culture proven GAS pharyngitis was 0.2%. Despite the high incidence in some ethnic groups (such as Māori and Pacific people in New Zealand), a genetic predisposition to ARF remains unproven. Some strains of GAS have been repeatedly identified as causative for ARF at least in some environments (and therefore labelled “rheumatogenic”) but in other circumstances a wide range of strains appear to be associated with ARF. The role of skin infections remains uncertain.

Following GAS infection, there is a latent period averaging three weeks before the symptoms of ARF begin. By the time the symptoms develop, the infecting strain of GAS has usually been eradicated by the host immune response.
Epidemiology

While once a relatively common disease in previous centuries, the burden of ARF in industrialised countries declined dramatically during the 20th Century, due mainly to improvements in living standards (and hence reduced transmission of GAS) and better availability of medical care. In most affluent populations ARF is now rare. RHD is also rare in younger people in industrialised countries, although it is still seen in some elderly patients, a legacy of ARF half a century earlier.

By contrast, ARF and RHD remain common in many developing countries. A review of the global burden of GAS-related disease estimated that there is a minimum of 15.6 million people with RHD, another 1.9 million with a history of ARF but no carditis who still require preventive treatment, 470,000 new cases of ARF each year and over 230,000 deaths due to RHD annually. Robust population-based epidemiological data for ARF (and RHD) is lacking and the burden of disease is likely to be several times higher than estimates so far published.

There is substantial regional variation in the burden of ARF and RHD. The highest documented rates in the world so far have been found in Māori and Pacific people in New Zealand, Aboriginal Australians and those in Pacific Island nations. Where the prevalence of RHD has been recorded it has been found to be high in Sub-Saharan Africa, Latin America, the Indian subcontinent, the Middle East and Northern Africa. New Zealand has had sustained high rates of ARF and RHD for many decades with RHD being a significant cause of premature death in this country. A number of surveys of ARF and RHD incidence have been conducted since the early 1900s in New Zealand. In the 1920s, surveys of school records in New Zealand determined an approximate annual total population (school aged) incidence of ARF of 65 per 100,000. From 1956 to 1973, the Wairoa College Study determined that the decline in incidence of ARF seen in other developed countries was not evident in New Zealand and those pockets of the country which experienced isolation and socio-economic deprivation had significantly higher rates of both ARF and RHD.

From 1995 to 2000, around 100 cases of ARF (first and recurrent cases) were notified annually in New Zealand, with an incidence of 13.8 per 100,000 population in 5 to 14 year olds. From 1993 to 1999, the Auckland Register recorded an incidence of 21.9 per 100,000 population in 5 to 14 year olds. Auckland accounts for 60% of the active cases on New Zealand registers. Recently in New Zealand, hospitalisation data (2000-2009) which provides the most comprehensive New Zealand population based data to date has been published on index cases of ARF i.e. first case of ARF only. Recurrent ARF admissions were excluded from this analysis. For individuals less than 25 years of age there were 1,225 ARF admissions with most in the 5-14 year old age group (1007/1225, 82%). Rates for 5-14 year old children were 20 or 40 fold higher respectively for those self-identified as Māori or Pacific than non-Māori/non-Pacific.

The peak of ARF is around eight years of age. It is rare to diagnose ARF under the age of three (perhaps because the immune system needs to fully mature). As RHD represents the cumulative heart damage of previous ARF episodes, the prevalence of RHD peaks in the third and fourth decades of life. Therefore, although ARF is a disease with its roots in childhood, its effects are felt throughout adulthood, especially in the young adult years when people might otherwise be at their most productive. In recent times studies on the prevalence of RHD have proliferated with the advent of echocardiography following the landmark study in Mozambique. Some studies show that up to 40% of adults with RHD have no recollection or recognition nor evidence of preceding episodes of ARF. However it is not clear whether this is lack of awareness of the importance of a sore joint(s) either by the patient and family or the health system or problems with access to health care or knowledge. The pathogenesis of RHD without previous documentation of acute symptoms may be recurrent asymptomatic episodes of carditis. In the absence of painful arthritis/arthralgia medical help is not sought. Cardiac symptoms only occur when there is severe valve regurgitation and cardiac decompensation with heart failure. True population based incidence studies of ARF are rare. New Zealand, with a high rate of ARF and RHD, and a highly developed medical care system is in a unique position to study RHD/ARF (see references above).

Disparity by ethnicity in rheumatic fever populations has been described in many world centres where population groups experiencing low socio-economic status and living in overcrowded situations present with a high incidence of ARF. Historically in New Zealand, Māori and Pacific peoples have the highest burden of both ARF and RHD. Despite the significant issues regarding the accuracy of ethnicity data in past morbidity and mortality statistics, the rates of ARF in Māori have always been reported as significantly greater than those seen in non-Māori. For example, from 1949 to 1953 the reported incidence of ARF in Māori children (rates of greater than 1000 per 100,000) was 11 times
that of the non-Māori population.\textsuperscript{21} Using hospitalisation data the incidence rates between 1993 and 2009 for children 5 to 14 years of age was 81.2 per 100,000 for Pacific, 40.2 per 100,000 for Māori and 2.1 per 100,000 for non-Māori/Pacific children.\textsuperscript{31} These discrepancies are similar in District Health Boards where ARF occurs.\textsuperscript{31} Depending on the year analysed, the Pacific incidence rates for ARF are about 40 fold higher and for Māori, about 20-fold higher than non-Māori/Pacific children.\textsuperscript{31}

However from New Zealand hospitalisation data using the NZ Deprivation index ARF incidence is clearly linked to socio-economic status.\textsuperscript{31} Jaine et al found ARF rates significantly related to household crowding.\textsuperscript{38}

As well as higher rates of initial ARF incidence, Māori and Pacific people also have the highest rates of ARF recurrence. From 1973 to 1982 (prior to the introduction of systematic prophylaxis delivery) recurrence rates in Māori were 40% compared to 22% in non-Māori.\textsuperscript{39} A review of cases in the Auckland rheumatic fever register from 1993 to 1999 found that although the total recurrence rates had dropped significantly from the 1980s (22% to 5.5%), all of the recurrences found were in Māori and Pacific people.\textsuperscript{29,30} It is therefore not surprising that Māori and Pacific people have much higher rates of carditis, RHD and consequent heart failure, as the risk of these complications increases with each attack of ARF. However in most regions of New Zealand where ARF is an issue, there are prophylaxis programmes in place, demonstrably reducing the ARF recurrence rate.\textsuperscript{30,40,41,42}

There is no evidence to date Māori and Pacific people have increased genetic susceptibility to rheumatic fever. It is more likely that the over-representation of these sectors of the population reflects a combination of overcrowded conditions, socio-economic deprivation, an increased incidence of upper respiratory infections with GAS, and different treatment options or opportunities for appropriate and effective health care.\textsuperscript{23,33,43}

**Cost to New Zealand**

There are significant personal, community and national costs associated with ARF and RHD. These result from repeated and prolonged hospitalisation, the resources required for medical prophylaxis and treatment, surgical intervention, negative physical and psychological experience, disruption of the lives of cases and their families and often premature death.\textsuperscript{44} In 1991, it was estimated that the total cost of ARF and RHD to the Auckland health service alone was $3.6 million per annum, with chronic RHD accounting for 71% of the costs. Costs involved were the direct costs of GP and outpatient visits, prescription charges, travel, radiology and the costs of informal care given by household members.\textsuperscript{34}

In addition to these direct costs, there are a number of indirect costs of ARF and RHD, which are often difficult to measure. These include the physical impacts such as loss of life (it has been estimated that five to ten young people die each year as a direct result of ARF or RHD) and physical development as well as the loss of quality of life. This occurs through time away from education and occupation, impacts on family/whānau relationships, psychological effects and the loss of ability for children and young adults to realise their full potential.\textsuperscript{24,34}

More recent publications have highlighted different aspects. Over a two year period paediatric cardiology at Starship Children’s hospital admitted 36 children 49 times (mean age 11.8 years +/- 2.4 years). The cost was $1.9 million.\textsuperscript{45} A study reviewing New Zealand hospitalisations (2000-2009) and deaths (2000-2007) of ARF and RHD found age-adjusted mortality to be 5-10 fold higher for Māori and Pacific peoples than for non-Māori/Pacific.\textsuperscript{46} There were on average 159 RHD deaths per year. New Zealand European with RHD die approximately 25 years older than Māori/Pacific peoples (mean 56.4 years vs 79.4 years), reflecting an earlier disease burden before the virtual disappearance of ARF in non-Māori.\textsuperscript{21} The average annual DRG-based cost of hospitalisations for ARF/RHD across all age groups (2000-2009) was $12 million, with heart surgery accounting for 71% of the cost.\textsuperscript{46}

**Population Projections**

Currently Māori and Pacific people in New Zealand make up a sizeable percentage of the childhood population. In 2013, approximately 33.80% of Māori and 35.65% of Pacific people in New Zealand were under the age of 15 (compared to 14.64% European). The median age of New Zealand Europeans was 41.0 years, while for the Māori and Pacific ethnic groups the comparable figures were 23.9 and 22.1 years respectively.\textsuperscript{47}
It is reasonable to predict that the New Zealand population in the future will represent high growth and a sustained youthful age structure in the Māori and Pacific populations with many (particularly children) living in poor socio-economic circumstance. All these features have significant implications for ARF incidence, prevalence and prevention.

**Prevention of Acute Rheumatic Fever and Rheumatic Heart Disease**

**Primordial prevention**
ARF has virtually disappeared in the developed world, beginning its decline before the discovery of penicillin but coinciding with a rise in standard of living and improved access to health care. However, in the less developed world and including disadvantaged populations in New Zealand and Australia, ARF and its sequela RHD persist. In a systematic review numerous studies were found on the association between crowding and ARF. Studies in a population in inner city Baltimore, USA when ARF was prevalent revealed that when household crowding was held constant the difference between the rate of ARF between African American and “White” populations disappeared.

**Primary prevention**
In the future, a cost-effective vaccine for group A streptococcus may be the ideal solution for the primary prevention of ARF. Scientific challenges have so far prevented the development of such a vaccine, although progress is being made. Currently prevention of an initial attack of ARF requires the prompt and accurate diagnosis and adequate antibiotic treatment of GAS throat infections. ARF can be prevented if the preceding throat infection is treated in a timely and effective way. Recommended treatment of streptococcal throat infection is intramuscular (IM) benzathine penicillin or a ten-day course of oral (twice a day) phenoxymethylpenicillin or once a day amoxicillin which eradicates the streptococci from the pharynx. The oral treatment is often used because it is safe, inexpensive and less painful.


**Secondary prevention**
Over the last 30 years one of the major successes in RHD management has been the marked decline in recurrent (and often disabling) attacks of rheumatic fever, due to the availability of effective antibiotics for secondary prophylaxis. The success of this approach was initially demonstrated in New Zealand in the 1990’s and again more recently. Secondary prevention of ARF is defined as the continuous administration of antibiotics (usually parenteral benzathine penicillin every 28 days) to cases with previous ARF or well-documented RHD. The aim of secondary prevention is to stop recolonisation or reinfection of the throat with group A streptococci and thereby preventing recurrence of ARF. The risk of ARF after the first attack of group A streptococci is approximately 0.3-3%, but with subsequent infection this risk rises to 25-75%. In addition, those who suffer carditis during their initial attack are significantly more likely to develop further carditis with subsequent streptococcal throat infections. The systematic use of regular antibiotic prophylaxis in known ARF cases has been shown to reduce the incidence of recurrent rheumatic fever, reduce the need for hospitalisation and surgery, decrease the rapidity and severity of RHD and improve quality of life. Furthermore, national prevention programmes based on secondary prevention have the potential for considerable cost savings, and have been found to be a cost-effective method of reducing mortality and morbidity from ARF internationally and in New Zealand.
A. DIAGNOSIS & MANAGEMENT

Diagnosis of Acute Rheumatic Fever (ARF)

Importance of Accurate Diagnosis
It is important that an accurate diagnosis of ARF is made as:

- Over-diagnosis will result in the individual receiving benzathine penicillin injections unnecessarily every four weeks for a minimum of ten years
- Under-diagnosis of ARF may lead to the individual suffering a further attack of ARF, cardiac damage and premature death.

The diagnosis of ARF relies on health professionals being aware of the diagnostic features, particularly when presentation is delayed or atypical. In Auckland for example, between 1993 and 1999, four patients diagnosed with septic arthritis by general medicine and orthopaedic surgeons, subsequently developed ARF.29,30

Currently, there is no laboratory test diagnostic for ARF, so diagnosis remains a clinical decision. The pre-test probability for diagnosis of ARF varies according to location and ethnicity. For example, in a region with high incidence of ARF (such as the Northern half of the North Island), a person with fever and arthritis is more likely to have ARF than one in a low incidence region (such as the South Island). Māori and Pacific people are also more likely than non-Māori and Pacific people to have ARF.

Current Approaches to Diagnosis
It is recommended that the New Zealand criteria are used for the diagnosis of ARF in New Zealand (Table 3) not the Jones criteria.61

### Table 3: New Zealand Guidelines for the Diagnosis of ARF

<table>
<thead>
<tr>
<th>Category</th>
<th>Diagnostic Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial episode of ARF</td>
<td>2 major or 1 major and 2 minor manifestations plus evidence of a preceding GAS infection*</td>
</tr>
<tr>
<td></td>
<td>Definite ARF</td>
</tr>
<tr>
<td>Initial episode of ARF</td>
<td>1 major and 2 minor with the inclusion of evidence of a preceding GAS infection* as a minor manifestation (Jones, 1956)62</td>
</tr>
<tr>
<td></td>
<td>Probable ARF</td>
</tr>
<tr>
<td>Initial episode of ARF</td>
<td>Strong clinical suspicion of ARF, but insufficient signs and symptoms to fulfil diagnosis of definite or probable ARF</td>
</tr>
<tr>
<td></td>
<td>Possible ARF</td>
</tr>
<tr>
<td>Recurrent attack of ARF</td>
<td>2 major or 1 major and 2 minor or several† minor plus evidence of a preceding GAS infection* (Jones, 1992)4</td>
</tr>
<tr>
<td>in a case with known past</td>
<td>Recurrent ARF</td>
</tr>
<tr>
<td>ARF or RHD</td>
<td></td>
</tr>
<tr>
<td>Major manifestations: modified† from Jones 1992 (see Table 5 for key points in identifying major manifestations)</td>
<td>Carditis (including evidence of subclinical rheumatic valve disease on echocardiogram)§ Polyarthritis§ or aseptic monoarthritis (with or without a history of NSAID use) See footnote to Table 4 Chorea (can be stand-alone for ARF diagnosis) Erythema marginatum Subcutaneous nodules</td>
</tr>
<tr>
<td>Minor manifestations: (see Table 6 for key points in identifying minor manifestations)</td>
<td>Fever Raised ESR or CRP Polyarthralgia§ Prolonged P-R interval on ECG</td>
</tr>
</tbody>
</table>
Categories of Definite, Probable and Possible ARF can be determined by the application of the New Zealand criteria to each case, including recurrences\(^30\) (Table 5 and 6).

All categories assume that other more likely diagnoses have been excluded. Please see additional tables for details about specific manifestations.

CRP=C-reactive protein; ECG=electrocardiogram; ESR=erythrocyte sedimentation rate; GAS=group A streptococcus; RHD=rheumatic heart disease

* Elevated or rising antistreptolysin O or other streptococcal antibody (Table 7), is sufficient for a diagnosis of definite ARF. A positive throat culture or rapid antigen test for GAS alone is less secure as 50% of those with a positive throat culture will be carriers only. Therefore, a positive culture alone demotes a case to probable or possible ARF.

† Most cases of recurrence fulfil the New Zealand criteria. However in some cases (such as new carditis on previous RHD) it may not be clear. Therefore in order to avoid under-diagnosis, a presumptive diagnosis of rheumatic recurrence may be made where there are several minor manifestations and evidence of a preceding GAS infection in a person with a reliable history of previous ARF or established RHD. In addition, WHO (2004) recommendations state that where there is established RHD, a recurrent attack can be diagnosed by the presence of two minor manifestations plus evidence of a preceding group A streptococcal infection.\(^51\)

‡ Acceptance of echocardiographic evidence of carditis as a major criterion was the New Zealand modification to the Jones (1992) update

§ When carditis is present as a major manifestation (clinical and/or echocardiographic), a prolonged P-R interval cannot be considered an additional minor manifestation in the same person

‖ Other causes of arthritis/arthralgia should be carefully excluded, particularly in the case of monoarthritis e.g. septic arthritis (including disseminated gonococcal infection), infective or reactive arthritis and auto-immune arthropathy e.g. juvenile chronic arthritis, inflammatory bowel disease, systemic lupus erythematosus, or other systemic vasculitis and sarcoidosis. Note that if polyarthritis or monoarthritis is present as a major manifestation, polyarthralgia cannot be considered an additional minor manifestation in the same person. Special consideration should be given to high-risk population groups such as Māori and Pacific people, and those residing in poor socio-economic circumstances. In these cases, it may be important to err on the side of diagnosis and prophylaxis.

The history and evolution of the Jones criteria for the diagnosis of ARF is detailed in Appendix B.

For the 1st edition of the New Zealand Rheumatic Fever guideline (2006) the main modification made to the Jones 1992 criteria was the acceptance of echocardiographic evidence of carditis as a major manifestation.\(^2,3,63\) In addition it was emphasized that monoarthritis could be a presenting feature if there was a history of non-steroidal anti-inflammatory drug (NSAID) use that may have modified the more typical migratory polyarthritis. It was recommended that a diligent search for alternative causes of polyarthritis/polyarthralgia in the absence of demonstrated carditis be undertaken (see Table 10). This approach has been vindicated with alternative diagnoses emerging in approximately 2% of ARF presenting to the Auckland ARF register and other published evidence.\(^64,65,66,67,68\) In addition it was recommended that the PR interval measurements on ECG be age adjusted.\(^69\)

**Table 4:** Comparison of New Zealand, Australian (RHD Australia) and the Revised Jones\(^4\) ARF Diagnostic Criteria

<table>
<thead>
<tr>
<th>Manifestation</th>
<th>NZ Criteria 2014 *</th>
<th>Revised Jones Criteria 1992</th>
<th>Australian (High Risk)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carditis</td>
<td>Major</td>
<td>Major</td>
<td>Major</td>
</tr>
<tr>
<td>Subclinical carditis</td>
<td>Major</td>
<td>N/A</td>
<td>Major</td>
</tr>
<tr>
<td>Polyarthritis</td>
<td>Major</td>
<td>Major</td>
<td>Major</td>
</tr>
<tr>
<td>Aseptic monoarthritis</td>
<td>Major</td>
<td>N/A</td>
<td>Major</td>
</tr>
<tr>
<td>Polyarthralgia</td>
<td>Minor</td>
<td>Minor</td>
<td>Major</td>
</tr>
<tr>
<td>Monoarthralgia</td>
<td>N/A</td>
<td>N/A</td>
<td>Minor</td>
</tr>
<tr>
<td>Prolonged PR interval</td>
<td>Minor</td>
<td>Minor</td>
<td>Minor</td>
</tr>
</tbody>
</table>
The substantive change for the New Zealand Criteria from 2006 to 2014 is that aseptic monoarthritis is accepted as a major criteria even when NSAID have been used. Data from Auckland since 2006 has shown that even in the absence of NSAID use, monoarthritis is a frequent presenting symptom in patients with ARF. Importantly 29 of 34 (85%) of cases of monoarthritis with ARF had echocardiographic changes supporting the probability that the monoarthritis was due to ARF. Of these, 25 of the 34 cases had echocardiographic changes on admission and four developed mild regurgitation on follow up echocardiography. Thus monoarthritis is now included as a major criterion even in the absence of NSAID use in this 2014 guideline.

Note that polyarthralgia (as a major criterion) or monoarthralgia (as a minor criterion) are not accepted in New Zealand (in comparison to the current Australian guidelines) as this is unsupported by evidence in the New Zealand setting. In addition the New Zealand Criteria do not have high and low risk categories as this is accommodated in the ‘Definite’ and ‘Probable’ categories as described in Table 3.

All of the criteria above stress the importance of evidence of a preceding streptococcal infection as a pre requisite for the diagnosis of ARF. An update by the advisory group to the American Heart Association of the Jones Criteria (2014) will be available shortly.

Exceptions to the above criteria for a diagnosis of ARF:
- Chorea as the only manifestation of ARF
- Indolent carditis (carditis of insidious onset and slow progression with evidence of inflammatory disease as distinguished from chronic RHD) as the only manifestation of ARF.

Both these types of patients may have insufficient supporting historical, clinical or laboratory findings to fulfil the Jones criteria.

Patients who do not fulfil these criteria, but in whom the clinician remains suspicious that the diagnosis may be ARF, should be maintained on oral penicillin and reviewed in two to four weeks with a second echocardiogram to detect the appearance of new lesions. If there is evidence of carditis by clinical examination or on echocardiogram, the diagnosis is confirmed and long-term secondary prophylaxis can be commenced. If there is no evidence of carditis and no alternative diagnosis has been found then ARF may be the diagnosis by exclusion. Those with epidemiological risk factors (Māori, Pacific and low socio-economic status) should be commenced on secondary prophylaxis with due consideration of an alternative diagnosis (such as rheumatological) and the need for ongoing review.

In New Zealand, as outlined below (Epidemiology section page 11), certain sectors of the population carry the burden of ARF with respect to Māori and Pacific People. Practitioners should be acutely aware of the consequences of missing a case of ARF with increasing cardiac damage without secondary prophylaxis with penicillin. Hospitalisation is recommended to ensure correct diagnosis for this potentially chronic disease with long term consequences.

When the first registers and prophylaxis programmes were set up, to ensure accurate epidemiologic data the Jones criteria of 1965 and 1956 were honed to produce Definite and Probable categories of ARF diagnosis. These are now incorporated into the New Zealand Criteria. Definitions of raised temperature, ESR and CRP were used. However the criteria need not be rigidly adhered to when ARF is the most likely diagnosis i.e. a possible case of ARF.

Recurrences of Acute Rheumatic Fever
See also the section on Secondary Prophylaxis (page 34), footnote to Table 21, page 38.

Diagnosis
As per Table 3 above, a recurrence of ARF in a patient with known past ARF or RHD requires:
- 2 major criteria or
- 1 major criterion and 2 minor criteria or
- Several minor criteria

**Plus**
- Evidence of a preceding GAS infection.
Aetiology
Most recurrences occur due to programme failure of delivery of secondary prophylaxis i.e. the person has stopped benzathine penicillin (for a variety of reasons). True penicillin failure in patients on four weekly penicillin can occur although this appears to be uncommon in the New Zealand setting.

Management
• Benzathine penicillin should be recommenced four weekly if patient not already on benzathine penicillin
• If there is a failure of benzathine penicillin on four weekly regimen, then this should be administered three weekly
• There is no proven data that severity of RHD should influence the frequency of benzathine penicillin regimen
• There can be difficulty deciding if there is new onset carditis in those with previous severe RHD; in these cases the minor criteria plus evidence of recent GAS pharyngitis allow a diagnosis of recurrent ARF or not
• It has been suggested that ‘root-cause analysis’ of ARF at the time of hospital admissions may reveal a higher proportion of missed opportunity cases of previous ARF but this is unproven as of 2014
• Those with recurrences of ARF are at risk of other poor health outcomes.

Clinical Features of Acute Rheumatic Fever - Major Manifestations
The major manifestations of ARF and features for their diagnosis are presented in Table 5.

Table 5: Major Manifestations of ARF

<table>
<thead>
<tr>
<th>Major Manifestation</th>
<th>Points for Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arthritis*</td>
<td>• Most common presenting symptom of ARF (occurring in up to 75% of first attacks)</td>
</tr>
<tr>
<td></td>
<td>• Classified as swelling of the joint in the presence of two or more of the following:</td>
</tr>
<tr>
<td></td>
<td>limitation of movement, hotness of the joint and pain in the joint and/or tenderness.</td>
</tr>
<tr>
<td></td>
<td>Typically, the arthritis of ARF is extremely painful</td>
</tr>
<tr>
<td></td>
<td>• Large joints are usually affected, especially knees and ankles</td>
</tr>
<tr>
<td></td>
<td>• Polyarthritis is usually asymmetrical and migratory (one joint becoming inflamed as another subsides) but can be additive (multiple joints progressively becoming inflamed without warning)</td>
</tr>
<tr>
<td></td>
<td>• Highly responsive to salicylate and NSAID therapy - usually responds within 3 days</td>
</tr>
<tr>
<td></td>
<td>• Monoarthritis is now permissible as a major criterion whether or not there is a history of NSAID use early in the course of the illness that might modify polyarthritis.[70] † This diagnosis is best made by a physician experienced in ARF</td>
</tr>
<tr>
<td></td>
<td>• The diagnosis of arthritis of the hip is accepted by history of pain precluding weight bearing and/or limitation of movement on examination</td>
</tr>
<tr>
<td></td>
<td>• In order to satisfy polyarthritis as a manifestation, at least one joint should have been observed in a clinical setting accompanied by a definite history of arthritis in other joints (Grade D)</td>
</tr>
<tr>
<td>Carditis</td>
<td>• Carditis (some use the term valvulitis) may be clinical or subclinical. Clinical carditis presents as an apical holosystolic murmur (mitral regurgitation) with or without a mid-diastolic flow murmur (Carey-Coombs murmur)</td>
</tr>
<tr>
<td></td>
<td>• Aortic regurgitation occurs less frequently with an early diastolic murmur heard at the base of the heart. Mitral and aortic regurgitation may occur together</td>
</tr>
<tr>
<td></td>
<td>• Subclinical carditis i.e. valve regurgitation detected with echocardiography but not associated with a murmur typical of mitral or aortic regurgitation, is included as a major manifestation</td>
</tr>
<tr>
<td></td>
<td>• Although pericarditis and myocarditis may occur, cardiac inflammation in ARF almost always affects the valves, especially the mitral and aortic valves[76,77]</td>
</tr>
<tr>
<td></td>
<td>• Early disease leads to valvular regurgitation, whereas prolonged or recurrent disease</td>
</tr>
</tbody>
</table>
may lead to valvular regurgitation, valvular stenosis or combination of both

- The rheumatic aetiology can usually be confirmed by a typical appearance on echocardiography (see Tables 8 and 9)
- Congestive heart failure in ARF results from valvular dysfunction secondary to valvulitis and is not due to primary myocarditis
- Valve regurgitation will improve in 25-50% within one year of the acute episode if secondary prophylaxis is well delivered
- If pericarditis is present, the friction rub may obscure valvular murmurs

### Sydenham’s chorea

- Consists of jerky, uncoordinated movements, especially affecting the hands, feet, tongue and face. The movements disappear during sleep. They may affect one side only (hemichorea)
- Useful signs include:
  - The “milkmaid’s grip” (rhythmic squeezing when the patient grasps the examiner’s fingers)
  - “Spooning” (flexion of the wrists and extension of the fingers when the hands are extended)
  - The “pronator sign” (turning outwards of the arms and palms when held above the head)
  - Inability to maintain protrusion of the tongue
- This manifestation affects females predominantly, particularly but not only in adolescence
- Chorea may occur after a prolonged latent period following GAS infection. Thus chorea can be a standalone criterion for the diagnosis of ARF without additional manifestations (such as raised antibody titres or inflammatory markers)
- Chorea has a strong association with carditis, hence echocardiography is essential for assessment of all patients with chorea, regardless of the presence of cardiac murmurs (Level IV, Grade C). A finding of subclinical carditis by echo will further support the diagnosis of chorea as a manifestation of ARF (Grade D). Even in the absence of echocardiographic evidence of carditis, patients with chorea should be considered at risk of subsequent cardiac damage. Therefore, they should all receive secondary prophylaxis, and be carefully followed up for subsequent development of RHD
- Chorea is the ARF manifestation most likely to recur and is often associated with pregnancy or oral contraceptive use. The vast majority of cases resolve within 6 months (usually within 6 weeks) although rare cases lasting as long as 3 years have been documented

### Subcutaneous nodules

- Rare (less than 2% of cases) but highly specific manifestation of ARF
- 0.5-2.0 cm in diameter, round, firm, freely mobile and painless nodules that occur in crops of up to 12 over the elbows, wrists, knees, ankles, Achilles tendon, occiput and posterior spinal processes of vertebrae
- Tend to appear 1-2 weeks after the onset of other symptoms, last only 1-2 weeks (rarely more than 1 month)
- Strongly associated with carditis
- Subcutaneous nodules are rarely seen as the sole major criterion in ARF and should be accompanied by additional major criteria in order to make the diagnosis

### Erythema marginatum

- Rare as well as difficult to detect (especially in dark-skinned people)
- Occurs as circular patterns of bright pink macules or papules that blanch under pressure and spread outwards in a circular or serpiginous pattern on the trunk and proximal extremities (almost never on face). The rash may be more apparent after showering
- Not itchy or painful and not affected by anti-inflammatory medication
- May recur for weeks or months, despite resolution of the other features of ARF
- Erythema marginatum is rarely seen as the sole major criterion in ARF and should be accompanied by additional major criteria in order to make the diagnosis.

* ARF should always be considered in the differential diagnosis of patients presenting with arthritis in high-risk populations. In the hospital setting, physicians and surgeons should collaborate when the diagnosis of arthritis is unclear. Patients with sterile joint aspirations in the absence of previous antibiotic exposure should never be treated speculatively for septic arthritis without further investigation, particularly in areas with high ARF/RHD prevalence*
† Note that in New Zealand, NSAIDs are readily available over the counter and are often used prior to presentation.
‡ During recent outbreaks of ARF in the USA, up to 71% of patients with chorea had carditis. Even though clinically evident carditis increases the risk of later development of RHD prior to cardiac echocardiography approximately 25% of patients with “pure” chorea also eventually developed RHD. This is explained by the finding that over 50% of patients with chorea, but without cardiac murmurs, have echocardiographic evidence of mitral regurgitation.

Clinical Features of Acute Rheumatic Fever - Minor Manifestations

The minor manifestations of ARF and features for their diagnosis are presented in Table 6.

Table 6: Minor Manifestations of ARF

<table>
<thead>
<tr>
<th>Minor Manifestation</th>
<th>Points for Diagnosis</th>
</tr>
</thead>
</table>
| Arthralgia                  | • May suggest ARF if the arthralgia occurs in the same pattern as rheumatic polyarthritis (migratory, asymmetrical and affecting large joints)
  | • If polyarthritis is present as a major manifestation, polyarthralgia cannot be considered an additional minor manifestation
  | • Alternative diagnoses (as suggested in Table 10) should be considered in a patient with arthralgia that is not typical of ARF                                |
| Fever                       | • Most manifestations of ARF are accompanied by fever (with the exception of chorea)
  | • In New Zealand, an oral, tympanic or rectal temperature greater than or equal to 38°C on admission, or documented during the current illness, should be considered as fever (Level IV, Grade C)
  | • Fever, like arthritis and arthralgia, is usually quickly responsive to NSAID/salicylate therapy                                                    |
| Elevated acute phase reactants | • In New Zealand, a serum CRP level of $\geq 30$mg/L or ESR of $\geq 50$mm/h meets this diagnostic criterion (Grade D)                                 |
  | • The peak ESR in ARF is typically $>80$mm/hr, usually remains elevated for $>4$ weeks, and may remain elevated for 3-6 months despite a much shorter duration of symptoms
  | • The serum CRP concentration rises more rapidly than the ESR and also falls more rapidly with resolution of the attack. It is less consistently raised on admission in ARF compared to the ESR |
| Prolonged P-R interval      | • An electrocardiogram (ECG) should be performed in all cases of suspected ARF (Level IV, Grade C)
  | • The P-R interval increases normally with age therefore needs to be age-adjusted. The following upper limits of normal are used in New Zealand: $^*$
    | • Age 3-12 years: 0.16 seconds
    | • Age 12-16 years: 0.18 seconds
    | • Age 17+ years: 0.20 seconds
  | • A prolonged P-R interval is occasionally a normal variant, but one that resolves over the ensuing days to weeks may be a useful diagnostic feature of ARF in cases where the clinical features are not definitive.$^*$ In these cases, a repeat ECG after 1-2 months may be useful
  | • Extreme first degree heart block is sometimes associated with junctional escape rhythm, usually with a heart rate similar to the sinus rate
  | • Second degree, and even complete heart block, can occur and, if associated with a slow ventricular rate, may give the false impression that carditis is not significant$^*$_1
  | • In the absence of clinical or echocardiographic carditis, a second or third degree block accompanied by other manifestations of ARF is highly supportive of the diagnosis (Grade D)
  | • When carditis is present as a major manifestation prolonged P-R interval cannot be considered an additional minor manifestation |

$^*$ Adapted from Park MK.$^{69}$ p42.
In the resurgence of ARF in the USA in the 1980’s, 32% of patients had abnormal AV conduction, usually a prolonged P-R interval. A small proportion had more severe conduction abnormalities, which were sometimes found in the absence of valvular regurgitation.\(^9\)

### Evidence of a Preceding Group A Streptococcal Infection

Evidence of a preceding GAS pharyngitis is critical to the diagnosis of ARF. A positive culture without supportive antibody elevation may be carriage in up to 50% of cases.\(^4\) Streptococcal antibody titres are therefore crucial in confirming the diagnosis.

In the New Zealand School Primary Prevention randomised controlled trial (RCT) of patients with ARF who reported sore throats, GAS were isolated from throat swabs in 54% (14 out of 26) closely observed ARF cases.\(^1\) However, a study in Australia found GAS was isolated in less than five percent of cases in Aboriginal Australians.\(^5\) This latter figure may be a result of later presentation of ARF, as 28% of Aboriginal Australians have been found to present as chorea\(^9\) compared to six percent of ARF cases in Auckland (1993-1999).\(^4,3\)

The most commonly used tests are the plasma antistreptolysin O (ASO) and the antideoxyribonuclease B (anti-DNase B) titres. The serum ASO titre reaches a maximum at about three to six weeks after infection and the serum anti-DNase B titre can take up to six to eight weeks to reach a maximum.\(^9\) The rate of decline of these antibodies varies considerably, with the ASO titre starting to fall six to eight weeks and the anti-DNase B titre three months after infection.\(^9\) In the absence of reinfection, the ASO titre usually approaches preinfection levels after six to 12 months, whereas the anti-DNase B titre tends to remain elevated for longer.\(^9\)

The reference range for these antibody titres varies with age and geographical location. Ideally this should be determined for each geographic location.\(^9\)

In a population with a high rate of streptococcal infections, many children will have high background streptococcal titres. The upper limit of normal approach attempts to determine a raised titre over and above this background, and therefore select out those children who have had a recent streptococcal infection.\(^9\) In New Zealand, an ASO titre of greater than or equal to 480 and/or an anti DNase B titre of greater than or equal to 680 is accepted as significant (Grade D) Table 7.

### Table 7: Upper Limits of Normal for Serum Streptococcal Antibody Titres Used in New Zealand for ARF Diagnosis

<table>
<thead>
<tr>
<th>Antibody Test</th>
<th>Titre (Iu/ML)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASO (Anti-streptolysin O)</td>
<td>≥480</td>
</tr>
<tr>
<td>Anti-DNase B</td>
<td>≥680</td>
</tr>
</tbody>
</table>

Established from residual sera from children (under 15 years) emanating from the population at risk of ARF and hospitalised in Auckland in 1982 for another reason. Lower levels may be acceptable in the very young or those over the age of 15 years. A four-fold (two-tube) rise or fall in antibody titres after 10-14 days would also be diagnostic.\(^9\)

Note that evidence of a preceding GAS infection is not necessary for the diagnosis of chorea as ARF.

All cases of suspected ARF (chorea is an exception) should have elevated serum streptococcal serology demonstrated. If the initial titre is below the upper limit of normal, testing should be repeated 10 to 14 days later (Grade D).

### Other Less Common Clinical Features

These include epistaxis, abdominal pain, rheumatic pneumonia (pulmonary infiltrates in patients with acute carditis), mild elevations of plasma transaminase levels and microscopic haematuria, pyuria or proteinuria. None is specific for ARF but epistaxis and abdominal pain occur commonly.
Echocardiography

All patients with suspected or definite ARF should undergo echocardiography, to identify sub clinical carditis and to assess the severity of regurgitation and left ventricular size and function on those with clinical carditis (Grade C).

In New Zealand, echocardiography is widely available for populations at high-risk of ARF. The use of colour-Doppler echocardiography, permitting definitions of echocardiographic findings as a major criterion for ARF diagnosis, has evolved over the past two decades. The original studies were summarized by Wilson and Neutze. These criteria further evolved as part of the development of both the New Zealand and the Australian guidelines on rheumatic fever diagnosis (2006) and the WHO working groups. The minimal colour-Doppler criteria for valvulitis of ARF is the same as the minimal colour-Doppler requirement for the diagnosis of rheumatic mitral regurgitation and aortic regurgitation. WHF guidelines for echocardiographic diagnosis of rheumatic heart disease were published in 2012. As there is no differentiation of the colour-Doppler findings of acute carditis and that of chronic rheumatic valve regurgitation we recommend the same criteria for defining the acute phase and the chronic phase. These standards are summarised in Table 8 (Level IV).

Table 8: Minimal Echocardiographic Criteria to Allow a Diagnosis of Pathological Valvular Regurgitation

<table>
<thead>
<tr>
<th>Mitral Regurgitation</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Seen in 2 views</td>
<td></td>
</tr>
<tr>
<td>• In at least 1 view jet length &gt;2cm*</td>
<td></td>
</tr>
<tr>
<td>• Peak velocity ≥ 3m/sec</td>
<td></td>
</tr>
<tr>
<td>• Pan-systolic jet in at least one envelope</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Aortic Regurgitation</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Seen in 2 views</td>
<td></td>
</tr>
<tr>
<td>• In at least one view jet length &gt;1cm*</td>
<td></td>
</tr>
<tr>
<td>• Peak velocity ≥3m/sec</td>
<td></td>
</tr>
<tr>
<td>• Pan-diastolic jet in at least one envelope</td>
<td></td>
</tr>
</tbody>
</table>

These criteria can usually readily distinguish a small colour jet of physiological regurgitation in a normal child from pathological regurgitation in a child with ARF or RHD. The proportion of children with physiological valve regurgitation in a New Zealand population was 15% and this proportion increases in later decades.

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 excessive leaflet motion of the tip of anterior mitral valve leaflet (often referred to as prolapse) is the commonest mechanism of mitral regurgitation. Anterior leaflet prolapse is more common than posterior valve prolapse

• Multiple jets of mitral regurgitation

• The presence of morphological or anatomical changes consistent with chronic RHD are:
  • Excessive leaflet motion of the tips of the AMVL or PMVL
  • Restrictive leaflet motion (including subchordal thickening)
  • Definite thickening of anterior mitral valve leaflets > 3mm
  • Mitral stenosis with a mean valve gradient ≥ 4mmHg

These features of RHD take time to develop but may be present in ARF on presentation indicating an acute on chronic presentation.

Source: Original studies described by Wilson N J. & Neutze J M. These criteria further evolved as part of the development of both the New Zealand and the Australian guidelines on rheumatic fever diagnosis (2006) and the WHO working groups on echocardiography and most recently in the 2012 WHF guidelines for echocardiographic diagnosis of rheumatic heart disease.

* 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 occurs in the first weeks of acute rheumatic carditis (Level IV)
† 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. Although none of these morphological features is unique to ARF, the experienced echocardiographic operator can use their presence as supportive evidence of a rheumatic aetiology of valvulitis.

‡ It is recommended that descriptive terms such as ‘elbow’ or ‘dog leg’ or ‘hockey stick’ deformity of anterior mitral valve leaflet be avoided: such appearances are due to the combination of valve thickening and restrictive valve motion.

In New Zealand, ARF carditis is classified mild, moderate or severe (Table 9) and these categories are used to guide the projected duration at diagnosis of secondary prophylaxis (see Table 21).

**Table 9: Severity of ARF Carditis**

<table>
<thead>
<tr>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild Carditis*</td>
</tr>
<tr>
<td>- Mild mitral or aortic regurgitation clinically and/or on echocardiography (fulfilling the minimal echocardiographic standards in Table 8) without heart failure, without cardiac chamber enlargement on CXR, ECG or echocardiography</td>
</tr>
<tr>
<td>Moderate Carditis</td>
</tr>
<tr>
<td>- Any valve lesion of moderate severity on clinical examination or</td>
</tr>
<tr>
<td>- Cardiac chamber enlargement seen on echocardiogram or</td>
</tr>
<tr>
<td>- Any valve lesion graded as moderate on echocardiogram†</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Severe Carditis</td>
</tr>
<tr>
<td>- Any impending or previous cardiac surgery for RHD, or</td>
</tr>
<tr>
<td>- Any valve lesion associated with significant cardiomegaly or heart failure, or graded as severe on clinical examination</td>
</tr>
<tr>
<td>- Any valve lesion graded as severe on echocardiogram:</td>
</tr>
<tr>
<td></td>
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<tr>
<td></td>
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</tr>
</tbody>
</table>

* 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 Zealand72

† When there is both mitral and aortic regurgitation, one 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.

If valvulitis is not found at presentation, it may appear within two weeks,71 or occasionally within one month but no longer. Thus an equivocal initial echocardiograph should be followed with a further study in two to four weeks if the diagnosis of ARF is uncertain. In a New Zealand series from the late 1990s clinical carditis occurred in 50% and subclinical carditis 30%. Thus only 20% of cases in the New Zealand setting have no evidence of carditis in this Auckland series.
Recent data from the Auckland series of presentation of monoarthritis in ARF showed that 85% had the supportive evidence of subclinical carditis, again helpful confirmatory evidence that the presentation is ARF.70

Usually it is not possible to distinguish between acute carditis and pre-existing rheumatic valve disease confidently by echocardiography.

In a patient with known previous RHD, the diagnosis of acute carditis during a recurrence of ARF relies on accurate documentation of the cardiac findings before the recurrence, so that new clinical or echocardiographic features can be confirmed. But, in a patient with no prior history of ARF or RHD, it makes little difference whether echocardiographic changes are new or old.

Further details on the use of echo in ARF can be found in Appendix C.

**Indolent Carditis**

First described in the USA in earlier decades4,106 and sometimes called insidious onset carditis, this is characterised by a subacute illness of several weeks or months with severe cardiac involvement and little or no joint symptoms. This is a rare scenario and is recognised in about two to three children per year in New Zealand.105 The usual case would have a modest elevation of inflammatory markers (ESR and CRP). Evidence of a streptococcal infection is not required.65 Younger children especially may have cardiac cachexia with weight loss.

Another subset of older children present with ARF severe chronic rheumatic valve disease and impaired ventricular function to the extent that heart valve surgery is contraindicated. The only option for these children and young adults is cardiac transplantation. Since cardiac transplantation began in New Zealand in 1987, eight patients (of the 268 heart transplants to date) received a heart transplant for end-stage RHD, all of Māori or Pacific ethnicity.107

**Differential Diagnosis**

Many of the clinical features of ARF are non-specific, so a wide range of differential diagnoses should be considered as shown in Table 10.56,108

<table>
<thead>
<tr>
<th>Table 10: Differential Diagnoses of Common Major Manifestations of ARF</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Polyarthritis and Fever</strong></td>
</tr>
<tr>
<td>- Other infections*(including gonococcal)</td>
</tr>
<tr>
<td>- Connective tissue and other auto-immune disease†</td>
</tr>
<tr>
<td>- Reactive arthropathy</td>
</tr>
<tr>
<td>- Sickle cell anaemia</td>
</tr>
<tr>
<td>- Infective endocarditis</td>
</tr>
<tr>
<td>- Leukaemia or lymphoma</td>
</tr>
<tr>
<td>- Gout and pseudogout</td>
</tr>
<tr>
<td>- Henoch-Schönlein purpura</td>
</tr>
<tr>
<td>- Post-streptococcal reactive arthritis‡</td>
</tr>
<tr>
<td>- Other, e.g. HIV/AIDS, leukaemia</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>
* Includes septic arthritis (e.g. Staphylococcus aureus, Neisseria gonorrhoea), and reactive arthritis from e.g. cytomegalovirus, Epstein-Barr Virus, mycoplasma, rubella (also post-vaccination), hepatitis B, parvovirus, and Yersinia species and other gastrointestinal pathogens

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

‡ Some patients present with arthritis not typical of ARF, but with evidence of recent streptococcal infection and are said to have post-streptococcal reactive arthritis. 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. These patients are said not to be at risk of carditis, and therefore do not require secondary prophylaxis. However, some patients diagnosed with post-streptococcal reactive arthritis have developed later episodes of ARF, indicating that the initial diagnosis should have been atypical ARF (Level IV)110,111

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). Patients so diagnosed should receive secondary prophylaxis for at least 5 years (Grade D). Echocardiography (see algorithm 2) should be used to confirm the absence of valvular damage in all of these cases before discontinuing secondary prophylaxis (Grade D)

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

¶ Some cases of chorea are mild or atypical and may be confused with motor tics or the involuntary jerks of Tourette’s syndrome. There may therefore be confusion between Sydenham’s chorea and these conditions. The term PANDAS (Pediatric Auto-immune Neuropsychiatric Disorder Associated with Streptococcal infection) refers to a subgroup of children with tic or obsessive-compulsive disorders (OCD), whose symptoms may develop or worsen following GAS infection. Five criteria have been used to define the PANDAS subgroup,112,113

- The presence of a Tic disorder and/or OCD
- Pre-pubertal age of onset (usually between 3 and 12 years of age)
- Abrupt symptom onset and/or episodic course of symptom severity
- Temporal association between symptom exacerbations and streptococcal infection (approx 7-14 days)
- Presence of neurologic abnormalities during periods of symptom exacerbation (typically adventitious movements or motoric hyperactivity)

However, the evidence supporting PANDAS as a distinct disease entity has been questioned.113 Hence, in New Zealand populations with a high prevalence of ARF, clinicians should rarely (if ever) make a diagnosis of PANDAS, and should rather err on the side of over-diagnosis of ARF and secondary prophylaxis (Grade D). If ARF is excluded, secondary prophylaxis is not needed, but such cases should be carefully followed up to ensure that they do not develop carditis in the long term

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

Investigations
The recommended investigations in ARF are listed in Table 11. Other investigations may be appropriate depending on the clinical picture and potential differential diagnoses.

Table 11: Investigations in Suspected ARF

<table>
<thead>
<tr>
<th>Recommended for All Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>White blood cell count</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate (repeat weekly once diagnosis confirmed)</td>
</tr>
<tr>
<td>C-reactive protein</td>
</tr>
<tr>
<td>Blood cultures if febrile</td>
</tr>
<tr>
<td>Electrocardiogram (repeat as necessary if conduction abnormality more than first degree)</td>
</tr>
<tr>
<td>Chest x-ray if clinical or echocardiographic evidence of carditis</td>
</tr>
<tr>
<td>Echocardiogram (repeat as necessary in 2-4 weeks if equivocal or if serious carditis)</td>
</tr>
<tr>
<td>Throat swab (preferably before giving antibiotics) - culture for group A streptococcus</td>
</tr>
<tr>
<td>Anti-streptococcal serology: both anti-streptolysin O and anti-DNase B titres, if available (repeat 10-14 days later if 1st test not confirmatory)</td>
</tr>
</tbody>
</table>
Tests for Alternative Diagnoses, Depending on Clinical Features

- Serology or reactive arthritis*
- Anti Nuclear Antibody (ANA) for autoimmune arthritis
- 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.‡

* Includes reactive arthritis from e.g. cytomegalovirus, Epstein-Barr Virus, mycoplasma, rubella (also post-vaccination), hepatitis B, parvovirus, influenza, and Yersinia species and other gastrointestinal pathogens

† Typically, the synovial fluid in joints affected by ARF contains 10,000 to 100,000 white blood cells/mm³ (predominantly neutrophils). The protein concentration is approximately 4g/dL, glucose levels are normal, gram stain negative and a good mucin clot is present.

‡ The chorea of ARF can be readily diagnosed on the basis of history, physical examination and laboratory evaluation. Neuroimaging is seldom necessary and should be reserved for cases who have an atypical presentation such as hemichorea.

Outbreak of Rheumatic Fever
Refer to the Ministry of Health's Communicable Disease Control Manual 2012 (currently being revised) for information on management of outbreaks of rheumatic fever, available at:

In New Zealand, as outlined below (Epidemiology section page 11), certain sectors of the population carry the burden of ARF with respect to Māori and Pacific People. Practitioners should be acutely aware of the consequences of missing a case of ARF with increasing cardiac damage without secondary prophylaxis with penicillin. Hospitalisation is recommended to ensure correct diagnosis for this potentially chronic disease with long term consequences.

Initial Management of Acute Rheumatic Fever

The major priority in the first few days after presentation in ARF is confirmation of the diagnosis. Except in the case of heart failure management, none of the treatments offered to cases with ARF have been proven to alter the outcome of the acute episode or the amount of damage to heart valves. Thus, there is no urgency to begin definitive treatment. The priorities in managing ARF are outlined in Table 12.

Table 12: Priorities in the Initial Management of ARF

<table>
<thead>
<tr>
<th>Admission to Hospital*</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Ideally, all those with suspected ARF (first episode or recurrence) should be hospitalised as soon as possible after onset of symptoms (Grade D). This ensures that all investigations are performed and, if necessary, observations completed for a period prior to commencing treatment to confirm the diagnosis. Hospitalisation also provides an ideal opportunity for education.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Confirmation of the Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Observation prior to anti-inflammatory treatment (use paracetamol [1st line] for fever or joint pain)</td>
</tr>
<tr>
<td>- Investigations (as per Table 11)</td>
</tr>
<tr>
<td>- Once diagnosis of ARF or recurrence is made, refer to rheumatic fever register for prophylaxis programme and public health for contact tracing.</td>
</tr>
<tr>
<td>- ARF is a notifiable disease in New Zealand. All patients should be notified to the regional Public Health service. The Public Health service will refer to Episurv, the national notifiable disease data base at ESR.</td>
</tr>
</tbody>
</table>
Treatment

All cases

**Antibiotics**

- Oral penicillin V (250mg two or three times daily) should be commenced in all cases while the diagnosis is being established. To reliably eradicate GAS, oral penicillin or amoxicillin should be given for the full 10 days.
- The first dose of intramuscular benzathine penicillin (1,200,000 U [900mg] or 600,000 U [450mg] if less than 30kg) should also be given in hospital in association with education about the importance of secondary prophylaxis. Once the first dose of benzathine penicillin is given, the oral penicillin is stopped.
- Oral macrolides used in cases with reliably documented penicillin allergy‡ (10 days of erythromycin ethylsuccinate (EES) 40mg/kg per day in 2-3 divided doses, maximum 1g/day).
- Intravenous antibiotics are not indicated.
- For guidance on antibiotic therapy, refer to the Group A Streptococcal Sore Throat Guideline Update 2014,1 available online at: www.heartfoundation.org.nz.

* Occasionally, when the diagnosis has already been confirmed and the patient is not unwell (e.g. mild recurrent chorea in a child with no other symptoms or signs), outpatient management may be appropriate. In such patients health staff must ensure that investigations, treatment, health education, registration (where available) and notification are all completed and prophylaxis commenced.

† Controlled studies have failed to show that treating ARF with large doses of penicillin affects the outcome of rheumatic valvular lesions one year later.119,120 Despite this, most authorities recommend a course of penicillin, even if throat cultures are negative, to ensure eradication of streptococci that may persist in the upper respiratory tract (Grade D).

‡ Most people labeled as being allergic to penicillin are not. Because penicillin is the best antibiotic choice for secondary prophylaxis it is recommended that those with stated penicillin allergy be investigated carefully, preferably with the help of an allergist, before being accepted as truly allergic (Grade D).

---

Ongoing Management of Acute Rheumatic Fever

The ongoing management of ARF are the symptomatic treatment of arthritis/arthralgia and/or chorea, management of fever and carditis/heart failure, recommendations for activity levels, and advice on long-term preventive measures prior to discharge.

1. Arthritis/Arthralgia

Table 13: Medications Used in the Symptomatic Management of Arthritis/Arthralgia

(See also Table 16)

**Medications**

- Mild arthralgia and fever may respond to paracetamol alone.
- Paracetamol for first line treatment of the pain of arthritis or severe arthralgia is recommended as early use of NSAID’s including salicylates, naproxen or ibuprofen may mask the evolution of the typical migratory polyarthritis which may be helpful to pin point the diagnosis particularly in the absence of echocardiographic changes or when an alternative diagnosis does not eventuate (see Table 10).
- Naproxen, a newer NSAID, has a dramatic effect similar to aspirin, and has been used (10-20mg/kg/day; maximum dose 1250mg) successfully in those with ARF, including one small randomised trial. It has been advocated as a safer alternative to aspirin (which is no longer recommended in New Zealand) (Level III-I)121,122 because of the risk of Reye’s syndrome in children receiving salicylates who develop certain viral infections, particularly influenza. Naproxen has the advantage of only twice-daily dosing and less hepatotoxicity. However it is not available as an elixir in New Zealand. Serum level monitoring is unnecessary (Grade D). There is no published evidence of Reye’s Syndrome being associated with naproxen (or ibuprofen).
- Many cases require 10 days or less of naproxen therapy.8 Joint symptoms may recur e.g. within three weeks and may be helped by staged reduction. This does not indicate recurrence. Most ARF episodes subside within six weeks, and 90% resolve within 12 weeks. Approximately 5% of cases require 6 months or more of salicylate therapy.123 Currently in New Zealand severe and persistent poly-arthritis is uncommon.
- The arthritis of ARF has also been noted to respond to other NSAID therapy e.g. ibuprofen (expert opinion). There are no randomised trials or other published data. Severe arthritis may not be completely controlled.
The use of glucocorticoids and other anti-inflammatory medications in rheumatic carditis has been studied in two meta-analyses. All of these studies of glucocorticoids were performed more than 40 years ago, and did not use drugs in common use today. These meta-analyses failed to suggest any benefit of glucocorticoids or IVIG over placebo, or of glucocorticoids over salicylates, in reducing the risk of long-term heart disease (Level I). The available evidence suggests that salicylates do not decrease the incidence of residual RHD (Level IV). Therefore, salicylates are not recommended to treat carditis (Grade C). Glucocorticoids may be considered for those with heart failure in whom acute cardiac surgery is not indicated (Grade D). This recommendation is not supported by evidence, but is made because many clinicians believe that

with short course or prn ibuprofen but then respond to naproxen

The most experience and published evidence for the management of arthritis is with salicylates. Characteristically the arthritis of ARF has been shown in controlled trials to respond dramatically to salicylates, often within hours and almost always within three days (Level II). Historically, salicylates were recommended as first line treatment because of the extensive experience with their use in ARF.

2. Fever
Low-grade fever does not require specific treatment. Fever will usually respond dramatically to NSAIDs or salicylate therapy. Fever alone, or fever with mild arthralgia or arthritis, may not require naproxen or salicylates, but can instead be treated with paracetamol.

3. Carditis/Heart Failure
Priorities in the management of carditis/heart failure are detailed in Table 14.

Table 14: Priorities in the Management of Carditis/Heart Failure

<table>
<thead>
<tr>
<th>Echocardiogram</th>
<th>Anti-Failure Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>An urgent echocardiogram and cardiology assessment are recommended for all cases with heart failure</td>
<td></td>
</tr>
<tr>
<td>• Diuretics/fluid restriction for mild-moderate failure</td>
<td></td>
</tr>
<tr>
<td>• ACE inhibitors for more severe failure, particularly if aortic regurgitation present</td>
<td></td>
</tr>
<tr>
<td>• Glucocorticoids optional for severe carditis</td>
<td></td>
</tr>
<tr>
<td>• Digoxin if atrial fibrillation present</td>
<td></td>
</tr>
<tr>
<td>• There is little experience with beta-blockers in heart failure due to acute carditis, and their use is not recommended (Grade D)</td>
<td></td>
</tr>
</tbody>
</table>

Detailed recommendations for the management of heart failure can be found in a separate Heart Foundation clinical guideline (available at http://www.heartfoundation.org.nz)

<table>
<thead>
<tr>
<th>Valve Surgery</th>
</tr>
</thead>
</table>
| Surgery is usually deferred until the acute inflammation has subsided. Rarely, valve leaflet or chordae tendinae rupture leads to severe regurgitation into a noncompliant left atrium resulting in acute pulmonary oedema. This condition is often mis-diagnosed as pneumonia as the pulmonary venous congestion is often unilateral. Such cases require emergency surgery to repair the flail leaflet. Four such patients presenting within a two year period are described by Anderson et al with all cases achieving valve repair rather than replacement in this life threatening clinical scenario. More commonly acute cases with severe valve disease and mild cardiac failure respond well to diuretics. Surgery is then deferred until the acute phase reactants have normalised as the surgeons can achieve more durable repairs when the early active valve inflammation has reduced. A recent review of the issues of cardiac surgery for acute and chronic RHD was based significantly based on the experience of the Starship Children’s cardiac unit. The philosophy for cardiac surgery in the young is always to repair rather than replace the mitral valve. This is supported by a recent report based on 81 cases aged 3-19 years from the Greenlane and Starship Children’s Hospital experience. Not only was there lower morbidity (less endocarditis, no thromboembolism) for repairs but the need for reoperation was not increased compared to the mitral valve replacement group.

The use of glucocorticoids and other anti-inflammatory medications in rheumatic carditis has been studied in two meta-analyses. All of these studies of glucocorticoids were performed more than 40 years ago, and did not use drugs in common use today. These meta-analyses failed to suggest any benefit of glucocorticoids or IVIG over placebo, or of glucocorticoids over salicylates, in reducing the risk of long-term heart disease (Level I). The available evidence suggests that salicylates do not decrease the incidence of residual RHD (Level IV). Therefore, salicylates are not recommended to treat carditis (Grade C). Glucocorticoids may be considered for those with heart failure in whom acute cardiac surgery is not indicated (Grade D). This recommendation is not supported by evidence, but is made because many clinicians believe that
Glucocorticoids may lead to more rapid resolution of cardiac compromise, and even be life-saving in severe acute carditis. The potential major adverse effects of short courses of glucocorticoids, including gastrointestinal bleeding and worsening of heart failure as a result of fluid retention, should be considered before they are used. If glucocorticoids are used, the drug of choice is oral prednisone or prednisolone (1-2mg/kg/day, to a maximum of 80mg once daily or in divided doses). Intravenous methyl prednisolone may be given in very severe cases. If a week or less of treatment is required, the medication can be ceased when heart failure is controlled, and inflammatory markers are improving. For longer courses (usually no more than 3 weeks is required), the dose may be decreased by 20-25% each week. Treatment should be given in addition to the other anti-failure treatments outlined below. Mild to moderate carditis does not warrant any specific treatment. As glucocorticoids will control joint pain and fever, salicylates can usually be discontinued, or the dose reduced, during glucocorticoid administration. Salicylates may need to be recommenced after glucocorticoids are discontinued to avoid rebound joint symptoms or fever.

4. Sydenham’s Chorea

Priorities in the management of Sydenham’s chorea are detailed in Table 15. Sydenham’s chorea may be the sole manifestation of ARF (see page 16).

Table 15: Priorities in the Management of Chorea

<table>
<thead>
<tr>
<th>Priorities in the Management of Chorea</th>
</tr>
</thead>
<tbody>
<tr>
<td>● Sydenham’s chorea is self-limited. Most patients will resolve within weeks and almost all patients within 6 months. Rare cases may last as long as 2-3 years. Mild or moderate chorea does not require any specific treatment, aside from rest and a calm environment. Over-stimulation or stress can exacerbate the symptoms. Sometimes hospitalisation is useful to reduce the stress that families face in dealing with abnormal movements and emotional lability.</td>
</tr>
<tr>
<td>● Because chorea is benign and self-limiting, and anti-chorea medications are potentially toxic, treatment should only be considered if the movements interfere substantially with normal activities, place the person at risk of injury or are extremely distressing to the patient, family and friends.</td>
</tr>
<tr>
<td>● Valproic acid* and carbamazepine† are now preferred to haloperidol, which was previously considered the first-line medical treatment for chorea. A small, prospective comparison of these 3 agents recently concluded that valproic acid was the most effective. Refer to Table 16 for medications for chorea management.</td>
</tr>
<tr>
<td>● Other anti-chorea medications should be avoided because of potential toxicity. Because of the small potential for liver toxicity with valproic acid, it is recommended that carbamazepine be used initially for severe chorea requiring treatment, and that valproic acid be considered for refractory cases. A response may not be seen for 1-2 weeks, and successful medication may only reduce, but not eliminate, the symptoms. Medication should be continued for 2-4 weeks after chorea has subsided and then gradually withdrawn. Recurrences of chorea are usually mild and can be managed conservatively but, in severe recurrences, the medication can be re-started if necessary.</td>
</tr>
<tr>
<td>● Aspirin and glucocorticoid therapy do not have a significant effect on rheumatic chorea. Corticosteroids can be considered for severe or refractory cases of chorea. Case series lend some support. One double blind randomised controlled trial (n=22 who received prednisone, and n=15 placebo) found a significant reduction in symptom intensity after one week and a significantly shorter time to complete remission of symptoms. Seven patients presented recurrences with no difference between groups.</td>
</tr>
<tr>
<td>● Small studies of intravenous immunoglobulin (IVIG) have suggested more rapid recovery from chorea, but have not demonstrated reduced incidence of long-term valve disease in non-chorea ARF. Until more evidence is available, IVIG is not recommended, except for severe chorea refractory to other treatments (Level II / IV, Grade C).</td>
</tr>
</tbody>
</table>

* Side effects of valproic acid include pancreatitis, hepatic toxicity, hyperammonaemia and thrombocytopenia.
† Side effects of carbamazepine include CNS adverse reactions (dizziness, headache, ataxia, drowsiness, fatigue and diplopia); gastrointestinal disturbances (nausea and vomiting), as well as allergic skin reactions. Uncommon side effects include abnormal involuntary movements (e.g. tremor, asterixis, dystonia and tics) and nystagmus. Rarely carbemazepine can cause orofacial dyskinesia, oculomotor disturbances, speech disorders (e.g. dysarthria and slurred speech), choreoathetotic disorders, peripheral neuritis, paresthesia, muscle weakness and paretic symptoms.
5. Medications Used in Acute Rheumatic Fever Management
The following table details recommended medications in the management of ARF.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Indication</th>
<th>Regimen</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antibiotics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Penicillin V PO Or</td>
<td>Treat or prevent streptococcal infection</td>
<td>Children &lt;20kg: 250mg two or three times daily</td>
<td>10 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Adolescents &amp; adults ≥20kg: 500mg two or three times daily</td>
<td></td>
</tr>
<tr>
<td>Amoxicillin PO Or</td>
<td>Treat or prevent streptococcal infection</td>
<td>Once daily: 50mg/kg once daily</td>
<td>10 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Weight &lt;30kg: 750mg once daily</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Weight ≥30kg: 1000mg once daily</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Twice daily: 25mg/kg twice daily</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Max dose 1000mg daily</td>
<td></td>
</tr>
<tr>
<td>Benzathine penicillin IM Or</td>
<td>Treat or prevent streptococcal infection</td>
<td>Children &lt;30kg: 450mg (600,000 U)</td>
<td>Single dose</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Adults &amp; children ≥30kg: 900mg (1,200,000 U)</td>
<td></td>
</tr>
<tr>
<td>Erythromycin ethyl succinate PO</td>
<td>If concern about allergic response to beta lactams</td>
<td>Children &amp; adults: 40mg/kg per day in 2-3 divided doses</td>
<td>10 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Max adult daily dose 1000mg</td>
<td></td>
</tr>
<tr>
<td><strong>Analgesia for the Management of Symptomatic Arthritis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paracetamol PO</td>
<td>Arthritis or arthralgia - mild or until diagnosis confirmed</td>
<td>60mg/kg/day given in 4-6 doses/day. May increase to 90mg/kg/day if needed, under medical supervision</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Max dose 4000mg daily</td>
<td></td>
</tr>
<tr>
<td>Naproxen PO *</td>
<td>Arthritis</td>
<td>10-20mg/kg/day given twice daily</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Max dose 1000mg daily</td>
<td></td>
</tr>
<tr>
<td>Ibuprofen *</td>
<td>Arthritis</td>
<td>5-10mg/kg/dose 8 hourly</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Max dose 400mg per dose</td>
<td></td>
</tr>
<tr>
<td><strong>Cardiac Drugs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Furosemide PO/IV (can also be given IM)</td>
<td>Heart failure, renal disease and hepatic disease.</td>
<td>Orally in children: 1 month-12 years: 0.5-2mg/kg 2-3 times daily. A medium dose is 1mg/kg bd. Max dose 80mg daily</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>12-18 years: 20-40mg daily (increase to 80-120mg daily in resistant oedema)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Slow intravenous injection in children: 1 month-12 years: 0.5-1mg/kg every 8 hours as necessary. Max dose 40mg (40mg) every 8 hours</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>12-18 years: 20-40mg every 8 hours as necessary (resistant cases may require higher doses)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Adults: 20-40mg/dose 12-24 hourly up to Max dose 250-500mg/day</td>
<td></td>
</tr>
<tr>
<td>Spironolactone PO</td>
<td>Heart failure</td>
<td>Orally in children: 1 month-12 years: 1-3mg/kg/day (max 100-200mg/day) in 1-2 doses. Round dose to multiple of 6.25mg (quarter of a tablet)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>12-18 years: 50-100mg daily in 1-2 divided doses</td>
<td></td>
</tr>
<tr>
<td>Enalapril PO</td>
<td>Impaired LV function</td>
<td>Children: 0.1mg/kg/day in 1-2 doses increased gradually over 2 weeks Max of 1mg/kg/day in 1-2 doses Initial: 2.5mg daily</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Adults:</td>
<td></td>
</tr>
</tbody>
</table>
### Lisinopril PO

**Impaired LV function**

<table>
<thead>
<tr>
<th>Children: Initial dose 70 mcg/kg (max. 5 mg) daily, increased in intervals of 1-2 weeks to max 600 mcg/kg/day (or 40 mg) daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults: 2.5-20mg daily</td>
</tr>
<tr>
<td>Max 40mg daily</td>
</tr>
<tr>
<td>Monitor blood pressure during initiation of therapy</td>
</tr>
</tbody>
</table>

### Digoxin* PO/IV

**Heart failure/atrial fibrillation**

<table>
<thead>
<tr>
<th>Children: Initial dose 15 mcg/kg oral stat and then 5 mcg/kg after 6 hours, then 3-5 mcg/kg/dose q12h 12 hourly</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults: 62.5-500 mcg daily</td>
</tr>
<tr>
<td>Check serum levels</td>
</tr>
</tbody>
</table>

**Intravenous use in children:** rarely indicated

Seek advice from specialist

Seek advice from cardiologist

### Captopril

**Heart failure**

<table>
<thead>
<tr>
<th>Children: Initial dose 0.1-0.2 mg/kg/dose 8 hourly increasing in increments to 1-1.5 mg/kg/dose 8 hourly</th>
</tr>
</thead>
<tbody>
<tr>
<td>12-18 years: 12.5-25 mg 2-3 times daily increasing to max 150 mg daily in divided doses</td>
</tr>
<tr>
<td>Adults: Up to 50 mg 8 hourly</td>
</tr>
</tbody>
</table>

As for furosemide

### Prednisone or Prednisolone PO

**Severe carditis, heart failure, pericarditis with effusion**

1-2 mg/kg/day. If used >1 week, taper by 20-25% per week

Max dose 60 mg daily

Usually 1 to 3 weeks

Seek advice from specialist

### Other Drugs

| Carbamazepine† PO |
| Severe chorea |
| 7-20 mg/kg/day (7-10 mg/kg/day usually sufficient) given three times a day |
| Until chorea controlled for several weeks, then trial off medication |
| Valproic acid† PO |
| Severe chorea (may affect salicylate metabolism) |
| Usually 15-20 mg/kg/day (can increase to 30 mg/kg/day) given three times a day |
| As for carbamazepine. |

---

* If the symptoms and signs do not remit substantially within three days of commencing anti-inflammatory medications, a diagnosis other than ARF should be considered.

† Always check drug interactions before prescribing.

### 6. Activity in Acute Rheumatic Fever

A guide for activity levels following diagnosis of ARF are based upon symptom management and severity of carditis.

#### Bed Rest

In the pre-penicillin era, prolonged bed rest in those with rheumatic carditis was associated with shorter duration of carditis, fewer relapses and less cardiomegaly. Bed rest has not been studied critically. Ambulation should be gradual and as tolerated in cases with heart failure, or severe acute valve disease, especially during the first four weeks, or until the serum CRP level has normalised and the ESR has normalised or significantly reduced. Those with milder or no carditis should only remain in bed as long as necessary to manage other symptoms, such as joint pain (Grade D).

A guide for activity levels is shown below in Table 17. (Adapted from Lennon D. 2004B) (Grade D).

Where echocardiography is freely available, echo can reassure there is no cardiac deterioration with mobilisation.
Table 17: Activity Recommendations in ARF

<table>
<thead>
<tr>
<th>Activity</th>
<th>Arthritis and Mild Carditis*</th>
<th>Moderate Carditis*</th>
<th>Severe Carditis*</th>
</tr>
</thead>
<tbody>
<tr>
<td>In hospital</td>
<td>1-2 weeks</td>
<td>4-6 weeks</td>
<td>2-4 months</td>
</tr>
<tr>
<td></td>
<td>Mobilise freely, unless carditis evolves</td>
<td></td>
<td></td>
</tr>
<tr>
<td>House arrest (activity and school work at home)</td>
<td>1-3 weeks</td>
<td>4-6 weeks</td>
<td>2-4 months</td>
</tr>
<tr>
<td>School</td>
<td>2 weeks</td>
<td>1-3 months</td>
<td>2-3 months</td>
</tr>
<tr>
<td></td>
<td>Gradually return to full activity over 2-4\textsuperscript{†} weeks</td>
<td>Avoid sport and physical education</td>
<td></td>
</tr>
<tr>
<td>Full activity (sport)</td>
<td>After 6 weeks</td>
<td>After 3-6 months</td>
<td>Variable</td>
</tr>
</tbody>
</table>

\* Based on echocardiography. See page 22, Table 9
\textsuperscript{†} ESR may guide.

7. Observation and General Hospital Care

Guidelines for general in-hospital care are provided in Table 18 (Grade D).

Table 18: Guidelines for General In-Hospital Care

<table>
<thead>
<tr>
<th>Nursing Recordings</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Temperature, pulse, RR, BP four times daily</td>
</tr>
<tr>
<td>- Sleeping pulse (e.g. 0200 hrs)</td>
</tr>
<tr>
<td>- If pulse &gt;100bpm, record apical HR</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diet</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Free fluids (if no heart failure)</td>
</tr>
<tr>
<td>- Normal diet (limit extras)</td>
</tr>
<tr>
<td>- Early dietary advice if overweight and in failure, to avoid further weight gain</td>
</tr>
<tr>
<td>- Weekly weight</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bed Rest and General Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Examine daily for the pattern of arthritis and the presence of heart murmur, choreiform movements, skin rash and subcutaneous nodules</td>
</tr>
<tr>
<td>- If clinical carditis present:</td>
</tr>
<tr>
<td>- Document cardiac symptoms and signs</td>
</tr>
<tr>
<td>- Daily weight and fluid balance chart</td>
</tr>
<tr>
<td>- Medications as appropriate (see Table 16)</td>
</tr>
<tr>
<td>- See general guidelines for bed rest (Table 16)</td>
</tr>
<tr>
<td>- Cardiology opinion</td>
</tr>
<tr>
<td>- Repeat investigations as necessary</td>
</tr>
<tr>
<td>- Provide cultural support (as relevant)</td>
</tr>
<tr>
<td>- Plan care to provide rest periods</td>
</tr>
<tr>
<td>- Provide age-appropriate activities</td>
</tr>
<tr>
<td>- Notify school teacher</td>
</tr>
<tr>
<td>- Involve family in care</td>
</tr>
</tbody>
</table>

Source: Adapted from Lennon D. 2004B\textsuperscript{66}

Note: RR = respiratory rate; BP = blood pressure; HR = heart rate.
8. Discharge Planning and Long Term Preventive Measures

Prior to discharge from hospital, it is recommended that patients diagnosed with ARF, have ongoing care and long-term preventive measures planned as detailed in Table 19.

Table 19: Discharge Planning and Long Term Preventive Measures

<table>
<thead>
<tr>
<th>Clinical Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>• All patients should receive regular review and outpatient follow-up initiated prior to discharge</td>
</tr>
<tr>
<td>• The frequency and duration of review is dependent on the individual clinical needs and local capacity and should become more frequent in the event of symptom onset, symptomatic deterioration or a change in clinical findings</td>
</tr>
<tr>
<td>• Mild and moderate cases are followed up by paediatric and internal medicine services, severe cases jointly with cardiology. In the South Island annual review for all the RF patients by Infectious Diseases specialists is recommended regardless of the severity of RHD</td>
</tr>
<tr>
<td>• Particular care should be taken when patients are transferred from paediatric to adult services. There is logic in maintaining less severe patients in the paediatric services as they will be discharged at age 21. This provides continuity of care including follow-up and benzathine penicillin delivery</td>
</tr>
<tr>
<td>• Further information regarding frequency and nature of routine review can be found in Table 26, page 46</td>
</tr>
<tr>
<td>• Contact GP to ensure patient is up to date with vaccines and recall placed in patient management system for annual flu vaccination</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Secondary Prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Obtain consent from caregiver/patient for IM benzathine penicillin treatment</td>
</tr>
<tr>
<td>• Administer first dose of IM benzathine penicillin whilst in hospital</td>
</tr>
<tr>
<td>• Refer the patient to the local regional ARF register for continuing free prophylaxis (see below). Community nurses need two weeks lead time to organise delivery of IM benzathine penicillin to a new patient</td>
</tr>
<tr>
<td>• Patients with recurrence of ARF need to be re-referred to the ARF register to ensure continuing secondary prophylaxis</td>
</tr>
<tr>
<td>• Raise awareness of importance of ongoing secondary prophylaxis through discussion at every health professional interaction with the patient</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Notification to the Regional Public Health Service</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Complete ARF Public Health Notification Form within seven days of diagnosis (Public Health refer to Episurv)</td>
</tr>
<tr>
<td>• ARF is a notifiable disease in New Zealand. Each possible, probable, or definite case of ARF (including recurrence) should be notified to the local public health unit for national infectious disease surveillance</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Contact Community Services to Ensure Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>• The register coordinator (if available) should inform community health staff about patients with ARF in their area</td>
</tr>
<tr>
<td>• The referring medical practitioner should also make direct contact with those in the community responsible for prophylaxis delivery in order to ensure that they are aware of the diagnosis, the need for secondary prophylaxis and any other specific follow-up requirements. This may include district nurses, public health nurses, medical officer of health and other public health staff</td>
</tr>
<tr>
<td>• A community nurse and/or community health worker for the area where the case resides should also do a ward and/or family visit if possible before discharge</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient and Family Education</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Offer the patient and their family education on rheumatic fever:</td>
</tr>
<tr>
<td>• At the time of diagnosis, it is essential that the disease process be explained to the patient and their family in a culturally appropriate way, using available educational materials and interactive discussion. Further education, using culturally appropriate educational materials should follow once the patient has returned home</td>
</tr>
<tr>
<td>• Importance of sore throat management for the patient and their family/household</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Oral Health Care and Infective Endocarditis Prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Refer to hospital dental service at time of diagnosis of ARF for evaluation and treatment if required of dental issues. Referral is then made to an ongoing community dental provider e.g. school dental service or dentist (preferably subsidised care)</td>
</tr>
<tr>
<td>• This is critical in the prevention of endocarditis. As those without rheumatic valve damage may still be at long-term risk of developing RHD, particularly in the event of recurrent episodes of ARF, oral health care</td>
</tr>
</tbody>
</table>
is essential, regardless of the presence or absence of carditis. See page 46

- Document whether patient requires infective endocarditis prophylaxis or not
- All those with carditis that have evolved to chronic RHD should have endocarditis prophylaxis (See www.heartfoundation.org.nz for guideline)\textsuperscript{148}
- Patients who have had ARF without cardiac involvement do not require prophylactic antibiotics

**Contact Management**

- All symptomatic and asymptomatic household contacts of the index case aged 3 years and older should have a throat swab if the contact was no longer than one month before the onset of ARF in the index case
  - This should be organised through the appropriate public health unit
- All contacts with positive GAS cultures should be offered antibiotic treatment.
  - Streptococcal acquisition rates of 25\% or greater have been recorded in family contacts of streptococcal pharyngitis\textsuperscript{124,149,150,151}

**Opportunistic Care**

- It is important to note this opportunity to provide information and other services for ARF patients, whom frequently have other challenges to their general wellbeing. This may include promoting a healthy diet, exercise and hygiene, as well as assistance with socioeconomic stressors, and the opportunity for ongoing support

**Eligible for Housing Review**

- The eligibility criteria for special assistance with health housing (DHB specific) can include:
  - A child aged between 4-19 years who is admitted with acute rheumatic fever
  - Other children in the household aged between 4 to 19 years
  - A Community Services Card (CSC) or income that falls within CSC threshold
  - A housing issue (cold, damp, overcrowded, mouldy etc).

**Discharge**

**Timing of Discharge**

The duration of treatment is dictated by the clinical response and improvement in inflammatory markers (ESR and CRP). Most ARF patients without severe carditis can be discharged from hospital after approximately two weeks. The length of admission will partly depend on the social and home circumstances. If patients come from remote communities or other settings with limited access to high quality medical care, it is advisable to discuss discharge timing with the person, family and the local primary health care team (particularly Māori or Pacific health providers where possible). In some patients, it may be advisable to prolong the hospital stay until recovery is well advanced.

**Advice on Discharge**

All patients should have a good understanding of the cause of rheumatic fever and the need to have sore throats treated early for themselves as well as in other family members. Contact management (as per Table 19) should be discussed.

Patients and their families should understand the reason for secondary prophylaxis and the consequences of missing a benzathine penicillin injection. The first dose of benzathine penicillin is usually given in a hospital setting. Arrangements for the first injection post discharge should be made. They should be given clear information about where to go for secondary prophylaxis once discharged, know who to contact with questions concerning their follow-up or secondary prophylaxis, and be given written information on appointments for follow-up with their local medical practitioner, physician/paediatrician and cardiologist (if needed). They should be advised of the appropriate activity level until their next clinic appointment.

Patients with RHD and their families should also be reminded of the importance of additional antibiotic prophylaxis for dental and other procedures to protect against endocarditis (Appendix D). Patients who have had ARF without cardiac involvement do not require prophylactic antibiotics.

Copies of the discharge summary should go to the following services: community nursing staff responsible for prophylaxis delivery (such as district nurse, public health nurse), rheumatic fever secretary or staff responsible for the register (where applicable), primary care provider and the family.
B. SECONDARY PREVENTION

Secondary prevention of rheumatic fever is defined as the continuous administration of antibiotics to cases who have had ARF or well-documented RHD. The purpose is to prevent infection of the upper respiratory tract with group A streptococcus (GAS) and the development of recurrent rheumatic fever.51

Prophylaxis Regimens

The regular administration of antibiotics to prevent infection with GAS and recurrent ARF is recommended for all people with a history of ARF or RHD.10 This strategy has been proven in randomised controlled trials to prevent recurrence of ARF. A Cochrane meta-analysis152 concluded that the use of penicillin (compared to no therapy) is beneficial in the prevention of recurrent ARF, and that intramuscular benzathine penicillin is superior to oral penicillin in the reduction of both recurrent ARF (87-96% reduction) (Level I) (Appendix E). There is strong evidence that secondary prophylaxis reduces the severity of RHD by preventing disease progression.153,154,155,156

Penicillin

In early studies of ARF prophylaxis using sulphonamides, 1.5% of treated cases developed ARF recurrences, compared to 20% of untreated cases. Subsequently, penicillin was found to be more efficacious than sulphonamides (Level I).60,123

Secondary prophylaxis also reduces the severity of RHD. It is associated with regression of heart disease in approximately 50-70% of those with adequate adherence over a decade (Level III 2),90,157,158 and reduces mortality (Level III 2).159

Dose

The internationally accepted standard dose of benzathine penicillin for the secondary prevention of ARF in adults is 900mg (1,200,000 U).10,127,160 The dose for children is less clear. In New Zealand, it is recommended that 1,200,000 U of benzathine penicillin should be used for secondary prophylaxis for all persons weighing 30kg or more (Level III-2, Grade B), and 450mg (600,000 U) for those weighing less than 30kg (Grade D).161

Frequency

While benzathine penicillin is usually administered every four weeks (28 days), serum penicillin levels may be low or undetectable 28 days following a dose of 1,200,000 U.162 Fewer streptococcal infections and ARF recurrences occurred among those receiving three weekly BPG (Level I).152,163,164 Moreover, the three-weekly regimen resulted in greater resolution of mitral regurgitation in a long-term randomised study in Taiwan (66% vs 46%) (Level II).165 Prospective data from New Zealand however, showed that recurrences were rare among people who were fully adherent to a four-weekly benzathine penicillin regimen.

An audit of practice in the Auckland region (1993 to 1999) showed that of 360 ARF patients, there were 20 recurrences in 19 patients (median age 21 years). The rate of recurrence in fully adherent individuals on a 28 day regime was 0.07 per 100 patient years. Failure on the prophylaxis programme (i.e. including those who were less than fully adherent) was 1.4 per patient years.29,30 Patient non-adherence accounted for 55% of recurrences. Two recurrences were following discharge from prophylaxis as per the New Zealand guideline, occurring three and 13 years later. Two young people (aged 16 and 17 years of age) suffered a recurrence following discontinuation of their prophylaxis regimen by a medical practitioner outside of recommended best practice guidance. An important contribution to failure of delivery of prophylaxis was the lack of register linkage both within New
Zealand and to the Pacific e.g. Samoa. This linkage has now been achieved in Auckland across three DHB’s and should be feasible between the North Island DHB’s where RF occurs most frequently.\textsuperscript{29,30} The Auckland study failure rate compares favourably to prophylaxis failure reported in Taiwan of 0.25 (21-day programme) and 1.29 (28-day programme) per 100 patient years.\textsuperscript{165} Furthermore, a four-weekly regime is preferable to a three-weekly regime because of the resource and compliance implications (Grade D). In New Zealand, three weekly (21-day) benzathine penicillin is recommended only for those who have confirmed recurrent ARF despite full adherence to four-weekly (28-day) benzathine penicillin delivery (Grade C).\textsuperscript{29,30}

An alternative strategy is the administration of larger doses of benzathine penicillin, leading to a higher proportion of people with detectable serum penicillin levels four weeks after injection.\textsuperscript{167} However, until more data are available, this strategy cannot be recommended.

In summary benzathine penicillin should be administered every 28 days (or 21 days for those with a proven recurrence on 28 day regimen). Administration three days early and up to five days late is considered reasonable (i.e. 25-33 days following the previous injection). Dose intervals can be adjusted for individual circumstances.

As of 2014, the Ministry of Health in New Zealand currently requires quarterly reporting of adherence to benzathine penicillin secondary prophylaxis.

The non-adherent and the non-presenting groups continue to be a major challenge to secondary prophylaxis. Transient living patterns or shifting without notifying staff of a forwarding address can create follow-up difficulties. As the populations at the highest risk of ARF are Māori and Pacific, the involvement of Māori and Pacific health workers, with their skills in outreach and their community knowledge, is important.

The presence of local ARF registers in New Zealand allows for inter-register referral (often nurse to nurse) of diagnosed ARF cases. This ensures continuity of care and prophylaxis when cases transfer to a new area. However a national register would ensure greater efficiency and effectiveness.

**Lignocaine with Benzathine Penicillin Injection**

Intramuscular benzathine penicillin injections can cause local pain and discomfort. This can lead to poor compliance in those requiring ongoing prophylaxis.\textsuperscript{168,169} Amir et al demonstrated that pain can be significantly reduced when 1% lidocaine (lignocaine) was used to reconstitute benzathine penicillin for injection. This did not affect serum penicillin levels.\textsuperscript{168}

A recent New Zealand study with rheumatic fever patients receiving monthly IM benzathine penicillin for prophylaxis has demonstrated a reduction in the subjective experience of pain when two analgesic interventions were offered: intramuscular delivery of benzathine penicillin with either 0.25ml of 2% lignocaine alone or 0.25ml of 2% lignocaine with a vibrating device with cold pack (Buzzy\textsuperscript{®}).\textsuperscript{170} Lignocaine and Buzzy\textsuperscript{®} together resulted in a greater reduction in pain than lignocaine alone, but only in children aged 13 years or younger. In this age group, the fear of injection was also reduced.

For the safe preparation and administration of lignocaine with benzathine penicillin refer to The KidzFirst Guideline on Analgesia for IM Penicillin injections (2011)\textsuperscript{171} in Appendix F. In many areas the vibrating device recommended will not be available but the use of lignocaine should still be considered.
Table 20: Recommended Antibiotic Regimens for Secondary Prevention of ARF/RHD

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dose</th>
<th>Route</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First line</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benzathine penicillin*</td>
<td>Children &lt;30kg: 450mg (600,000 U)</td>
<td>Most effectively given as a deep intramuscular injection†</td>
<td>4-weekly (28 days), or 3-weekly for those who have had confirmed recurrent ARF despite full adherence to 4-weekly benzathine penicillin†</td>
</tr>
<tr>
<td></td>
<td>Children &amp; Adults ≥30kg: 900mg (1,200,000 U)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Second line (If intramuscular route is not possible or refused)</strong>‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Penicillin V</td>
<td>Children &lt;20kg: 250mg</td>
<td>Oral</td>
<td>Two or three times daily</td>
</tr>
<tr>
<td></td>
<td>Adolescents &amp; Adults ≥ 20kg: 500mg</td>
<td>Oral</td>
<td>Two or three times daily</td>
</tr>
<tr>
<td><strong>Following documented penicillin allergy§</strong></td>
<td>Children &amp; Adults: 40mg/kg per day</td>
<td>Oral</td>
<td>2-3 divided doses (max adult daily dose 1000mg)</td>
</tr>
<tr>
<td>Erythromycin ethyl succinate (EES)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Benzathine penicillin can be given with lignocaine to reduce injection site pain
† The timing of administration may be advanced to aid compliance for extenuating circumstances such as tangi leave, overseas travel, school holidays etc. For people on a 28 day regimen it can be advanced as much as 14 days, and for those on a 21 days regime, up to 7 days
‡ Oral penicillin is less efficacious than benzathine penicillin in preventing GAS infections and subsequent recurrences of ARF. 127,123,172,173 Twice-daily oral regimens are also likely to result in poorer rates of adherence over long periods of time174 and less predictable serum penicillin concentrations, when compared to intramuscular benzathine penicillin. 60 In addition, oral penicillin V incurs a cost to the patient, while IM benzathine penicillin is free when provided through an ARF prevention programme. Oral penicillin should be reserved for cases who refuse intramuscular benzathine penicillin (Level II, Grade B). If a patient is offered oral penicillin, the consequences of missed doses must be emphasised and adherence carefully monitored (Grade D).
§ The benefits of long-term benzathine penicillin administration outweigh the rare risk of serious allergic reactions to penicillin and fatality as a result of anaphylaxis. 60,163,175,176 The rates of allergic and anaphylactic reactions to monthly benzathine penicillin are 3.2% and 0.2%, respectively, and fatal reactions are exceptionally rare. 176,177 There is no increased risk with prolonged benzathine penicillin use. A prospective study of 1,790 ARF/RHD patients found similar rates of allergic reactions in those receiving long-term penicillin therapy and those receiving short-term therapy for sexually transmitted diseases (Level III-2). 177 Before commencing penicillin treatment, cases should be carefully questioned about known allergies to penicillin and other beta-lactam antibiotics. When patients state they are allergic to penicillin or when a non-specific reaction has been reported but there is no unequivocal evidence, they should be investigated for penicillin allergy, preferably in consultation with an immunologist/allergist. The options include skin testing177 or a supervised challenge test. Most of these patients are not truly allergic. Penicillin desensitisation is not applicable to these patients, even with a regimen of more frequent injections, as it would have to be repeated before each dose of benzathine penicillin. 176,179 A RAST (RadioAllergoSorbent Test) may be used as a screening tool only. Because this is a specific but not very sensitive test, a negative RAST test must be followed up in all cases with penicillin skin testing and/or consideration of a graded challenge if appropriate (Grade D).

New Zealand has been affected by inconsistent supply of benzathine penicillin over recent years. This poses potential risks to those requiring four-weekly prophylaxis. Organisational approaches to secondary prevention should seek to ensure consistent supply at the national, regional and local levels. However, when benzathine penicillin is unavailable, oral penicillin or erythromycin can be given (as per Table 20).
Secondary Prophylaxis during Pregnancy, While Breast Feeding or While on Oral Contraceptives

Secondary Prophylaxis during Pregnancy

Penicillins and erythromycin are considered safe for use in pregnancy (Grade C).\textsuperscript{180}
Low dose lignocaine is safe in pregnancy (Grade C, Level III-2).\textsuperscript{180,182} A large number of pregnant women and women of child bearing age have been exposed to lignocaine.\textsuperscript{181,182} Lignocaine crosses the placenta but there is no evidence of an association with fetal malformations, cardiac rhythm disturbances or other significant side effects in pregnant women or their babies.

Secondary Prophylaxis While Breastfeeding

Penicillins are excreted into breast milk in low concentrations and are considered safe for use in breast feeding.\textsuperscript{180,183} Erythromycin is also excreted into breast milk and has been considered as compatible in breast feeding.\textsuperscript{180,183} There have been reports of a correlation between the use of erythromycin in breast feeding mothers and infantile hypertrophic pyloric stenosis in newborns.\textsuperscript{183} Monitor infants for vomiting, diarrhea and rash while breastfeeding mothers are on amoxicillin and erythromycin courses.\textsuperscript{183} Lignocaine can be administered to breast feeding women (Grade C, Level IV). Lignocaine is excreted into breast milk in small amounts,\textsuperscript{180,181,182,183,184} however the oral bioavailability of lignocaine is very low (35%).\textsuperscript{183} Given the small amount of lignocaine used with benzathine penicillin the amount excreted into breast milk to which the infant is therefore exposed, is minimal. Lignocaine is unlikely to cause adverse effects in breast feeding infants.\textsuperscript{180,181,182,183,184}

Secondary Prophylaxis While on Oral Contraceptive

Oral contraceptives are still recommended for women of child-bearing age while on benzathine penicillin prophylaxis. Progesterone-only oral contraceptives do not interact with benzathine penicillin therapy.\textsuperscript{185,186,187,188} An interaction between IM benzathine penicillin and the combined oral contraceptive is possible, although this interaction is suggested to only be of significance for short courses of antibiotic therapy (less than three weeks). In addition, the risk of interaction with antibiotics is small enough that it may not be identifiable from the one to three percent risk of oral contraceptive failure (Grade C).\textsuperscript{189} Caution is advised when considering the use of the combined oral contraceptive pill in women with complicated rheumatic heart disease/valve disease or atrial fibrillation, especially for cases also on warfarin due to the pro-thrombotic nature of oestrogens, later generation progestogens etc; advice should be sought.

A levonorgestrel-releasing intra uterine contraceptive device (such as Mirena™) would be more suitable (if in a stable relationship) (Grade D).

The risk benefit ratio of pregnancy versus side effects of oral contraception may need discussion with family planning and cardiology.

Secondary Prophylaxis in Anti-Coagulated Patients

Intramuscular bleeding from benzathine penicillin injections, used in conjunction with anticoagulation therapy in New Zealand, is rare. Thus, benzathine penicillin injections should be continued for those who are anti-coagulated, unless there is evidence of uncontrolled bleeding or the international normalised ratio (INR) is outside the defined therapeutic window (Grade D). Benzathine penicillin should not be administered if the INR is greater than 4.5. The INR level should be monitored monthly as a minimum for adults, more frequently in children. Patients discharged from hospital on oral penicillin following valve surgery should recommence benzathine penicillin as soon as is practical.
Duration of Secondary Prophylaxis

The appropriate duration of secondary prophylaxis depends on a number of factors. These include:

- **Age** (ARF recurrence is less common after the age of 25 and uncommon after the age of 30)\(^{29,30,127}\)
- **Clinical pattern** (presence or absence of carditis at presentation or RHD and severity of carditis or RHD)
- **Environment** (particularly the likelihood of ongoing exposure to GAS such as young children in the household)
- **Time elapsed since last episode of ARF** (ARF recurrences are less common greater than five years since last episode)\(^{29,30,127}\)

Based on these factors, the recommended duration of secondary prophylaxis is outlined in Table 21. The duration of prophylaxis recommended is also outlined in Algorithm 2, page 69.

Table 21: New Zealand Recommendations for the Duration of Secondary Prophylaxis

<table>
<thead>
<tr>
<th>Category of RHD*</th>
<th>Duration of Prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>None or mild RHD</td>
<td>Minimum of 10 years after most recent episode ARF or until age 21† years (whichever is longer)</td>
</tr>
<tr>
<td>Moderate RHD</td>
<td>Until age 30 and then reassess</td>
</tr>
<tr>
<td>Severe RHD</td>
<td>Until age 40 but reassess at age 30‡</td>
</tr>
</tbody>
</table>

* Definition of categories:

  - **Mild RHD:** Any valve lesion(s) graded mild clinically, or by echocardiography, with no clinical evidence of heart failure and no evidence of cardiac chamber enlargement on CXR, ECG or echo
  - **Moderate RHD:** Any valve lesion of moderate severity clinically (e.g. mild or moderate cardiomegaly), or any moderate severity valve lesion on echocardiography, or any echocardiographic evidence of cardiac chamber enlargement
  - **Severe RHD:** Any severe valve lesion clinically (significant cardiomegaly expected, and/or heart failure), or any severe valve lesion on echocardiography, or any impending or previous cardiac surgery for RHD

† **At age 21 (or 10 years after the first attack), reassess (clinical examination and echocardiography) severity of RHD.** A review of data from the Auckland Acute Rheumatic Fever Register (1993-1999) in New Zealand found that recurrences occurred up to 21 years after completion of prophylaxis programmes. 77% were within the first seven years, and 30% were greater than ten years. The mean overall recurrence interval between last attack and recurrence was 8.6 years. Of the cases that received ten years prophylaxis, there were two ARF recurrences after discharge and an estimated 2,200 patient years of follow-up (0.1/100 patient years). Two “breakthrough” recurrences occurred in this series in cases who were inadvertently discharged early off prophylaxis (aged 16 and 17 years).\(^{29,31}\) This data suggest that in the New Zealand environment, maintenance of prophylaxis to 21 years of age (or 10 years after the first attack) in cases with absent or mild heart disease is safe and effective (Level IV, Grade C). Advice re: ongoing sore throat management is important at the time of discharge.

‡ **Of the Auckland (1993-1999) cases, only five recurrences occurred after the age of 30.**\(^{29,30}\) Therefore it is reasonable to cease secondary prophylaxis at that age, except when individual circumstances warrant continuing (e.g. when cases wish to reduce even a small chance of a recurrence) (Level IV, Grade C)

- **Individuals working or living with children or in a living situation where there is overcrowding or close proximity to others** (such as boarding schools, barracks, and hostels) have a higher risk of exposure to GAS and subsequent development of ARF. In these cases, consideration should be given to extending the duration of prophylaxis (Grade D)

- **For those presenting at an older age (over the age of 21 years), with no or mild carditis, it is possible to consider discharge from prophylaxis after 5 years** (Grade D)

- **The duration of prophylaxis presented here refers to ‘definite’ and ‘probable’ cases of ARF** (see page 14). For those with ‘possible’ ARF (where there is strong clinical suspicion, but insufficient signs and symptoms to fulfill the diagnosis), a minimum of 5 years prophylaxis should be considered, with regular review (Grade D)
For those presenting with RHD for whom no initial episode of ARF can be identified, the decision to commence and cease penicillin prophylaxis should be taken on an individual basis with regard to the age of the case, severity of the disease, possible age of first attack and risk of exposure to GAS.

Before stopping prophylaxis the patient’s physician should discuss with a physician knowledgeable on rheumatic fever e.g. internal medicine physician with a special interest in RF/RHD, infectious diseases paediatrician/physician or cardiologist. Recipients who are known to have had carditis should be evaluated for symptomatic deterioration and the stability and severity of valve lesions. This should include echocardiographic assessment (Grade D). Where limited echocardiography is available, preference should be given to those with a history of moderate or greater carditis, a history of one or more ARF recurrences or clinical evidence of carditis (e.g. a murmur) (Grade D). The anticipated and actual dates of cessation should be documented in the medical records and on the ARF register where possible, (see page 42). The date of cessation may be reviewed if there is a change in clinical or echocardiographic severity, specialist recommendation, a change in environmental exposure to GAS, or a recurrence of ARF (Grade D).

Protocol for Secondary Prophylaxis Delivery

In the New Zealand environment, it is recommended that secondary prophylaxis is delivered by community nursing staff at schools, in the workplace or at home (Table 22). Local protocols should be available at public health units and in healthcare pathways in general practice (where these are available).

In each area this delivery should be supported by the presence of a rheumatic fever register (see page 42), and it is also recommended that in each area specific medical staff sign designated authorisation for the nurses to deliver benzathine penicillin. The generation of these prescriptions will also be assisted by a register system.

Table 22: Suggested Protocol for the Delivery of Secondary Prophylaxis by Community Nurses

For the safe preparation and administration of lignocaine with benzathine penicillin refer to The KidzFirst Guideline on Analgesia for IM Penicillin injections (2011) in Appendix F.

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Delivery†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identify client (full name and date of birth) *</td>
<td>Apply pressure to injection site for 10 seconds and consider other measures to reduce pain (Table 23)</td>
</tr>
<tr>
<td>Confirm that consent has been given for benzathine penicillin delivery by delegated authority i.e. usually at school (if appropriate) by nurses. This will include discussion about likely probable length of penicillin prophylaxis</td>
<td>Administer benzathine penicillin slowly into ventrogluteal, dorsogluteal area of buttock or vastus lateralis or thigh (or as per local area policy)</td>
</tr>
<tr>
<td>Check allergy status, if symptoms of allergy reported from previous injection then withhold injection, document and report to GP and specialist</td>
<td>Dispose of the used syringe in a sharps container</td>
</tr>
<tr>
<td>Refer to local clinical policies for anaphylaxis management</td>
<td></td>
</tr>
<tr>
<td>Check the prescription: date, route, frequency and dose</td>
<td></td>
</tr>
<tr>
<td>Check weight for children on 450mg (0.6 MU) of benzathine penicillin to ensure dose for next injection is appropriate (i.e. remain at &lt;30kg). Record weight in progress notes. If dose should change, document and inform the local prescriber and register coordinator to ensure the dose is changed for the next delivery</td>
<td></td>
</tr>
<tr>
<td>Give full explanation to client</td>
<td></td>
</tr>
<tr>
<td>Position client lying or as preferred</td>
<td></td>
</tr>
<tr>
<td>Wash hands</td>
<td></td>
</tr>
<tr>
<td>Prepare benzathine penicillin. If 450mg (0.6 MU) dose is required dispose of half the syringe contents prior to administration. Warm in hands</td>
<td></td>
</tr>
</tbody>
</table>
Observation

- Observe client for a minimum of 10 minutes after administration of benzathine penicillin for any signs and symptoms of an allergic reaction. Local policy may suggest a 20 minute observation period.

Evaluation

- Complete record of administration
- Review education needs/knowledge

* If under 16: confirm identification with another responsible person (i.e. caregiver, school receptionist)
† If the client is not available, and the full syringe has been maintained in cold chain (see vaccine storage protocols), it can be returned to the medicine fridge. If the full syringe has not been maintained within the cold chain, then it needs to be discarded.

Anaphylaxis

Anaphylaxis is an uncommon reaction following IM or IV antibiotics, immunisation or other medicines. Anaphylaxis to benzathine penicillin is rare. Hypersensitivity reactions to benzathine penicillin have been reported after multiple monthly injections. Anaphylaxis has been reported to occur in patients who have previously tolerated the injection for months and years without incident. In a prospective international study after 32,430 injections during 2,736 patient years of observation, 57 (3.2%) of the 1,790 patients had an allergic reaction and four (0.2% or 1.2 per 10 000 injections) had anaphylaxis. The long-term benefits of prophylaxis therefore far outweigh the potential risk of a serious allergic reaction. Refer to local clinical policies for guidance on the management of anaphylaxis.

It is recommended that the first benzathine injection be given in hospital, especially in the childhood age group with appropriate play therapy. Subsequent injections may then be given in the home environment before progressing to injections at school.

It is recommended that monitoring and screening for allergy should be completed at each injection. Following documented anaphylaxis to penicillin, immunological evaluation is recommended. Interim oral erythromycin is recommended until evaluation is undertaken.

Improving Adherence to Secondary Prophylaxis

The persistence of recurrent ARF in some areas of New Zealand highlights the continued failure of secondary prevention.

Failure to prevent recurrent ARF in a study from the Gisborne area, was thought to be due to a range of factors including a lack of recognition of the efficacy of parenteral benzathine penicillin compared to oral regimens, inadequate adherence, unreliable data collection and the lack of long-term continuity of care. Improved adherence to prophylaxis is seen with active follow-up of cases when benzathine penicillin doses are missed, the identification of local dedicated staff members responsible for delivery of secondary prophylaxis, developing a personal rapport with each case and coordinating routine care. Effective communication between health staff and families is important. In New Zealand, it is particularly important to support and utilise the expertise, experience, community knowledge, culture and language skills of Māori and Pacific health workers in order to assist with adherence to secondary prophylaxis.

Three methods for improving compliance will be discussed further in this guideline:

- Reducing the pain of the benzathine penicillin injection
- Education
- The use of rheumatic fever registers to plan a treatment programme for patient.

Reducing the Pain of Benzathine Penicillin Injections

The pain of benzathine penicillin injections is usually not a critical factor in determining adherence to secondary prophylaxis. Nonetheless, techniques that safely reduce injection pain (Table 23) should be promoted.
Table 23: Measures That May Reduce the Pain of Benzathine Penicillin Injections

<table>
<thead>
<tr>
<th>Measures Include:</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Use a 23-gauge needle*</td>
</tr>
<tr>
<td>- Apply pressure with thumb for 10 seconds before inserting needle†</td>
</tr>
<tr>
<td>- Warm syringe to room temperature before using‡</td>
</tr>
<tr>
<td>- Allow alcohol from swab to dry before inserting needle‡</td>
</tr>
<tr>
<td>- Use of ethylchloride spray prior to injection§</td>
</tr>
<tr>
<td>- Deliver injection very slowly (preferably over at least 2–3 mins)‡</td>
</tr>
<tr>
<td>- Distraction techniques during injection (e.g. with conversation)</td>
</tr>
<tr>
<td>- Good rapport with the case, assisted by having a designated nurse for each case, is a significant aid to injection comfort, compliance, and understanding.‡</td>
</tr>
<tr>
<td>- Use of lignocaine and vibrating device‖</td>
</tr>
</tbody>
</table>

* A smaller gauge needle and increasing the volume of injection to 3.5ml improved acceptability in Taiwan.¹⁶⁵
† Direct application of pressure to the injection site has been shown to decrease pain of intra-muscular injections.¹⁹¹
‡ As these measures are logical and benign they are recommended, despite the lack of evidence (Grade D)
§ Although merely a topical agent, some cases have reported reduced pain and bruising following the appropriate use of ethylchloride spray (Grade D)
‖ See The KidzFirst Guideline on Analgesia for IM Penicillin injections (2011) in Appendix F.

The addition of 0.25ml of 2% lignocaine has become standard practice in New Zealand. This is optional for the patient and informed consent is required before administration. It significantly reduces pain immediately and in the first 24 hours after injection, while not significantly affecting serum penicillin concentrations.¹⁶⁸ See The KidzFirst Guideline on Analgesia for IM Penicillin injections (2011) in Appendix F.

Education

Health education is critical at all levels.¹²⁷ Lack of parental awareness of the causes and consequences of ARF/RHD was a key contributor to poor adherence among children on long-term prophylaxis in Egypt.¹⁹² In a number of regions in India, comprehensive health education has improved community awareness of sore throat, ARF and RHD and assisted case identification.¹⁹⁴ Comprehensive health education and promotion was also a key component in the successful control of RHD in the French Caribbean.¹⁹⁵ Improved health staff awareness of the diagnosis and management of ARF and RHD is necessary in order to improve case findings, encourage compliance with prophylaxis and to improve the quality and delivery of health education delivered to cases and their families.

Education Provided to the Patient and Their Family Should Cover:

- The cause and complications of ARF
- The reason for secondary prophylaxis and the signs and symptoms of recurrence
- The prevention of endocarditis and the differences between this and secondary prophylaxis of ARF
- Sore throat management (for the person with rheumatic fever as well as their family/household members)
- The importance of medical and dental follow-up
- How to contact the relevant people or agencies should they require further information or assistance.

The National Heart Foundation of New Zealand produces a booklet in English, Tongan and Samoan called “What is Rheumatic Fever?” to assist in education provision to cases and their families. This is available to order from www.heartfoundation.org.nz
**ARF Registers**

Registers of people with RHD or a history of ARF are a key element in ARF recurrence and RHD control at an individual, community and national level.26,28,29,44,196

In 1978, the WHO promoted the use of disease registers as part of community programmes to help coordinate prevention of ARF recurrences and of RHD.197 The use of these registers has been proven in both developing and developed countries to enhance the impact of secondary prevention strategies for ARF and to effectively reduce morbidity and mortality.25,51,198

Register-based RHD control programmes have been successful in New Zealand. By the early 1980s, ARF registers had been implemented in Waikato, Northland, Auckland, Gisborne and Rotorua. Despite similarities, each programme developed independently of any national framework, and each was shown to be effective at reducing admissions for ARF recurrences.25 In New Zealand, ARF became a notifiable condition under the national surveillance and management framework in 1986.25

In 2001, a survey describing register-based ARF prevention programmes in New Zealand was conducted. Two types of registers were described: management and surveillance. Register-based ‘management’ programmes use a register to coordinate community based prophylaxis provided predominantly by district nursing services, collate information on prophylaxis delivery and encourage parenteral prophylaxis. Management programmes also use their registers to perform a varying range of other functions including informing health care workers (such as dentists and GPs) of those who are receiving prophylaxis, generating or prompting penicillin prescriptions and accumulating data for evaluation. Six register-based management programmes were operating in New Zealand in 2001 (predominantly through public health units in collaboration with clinicians). These were based in Northland, Auckland (district nurses in association with paediatricians), Rotorua (established by an association of GP’s), Hawkes Bay and Lower Hutt. Collectively, these programmes covered nine health districts containing 51.1% of the population and 81.9% of ARF notifications between 1995 and 2000. A further three ‘surveillance’ programmes, without clinician input, were described in Whakatane, Wanganui and Palmerston North. These programmes maintained a record of cases receiving prophylaxis, but did not have a role in coordinating the provision of prophylaxis.25 In total, these register systems covered 94% of notified ARF cases, and they were considered largely responsible for reducing ARF recurrence from 22% (of all ARF episodes) between 1972 and 1981 to only 6% between 1982 and 1992.199

The Auckland Acute Rheumatic Fever Register, established in 1982, is a population-based register covering 60% of New Zealand ARF registrations. The register is used both as a surveillance register and a tool to generate dental referrals and delegated authority prescriptions to aid penicillin delivery by the district nursing service. Those who miss their prophylaxis are actively sought for three to six months before being inactivated on the register. Community nurses from other areas can also refer confirmed cases to the register for ongoing prophylaxis. A study evaluated the effectiveness of the Auckland ARF Register and of 28 day penicillin prophylaxis by auditing recurrences notified to the register in this time period for those with mild or absent heart disease without active follow-up after at least ten years. In this study, an overall programme failure rate of 1.4 per 100 patient years was determined with a penicillin failure rate of 0.07 per 100 patient years.25,30 Earlier audits of the same register from 1972 to 1981 (1.5 per 100 patient years) and 1982 to 1992 (0.6 per 100 patient years) reached similar conclusions.39,200 These rates of programme failure are highly acceptable when compared to other published data (0.0-2.8 per 100 patient years).60,90,163,164,165,197,201,202,203,204

It is recommended that all regions of New Zealand with substantial populations with ARF or RHD establish a coordinated computer-based ARF register which provides individual and community reports, recall lists, reports on ARF/RHD epidemiology and monitors the effectiveness of the local prevention programme (Grade C).

The main aims of ARF registers are summarised in Table 24.

In the Auckland register review by Spinetto et al patients originating from outside Auckland were found to be at risk.28,30 This has led to re-affirming the need for a New Zealand based register with the rationale that cases who move between regions, a frequent cause of non-compliance, would have improved adherence. A recent study by paediatrician Dr John Malcolm and colleagues in the Bay of Plenty found that non-compliance was a risk factor for multiple poor health outcomes.74

At the time of writing the Ministry of Health do not regard a national based RF register as a priority.
Table 24: Primary Aims of ARF Register Systems

<table>
<thead>
<tr>
<th>Primary Aims</th>
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</thead>
<tbody>
<tr>
<td>● Increase uptake of and adherence to secondary prophylaxis(^59,205)</td>
</tr>
<tr>
<td>● Reduce recurrences of ARF(^25,59,199,295,206,207) and decrease hospitalisations from ARF/RHD (Level III)(^59,205)</td>
</tr>
<tr>
<td>● Improve case detection(^59,194,205,208,209)</td>
</tr>
<tr>
<td>● Record prophylaxis delivery</td>
</tr>
<tr>
<td>● Employ recall and reminder systems for ARF cases, identify individuals with poor adherence to long-term therapy for targeted educational activities and other interventions</td>
</tr>
<tr>
<td>● Monitor the movement of ARF cases (who are typically highly mobile), while conforming to privacy legislation and patient confidentiality</td>
</tr>
<tr>
<td>● Improve the coordination of ongoing care requirements and follow-up</td>
</tr>
<tr>
<td>● Identify and register new cases of ARF and RHD</td>
</tr>
<tr>
<td>● Use data to improve programme strategies and determine changes in disease epidemiology</td>
</tr>
<tr>
<td>● Fulfil legal requirements of disease notification</td>
</tr>
<tr>
<td>● Improve awareness amongst health professionals</td>
</tr>
<tr>
<td>● Centralised registers can also support the provision of prophylaxis for those who move between communities.(^208)</td>
</tr>
</tbody>
</table>

The register can then be used as the basis for a coordinated control programme. This is the most effective approach to improving benzathine penicillin adherence and clinical follow-up of people with RHD, including specialist review and echocardiography (Level III-3). Elements of such a programme are listed in Table 25 (Grade C). Key data elements of ARF/RHD registers can be found in Appendix G.

Table 25: Recommended Elements of a Register-Based Control Programme

<table>
<thead>
<tr>
<th>Recommended Elements</th>
</tr>
</thead>
<tbody>
<tr>
<td>● A local ARF register, established within existing health care networks or public health units, with all the properties and data as described in Tables 24 and 42</td>
</tr>
<tr>
<td>● Commitment from regional and local services, particularly to ensure long-term funding</td>
</tr>
<tr>
<td>● Activities guided by locally relevant, evidence-based guidelines</td>
</tr>
<tr>
<td>● A coordinator for each register programme*</td>
</tr>
<tr>
<td>● A commitment to partnerships between clinicians and public health services in order to support the needs of people with ARF/RHD and the community</td>
</tr>
<tr>
<td>● An ability to assess and monitor the burden of disease</td>
</tr>
<tr>
<td>● Provision of education for health practitioners, the community, those with rheumatic fever or rheumatic heart disease and their families</td>
</tr>
<tr>
<td>● Provision or support for the provision of health education within the local community, community health service and for community health workers</td>
</tr>
<tr>
<td>● A follow-up system (such as dedicated ARF/RHD clinics) that ensures that ongoing care is delivered, particularly to those at highest risk</td>
</tr>
<tr>
<td>● A mechanism for monitoring delivery of secondary prophylaxis and ongoing care, programme reporting and independent evaluation</td>
</tr>
<tr>
<td>● Some areas may also be able to have an effective advisory committee that may include cardiologists, paediatricians, general practitioners, physicians, epidemiologists, nurses, public health practitioners and relevant community representative.</td>
</tr>
</tbody>
</table>

* A dedicated coordinator with data entry support is critical to the success of the programme. This person should have skills in data management, basic epidemiology, and clinical medicine, or ready access to clinical expertise when individual case management issues arise. To ensure that the programme continues to function well despite staffing changes, activities must be integrated into the established health system.
Non-adherence

If a patient is non-adherent, it is recommended that a number of methods of contact, over a number of months are attempted. Every effort should be made to utilise community contacts in the area, and a period “on hold” with continued attempts to contact, should be used prior to considering discharge. In Auckland early discharge off prophylaxis due to persistent non-adherence, is rare.

A protocol for the management of non-adherent patients can be found in Appendix H.
C. RHEUMATIC HEART DISEASE

Chronic rheumatic heart disease (RHD) is the consequence of carditis of ARF. No other presenting sign or symptom of ARF has a significant long term effect. If RHD did not occur, then ARF would be an autoimmune disease with little long term consequence. RHD most frequently involves the mitral valve, initially with mitral regurgitation. Chronic mitral regurgitation leads to volume loading of the left ventricle. Progressive dilation results in myocardial fibrosis and eventually ventricular dysfunction and cardiac failure.

Mitral valve pathology evolves over many years after the acute inflammation has resolved, with fibrosis of the valve leaflets and subvalvular structures. The valve leaflets become immobile leading to mixed mitral regurgitation and stenosis. Mitral stenosis leads to atrial dilatation, setting the stage for atrial fibrillation (AF) and thromboembolism. The aortic valve is less frequently involved than the mitral valve in chronic RHD. Severe aortic regurgitation also leads to volume loading of the left ventricle. Evolution to aortic stenosis is extremely rare.

The American investigators of the first half of the 20th century called RHD the ‘long shadow of rheumatic fever’ as they recognised that the disease state lasted decades after the original episodes of ARF.

The individual lesions of mitral regurgitation, mitral stenosis, aortic regurgitation, aortic stenosis (a rare scenario), tricuspid regurgitation and multi-valvular disease have their own specific pathogenesis, symptoms, and signs. Excellent descriptions of their clinical presentation and management as part of chronic RHD arose from the Australian and New Zealand collaboration in 2005-06 (which led to their respective RF guidelines). The 2012 Australian RF guideline (2nd Edition) also provides an up-to-date guide for the description and management of significant RHD.

**Best Practice RHD Care Involves:**
- Secondary prevention with penicillin prophylaxis
- Timely reviews by a specialist experienced in RHD management; physician, paediatrician, infectious disease specialist (paediatric or adult) or cardiologist (paediatric or adult)
- Access to echocardiography to serially assess left ventricular function and valve function
- Adequate monitoring of anticoagulation therapy in patients with atrial fibrillation and/or mechanical prosthetic valves
- Access to oral healthcare
- Timely referral for heart surgery.

The fundamental goals in the long-term management of RHD are to prevent ARF recurrences (which lead to the progression of valve disease) and monitor left ventricular function. In many cases with mild or moderate RHD, resolution of RHD is observed over time. In mild and moderate RHD the left ventricle is not at risk of failing. Unfortunately, even without recurrences of ARF, those with severe RHD may develop progression of disease due to the irreversible damage of the valves and left ventricular myocardium.

All patients with RHD or a past history of ARF who develop new heart murmurs require echocardiography. Echocardiography can grade the severity of valvular disease and assesses left ventricular (LV) size and systolic function. Serial echocardiographic data plays a critical role in determining the timing of any surgical intervention and balloon mitral valvuloplasty. Cardiologists have a key role to reinforce the need for secondary prophylaxis for their patients.
Routine Review and Structured Care Planning

A structured care plan should be developed and recorded in the notes of all persons with a history of ARF, or with established RHD. Table 26 lists the recommended review frequency (Grade D). This schedule may be tailored to the needs of the individual and may also differ depending on local resources.

Table 26: Recommended Routine Clinical Review and Management Plan for RHD*

<table>
<thead>
<tr>
<th>Classification</th>
<th>Criteria</th>
<th>Review and Management Plan</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Secondary Prophylaxis</td>
</tr>
<tr>
<td>Low Risk</td>
<td>ARF with no evidence of RHD or Trivial or mild valvular disease</td>
<td>4-weekly§</td>
</tr>
<tr>
<td>Medium risk</td>
<td>Moderate RHD</td>
<td>4-weekly§</td>
</tr>
<tr>
<td>High risk II</td>
<td>Any severe valve lesion or Mechanical prosthetic valves or Tissue prosthetic valves and valve repairs</td>
<td>4-weekly§</td>
</tr>
</tbody>
</table>

**In addition:**
- Annual influenza vaccination (funded for RHD patients)
- Polysaccharide pneumococcal vaccination (Pneumovax® 23) repeated once after 5 years

<table>
<thead>
<tr>
<th>Additional considerations</th>
<th>Review and Management Plan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Following valve surgery</td>
<td>3 - 4 weeks following hospital discharge: Medical assessment to include ECG, chest radiograph, echocardiography, full blood count, urea, creatinine, electrolytes and INR if indicated.</td>
</tr>
</tbody>
</table>

* Review frequency should be determined according to individual needs and local capacity. Most critically, review should become more frequent in the event of symptom onset, symptomatic deterioration or a change in clinical findings

† In the South Island annual review for all the RF patients by Infectious Diseases specialists is recommended regardless of the severity of RHD

‡ Routine dental care is critically important in cases with a history of ARF and/or RHD. All patients should receive education about oral hygiene, and should be referred promptly for dental assessment and treatment when required. This is especially important prior to valvular surgery, when all oral/dental pathology should be investigated and treated accordingly (Grade D).

§ In New Zealand, 4-weekly benzathine penicillin is recommended unless confirmed recurrent ARF has occurred despite full adherence to prophylaxis. In this case, 3-weekly benzathine penicillin is recommended (Grade D)

‖ Anyone with severe valvular disease or moderate to severe valvular disease with symptoms should be referred for cardiological and surgical assessment as soon as is possible (Grade D).
Oral Health Care

People with rheumatic heart disease have an increased risk of developing infective endocarditis, a condition with significant morbidity and mortality. Oral bacteria have been identified as causative agents for infective endocarditis and so it is important that all people with RHD have meticulous dental and oral hygiene to reduce the risk of oral source for bacteraemia.

Regular oral health care, which includes assessment, treatment and preventive education should be part of the routine ongoing management of RHD. It is recommended that all patients with rheumatic heart disease (regardless of severity) undergo at least annual oral health review. Dental recall intervals should be based on clinical risk therefore people with moderate/severe RHD, prosthetic cardiac valves or higher dental risk factors (e.g. poor oral hygiene, dry mouth, untreated dental caries and inflammatory periodontal disease) should be offered more frequent dental reviews based on clinical risk.

Some dental procedures do have an increased risk of causing an oral bacteraemia. The effectiveness of additional antibiotic prophylaxis prior to dental procedures is controversial, however antibiotic prophylaxis is recommended for at risk patients having at risk dental procedures.

Current New Zealand Heart Foundation recommendations for antibiotic prophylaxis for dental procedures are detailed below:

Patients Requiring Antibiotic Prophylaxis

Patients with the following conditions require antibiotic prophylaxis have been selected because of a high lifetime risk of endocarditis and a high risk of mortality or major morbidity resulting from infective endocarditis, should it occur. Prophylaxis is recommended for people with rheumatic valvular heart disease but is not recommended for those who have had previous rheumatic fever without cardiac involvement.

- Prosthetic heart valves (bio or mechanical)
- Rheumatic valvular heart disease
- Previous endocarditis
- Unrepaired cyanotic congenital heart disease (includes palliative shunts and conduits)
- Surgical or catheter repair of congenital heart disease within six months of repair procedure.

Of note: Prophylaxis is recommended only for people with rheumatic valvular heart disease and is not recommended for those who have had previous rheumatic fever without cardiac involvement.

Dental Procedures Requiring Antibiotic Prophylaxis

Prophylaxis is recommended for all dental procedures that involve manipulation of gingival tissue or the periapical region of teeth for instances fillings that extend to or below the gum margin, cleaning teeth at or below the gingival margin and the earlier stages of a root filling when the length of the canal is still being measured.

The following procedures and events do NOT need prophylaxis:

- Routine anaesthetic injections through non-infected tissue
- Taking dental radiographs
- Placement of removable prosthodontic or orthodontic appliances
- Adjustment of orthodontic appliances
- Placement of orthodontic brackets
- Shedding of deciduous teeth
- Bleeding from trauma to the lips or oral mucosa.
Antibiotic Prophylaxis Regimen
The prophylaxis for dental procedures and tonsillectomy is directed against viridans streptococci. While they are not the only organisms that cause bacteraemia following these procedures, they are the organisms most likely to cause endocarditis.

Table 27: Antibacterial Regimen for Dental Procedures

<table>
<thead>
<tr>
<th>Antibacterial Regimen for Dental Procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Amoxicillin 2g (child: 50mg/kg up to 2g), administered:</strong></td>
</tr>
<tr>
<td>- Orally, 1 hour before the procedure, or</td>
</tr>
<tr>
<td>- IV, just before the procedure, or</td>
</tr>
<tr>
<td>Administer parenterally if unable to take medication orally; administer IV if IV access is readily available.</td>
</tr>
<tr>
<td>For penicillin allergy or if a penicillin or cephalosporin-group antibiotic is taken more than once in the previous month (including those on long-term penicillin prophylaxis for rheumatic fever):</td>
</tr>
<tr>
<td><em><em>Clindamycin</em> 600mg (child: 15mg/kg up to 600mg), administered:</em>*</td>
</tr>
<tr>
<td>- Orally, 1 hour before the procedure, or</td>
</tr>
<tr>
<td>- IV, over at least 20 minutes, just before the procedure, or</td>
</tr>
<tr>
<td>- IM, 30 minutes before the procedure.</td>
</tr>
<tr>
<td>Or</td>
</tr>
<tr>
<td><strong>Clarithromycin† 500mg (child: 15mg/kg up to 500mg) orally</strong>, 1 hour before the procedure.</td>
</tr>
</tbody>
</table>

**Source:** Adapted from the Heart Foundation of New Zealand. New Zealand Guideline for the Prevention of Infective Endocarditis Associated with Dental and Other Medical Procedures 2008.148
* Clindamycin is not available in syrup form in New Zealand
† Beware potential interactions between clarithromycin and other medications.

If the antibacterial agent is inadvertently not administered before the procedure, it may be administered up to two hours after the procedure.

For patients requiring more than one appointment to complete their care, if possible schedule appointments two weeks apart and alternate Clindamycin and Clarithromycin) if the patient is already taking a penicillin for secondary RHD prophylaxis or is allergic to penicillin.

If the antibacterial agent is inadvertently not administered before the procedure, it may be administered up to two hours after the procedure.

See the New Zealand Guideline for the Prevention of Infective Endocarditis Associated with Dental and Other Medical Procedures 2008 for more details.148 See:

Pregnancy and Childbirth
This section has been adapted from: RHDAustralia (ARF/RHD writing group) et al. Australian guideline for prevention, diagnosis and management of acute rheumatic fever and rheumatic heart disease (2nd edition). 2012 © by permission of RHDAustralia.5

Pregnancy in Women with Rheumatic Heart Disease
Normal pregnancy is associated with a 30-50% increase in blood volume, reduction in systemic vascular resistance and corresponding increase in cardiac output. These changes begin during the first trimester, peaking at 28-30 weeks of pregnancy and are then sustained until term. The increase in blood volume is associated with an increase in heart rate by 10–15 beats per minute. These circulatory changes of pregnancy will exacerbate any pre-existing valvular disease. Sometimes RHD, especially mitral stenosis (MS), is first diagnosed during pregnancy or soon after delivery when a woman develops symptoms of decompensated heart failure such as dyspnoea, orthopnoea and paroxysmal nocturnal dyspnoea.215

Ideally, women with known RHD should have a complete cardiac assessment before pregnancy. Discussion regarding pregnancy planning should be undertaken in all women even if immediate pregnancy is not planned; unplanned pregnancy is by no means uncommon in this disadvantaged
group. Assessment should include a full history and examination, with functional assessment and a detailed echocardiographic study. In women who are already symptomatic with significant RHD, consideration should be given to interventional therapy (such as balloon valvotomy) or valve repair or replacement prior to pregnancy, to avoid severe morbidity or even mortality as a result of physiological changes of pregnancy on cardiac work. The cardiac changes of pregnancy can result in development of significant symptoms in particular in women with mild or moderate stenotic valvular lesions, multiple valvular lesions or pre-existing impairment of ventricular function. Percutaneous balloon mitral valvotomy (PBMV) may be considered in women with anything more than mild mitral stenosis (MS) prior to pregnancy as it can lead to long-lasting improvements in valvular disease that will prevent development of significant clinical deterioration during pregnancy. Reliable contraception is paramount to avoid unplanned pregnancy especially while more definitive treatment of valvular lesions is being undertaken.

The physiological changes of pregnancy mean that women with RHD are likely to be at increased risk of developing cardiac complications in pregnancy. Women with moderate and severe RHD are at risk of obstetric complications such as preterm delivery and fetal complications such as fetal growth restriction. Cardiac complications can be compounded if pregnancy disorders such as preeclampsia or obstetric haemorrhage develop. Women with significant consequential left atrial disease as a result of their RHD are at particular risk for developing tachyarrhythmia (in particular atrial fibrillation) which can further compromise effective cardiac work. The risk is lowest in women with mild regurgitant valvular lesions affecting single valves with a preserved cardiac function. Other pregnant women with RHD should be under the care of multidisciplinary team with an obstetrician, in collaboration with a cardiologist and/or obstetric physician. Women with severe RHD should be delivered at a referral centre, with onsite cardiology and intensive-care facilities. Discussions regarding the timing, nature and site of planned delivery should preferably occur before or early in course of pregnancy.

Additional risk factors include the need for therapeutic anticoagulation in women with mechanical prosthetic heart valves or those who develop atrial fibrillation.

**Clinical Management during Pregnancy**

Women should have serial cardiac evaluations, (frequency determined by the severity of disease and clinical symptoms). Women with severe disease may require cardiac evaluation every two to four weeks after 20 weeks’ gestation, especially if there is clinical deterioration. Consideration should be given to stopping work for medical reasons if women develop significant symptoms.

**Mitral/Aortic Regurgitation**

Pregnancy is well tolerated in the majority of women with mild or moderate mitral regurgitation (MR) or aortic regurgitation (AR) especially if they are single valve lesions. The increase in blood volume and cardiac output in pregnancy increases LV volume overload, but the decrease in systemic vascular resistance partly compensates for this. Some women with severe MR or AR may develop congestive heart failure, especially during the third trimester and may need diuretics and vasodilator therapy. Angiotensin receptor antagonists and ACE inhibitors are contraindicated in pregnancy. Calcium channel blockers (e.g. nifedipine) or nitrates can be used in pregnancy.

The mode of delivery should be determined by obstetric indications with vaginal delivery or assisted vaginal delivery (with vacuum extraction or forceps) being the goal in the majority of women who have stable cardiac symptoms. An early epidural may be helpful in minimising the sympathetic response to labour of tachycardia and raised blood pressure.

**Mitral Stenosis**

Mitral stenosis is a common valvular lesion in RHD and can pose particular problems during pregnancy and at delivery. In mitral stenosis the narrowed mitral valve limits flow across the valve during diastole which leads to reduced filling of the ventricle resulting in reduced stroke volume, cardiac output and aortic pressure. The tachycardia of pregnancy further shortens diastolic filling time exacerbating the impact of MS. The increase in blood volume during pregnancy also exacerbates the increases in left atrial pressure leading to pulmonary vascular hypertension and pulmonary oedema.
In patients with mild or moderate symptoms during pregnancy, therapy with beta-blockers to slow the heart rate and diuretics to reduce volume overload should be given.

The development of AF requires rapid rate control with the use of beta blockers (e.g. metoprolol) and digoxin. A higher dose of digoxin is usually required in pregnancy (e.g. 250mcg bd). Electrical cardioversion may be considered if medical treatment does not provide sufficient rate control but is often unsuccessful in women with an enlarged left atrium as a result of high left atrial pressures. Chemical cardioversion with amiodarone should be avoided in pregnancy as amiodarone crosses the placenta and affects the fetal thyroid.

In women who remain symptomatic despite medical therapy or where there is minimal improvement, there is significant risk to both mother and fetus peri-delivery, and surgical intervention for MS is usually required. PBMV, carried out by an experienced operator, may be considered in women with suitable valve characteristics, who do not have significant MR and major atrial thrombus. The timing of the procedure requires multidisciplinary team discussion. If the fetus is viable, steroids for fetal lung maturation should be given prior to the PBMV. The safety of this procedure in pregnancy has been well established in a number of patient series and can lead to durable improvements in MS. Complications of PBMV include cardiac tamponade and development of severe MR. These complications can be managed medically but urgent cardiac surgery with cardiopulmonary bypass may be required.

In the majority of women the mode of delivery should be determined by obstetric indications and vaginal delivery is favoured, with assisted delivery to minimize the duration and effort of the second stage. Placement of an early epidural will minimize the tachycardia and blood pressure increases of labour. Furosemide should be given in the second stage of labour to reduce the impact of the autotransfusion that occurs with delivery of the placenta. Active management of the third stage of labour is recommended to reduce the risk of postpartum haemorrhage. Fluctuations in blood volumes in the first 24-72 hours postpartum should be anticipated with careful clinical monitoring for deterioration in cardiac symptoms over this period.

Definitive indications for elective delivery by Caesarean section (CS) are difficult to determine but many clinicians are concerned when women have severe MS with severe pulmonary hypertension. The risks of bleeding are increased with CS but arguments are made that elective CS enables delivery during daylight hours with full access the clinical team required to care for the woman and baby, whereas the timing of vaginal delivery is unpredictable should complications arise. This clinical scenario requires careful multidisciplinary team discussion and discussion with the woman and her family. The ultimate decision will depend on a number of factors including the availability of resources and staff out-of-hours, the previous obstetric history of the woman and her wishes.

A contingency plan for emergency delivery should be drawn up for all women as pregnancy can be unpredictable and there are a number of obstetric complications that may require urgent delivery, such as antepartum haemorrhage, development of severe pre-eclampsia or fetal distress.

### Aortic Stenosis

Severe rheumatic AS in pregnancy is far less common than MS. Suspected AS should be accurately assessed by Doppler echocardiography. Women with mild AS can generally be managed medically during pregnancy with rate control using beta-blockers and diuretics to minimize volume overload. Women with moderate or severe AS, although much less common, are at significant risk of adverse maternal and fetal outcomes. Myocardial ischaemia may occur. Effective rate control and diuresis are paramount. Women with any degree of AS must be cared for by a multidisciplinary team consisting of an obstetrician and cardiologist and/or obstetric physician in an appropriate clinical centre (and potentially a neonatal team). Women with severely symptomatic AS should be considered for percutaneous balloon aortic valvuloplasty or valve replacement prior to pregnancy preferable.

### Prosthetic Heart Valves in Pregnancy

In the child-bearing age group, tissue valves have the major advantage of not requiring therapeutic dose anticoagulation, for patients in sinus rhythm. However, reoperation later in life is likely because of structural valve degeneration. The choice of valve prosthesis in the child-bearing age group requires careful judgment balancing need for reoperation against the hazards of therapeutic
anticoagulation in pregnancy in women with mechanical prostheses. Pregnancy does not appear to accelerate structural valve degeneration of bioprosthetic valves. Women with normally-functioning bioprosthetic valves generally tolerate the haemodynamic changes of pregnancy. Heart failure may develop, especially if left ventricular (LV) function is impaired. The treatment of symptomatic heart failure requires rate control with beta-blockers and diuresis. angiotensin-converting enzyme (ACE) inhibitors and angiotensin antagonists are contraindicated in pregnancy, and should be stopped once pregnancy is detected.

Mechanical Prosthetic Valves: Management of Anticoagulation Therapy

Women with mechanical prosthetic heart valves (MPHV) are a very high-risk group as they must continue therapeutic dose anticoagulation throughout pregnancy to prevent valve thrombosis and its sequelae of valve failure and systemic thromboembolism. All anticoagulation options carry maternal and/or fetal risks. Therefore; patients with mechanical prosthetic valves should be given appropriate contraceptive advice to avoid unplanned pregnancy, and counselled about the risks to mother and fetus of pregnancy (Grade D).

The choice of anticoagulant for pregnant women with MPHV remains a highly contentious issue. Oral anticoagulants or vitamin K antagonists may be the most effective agents at preventing valve thrombosis but readily cross the placenta and are associated with development of warfarin-specific embryopathy, fetal ocular and neurological abnormalities and also late fetal loss and stillbirth. Unfractionated heparin (UFH) and more recently low molecular weight heparin (LMWH) do not cross the placenta and have been demonstrated to be associated with better fetal outcomes. However they are less effective at preventing valve thrombosis and this may occur in as many as 10% of women, although the risk of thrombosis is lower in women who are compliant with twice daily dosing and regular monitoring of anti-Xa levels. A number of reviews have summarised maternal and fetal outcomes with various anticoagulant options.

Recommendations for Anticoagulation in Pregnancy for Patients with Mechanical Valves

No randomised comparative studies of different anticoagulant regimens have been performed. Options for anticoagulation include:

1. Substitution of warfarin with therapeutic dose enoxaparin (1mg/kg twice daily) before six weeks’ gestation, continued until planned delivery.
2. Substitution of warfarin with therapeutic dose enoxaparin (1mg/kg twice daily) from six until 12 weeks’ gestation, then reverting to warfarin. Enoxaparin (1mg/kg twice daily) re-introduced at 34–36 weeks’ gestation until planned delivery.
3. Warfarin throughout pregnancy, switching to therapeutic enoxaparin (1mg/kg twice daily) at 34–36 weeks’ gestation until planned delivery.

All of these options are associated with risk to both mother and baby and must be discussed with a specialist.

Monitoring of both trough and peak anti-Xa levels is recommended. The trough anti-Xa level should be taken immediately before a dose (target range 0.6–0.8 IU/ml) and peak anti-Xa level three to four hours after the dose (target range 1.0–1.2 IU/ml). Daily aspirin 100mg is recommended for women with MPHV. Aiming for a higher trough level may be particularly important for women with multiple valve replacements, older generation ball-and-cage (Starr-Edwards valves), and women with previous thromboembolic complications.
**Management of Delivery**
Planned delivery of women on therapeutic anticoagulation is necessary to reduce the risk of haemorrhage. The mode of delivery should be determined by obstetric indications. A recommended plan for anticoagulation in the peridelpvery period is detailed in Table 28.

**Table 28: A Recommended Plan for Anticoagulation in the Perideltivery Period**

<table>
<thead>
<tr>
<th>Pre-delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td>● 36 hours prior to planned caesarian section (CS) or induction of labour (IOL): Take last dose of enoxaparin</td>
</tr>
<tr>
<td>● 24 hours prior to planned CS or IOL (when the next dose enoxaparin would have been due): Admit for intravenous (IV) Unfractionated heparin (UFH)</td>
</tr>
</tbody>
</table>

**Protocol For IV Unfractionated Heparin**
- Take baseline Activated Partial Thromboplastin Time (APTT) when IV line placed
- Bolus dose 5000 IU then infusion 1250 IU/hour
- Check APTT 6 hours later
- Adjust infusion rate to keep APTT 2-3 x baseline (or if using anti-Xa levels, target 0.4-0.7 anti-Xa units/ml)
- If dose adjusted recheck 6 hours later, otherwise check every 24 hours
- If planned elective CS:
  - Stop IV UFH 6 hours before
  - Check APTT 3-4 hours later (to ensure it has returned to normal prior to placement of epidural catheter for regional anaesthesia)
- If planned IOL: stop IV UFH once in established labour

**Postpartum Restarting IV Unfractionated Heparin**
- Uncomplicated vaginal delivery: restart IV UFH 4-6 hours post-delivery
- Caesarean section: restart IV UFH 6-10 hours post-delivery
  In any concerns re bleeding, discuss the time of restarting anticoagulation with obstetric and medical team looking after patient.

**Protocol For IV Unfractionated Heparin**
- First 6 hours: IV UFH 500 IU/hour
- Second 6 hours: increase IV UFH to 1000 IU/hour
- After this, measure APTT and adjust IV UFH dose aiming for APTT 2-3 x baseline. Ensure APTT result available within 1-2 hours (if using anti-Xa levels, target range 0.4-0.7 anti-Xa units/ml)
- Restart daily warfarin on Day 2 postpartum: 1st dose 10mg, 2nd dose 5mg
- Check INR daily. The 3rd dose as per INR
- Continue IV UFH until INR >2
  There is a high risk of bleeding in women who are anticoagulated postpartum. Close clinical observation and a high index of suspicion are required. In the event of bleeding, anticoagulation should be stopped or the dose modified under the guidance of a haematologist or obstetric physician.

All women on therapeutic dose anticoagulation should have anaesthetic review to discuss and advise on options and timing of regional anaesthesia/analgesia.

Breastfeeding is safe in women taking either heparin or warfarin.
Table 29: Key Points in the Management of Pregnancy in Women with RHD

<table>
<thead>
<tr>
<th>Predictors of Increased Maternal and Fetal Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>● Cardiac symptoms before pregnancy</td>
</tr>
<tr>
<td>● Stenotic valvular lesions</td>
</tr>
<tr>
<td>● Multiple valvular lesions</td>
</tr>
<tr>
<td>● Moderate or severe pulmonary hypertension</td>
</tr>
<tr>
<td>● Mechanical prosthetic heart valve(s)</td>
</tr>
<tr>
<td>● Atrial fibrillation requiring warfarin</td>
</tr>
<tr>
<td>● Left ventricular impairment</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cardiac Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>● Early comprehensive assessment with echocardiography to assess valves and LV function</td>
</tr>
<tr>
<td>● Plan multidisciplinary management</td>
</tr>
<tr>
<td>● Women with rheumatic valvular disease must be reviewed by cardiologist and/or obstetric physician during pregnancy</td>
</tr>
<tr>
<td>● The majority of women with RHD will require ongoing assessment during pregnancy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mitral/Aortic Regurgitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>● Usually well tolerated</td>
</tr>
<tr>
<td>● Treat medically with diuretics,</td>
</tr>
<tr>
<td>vasodilators (no ACE inhibitors/angiotensin II receptor blockers) for clinical</td>
</tr>
<tr>
<td>heart failure</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mitral Stenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>● Mild to moderate mitral stenosis: manage medically moderate to severe mitral stenosis</td>
</tr>
<tr>
<td>● (MVA &lt; 1.5 cm²) - consider PBMV during late second trimester, if patient remains symptomatic and PAS pressure &gt;50 mmHg</td>
</tr>
<tr>
<td>● Beta-blockers or digoxin for rate control of atrial fibrillation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Aortic Stenosis (Rare)</th>
</tr>
</thead>
<tbody>
<tr>
<td>● Mild aortic stenosis: usually well-tolerated.</td>
</tr>
<tr>
<td>● Beta-blockers for rate control.</td>
</tr>
<tr>
<td>● Diuretics to prevent volume overload</td>
</tr>
<tr>
<td>● Consider PTAV if severe symptoms</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mechanical/Prosthetic Valves and Anticoagulation in Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>● Very high maternal and fetal risk</td>
</tr>
<tr>
<td>● Risk of warfarin embryopathy in first trimester</td>
</tr>
<tr>
<td>● Risk of adverse outcome with any anticoagulant approach:</td>
</tr>
<tr>
<td>● Warfarin: most effective at preventing maternal thromboembolic complications. High rate of fetal complications</td>
</tr>
<tr>
<td>● Therapeutic dose adjusted LMWH: less effective at preventing maternal thromboembolic complications, improved fetal outcomes</td>
</tr>
</tbody>
</table>

Source: Adapted from Table 5.11 in RHDAustralia (ARF/RHD writing group) et al. Australian guideline for prevention, diagnosis and management of acute rheumatic fever and rheumatic heart disease (2nd edition). 2012 © by permission of RHDAustralia.⁵

ACE=angiotensin-converting enzyme; anti-Xa=antifactor Xa; INR=international normalised ratio; LMWH=low molecular weight heparin; LV=left ventricle; MVA=mitral valve area; PAS=pulmonary artery systolic; PBMV=percutaneous balloon mitral valvuloplasty; PTAV=percutaneous transluminal aortic valvuloplasty; UFH=unfractionated heparin.

Anticoagulation

Warfarin a vitamin K antagonist, is the drug of choice for anticoagulation for patients with prosthetic heart valves, for both RHD and non-rheumatic valve disease. As the absorption of warfarin is affected by diet the international normalised ratio (INR) must be measured on a regular basis with adjustments of the dose as required.
The usual recommended INR ranges are:

- Prosthetic mitral valves 2.5 - 3.5
- Prosthetic aortic valves 2.0 - 3.0
- Mitral and aortic prosthetic valves 2.5 - 4.0

The cardiologist of the patient should specify the INR range on an individual basis.

Titrating the warfarin dose can be difficult even with easy access to INR monitoring. Inadequate INR monitoring with low levels predisposes to valve thrombosis, thromboembolism and strokes. High INRs can lead to spontaneous bleeding with a risk of strokes. The patient should be encouraged to be active in their INR control, ideally holding their own INR card, the warfarin dosage and the date of their next test. Home INR testing kits have been used for the paediatric rheumatic (and congenital heart) children and their families.\textsuperscript{230}

There are current studies designed to study the safety of the On-X\textsuperscript{®} valve in the aortic position without warfarin.\textsuperscript{231}

Newer anticoagulants have been developed that dose-dependently inhibit thrombin or activated factorX offering potential advantages over vitamin K antagonists, such as rapid onset and offset of action. These include dabigatran, rivaroxaban and apixaban. Dabigatran is licensed in New Zealand for anticoagulation for individuals with atrial fibrillation to prevent thromboembolism. The advantage for patients is that INR levels do not need to be monitored. They have been proven to be as safe and effective as warfarin for prevention of stroke and systemic embolism in patients with atrial fibrillation.\textsuperscript{232}

However the efficacy and safety of these newer agents are still being studied in patients with prosthetic valves. Currently they are not recommended for anticoagulation for prosthetic heart valves. There are many causes of atrial fibrillation and it is more frequent with increasing age: its onset in an individual with a past history of ARF and mild RHD may not be related to the RHD. In such individuals dabigatran could be considered for anticoagulation.

**Prevention of Infective Endocarditis**

Persons with established RHD or prosthetic valves should receive antibiotic prophylaxis prior to procedures expected to produce bacteraemia. Individuals with a history of ARF but no valvular damage do not require antibiotic prophylaxis. Those already receiving penicillin for secondary prophylaxis should be offered a different antibiotic for prophylaxis of endocarditis.

Recommendations for the procedures that require endocarditis prophylaxis and the appropriate antibiotics can be found on the Heart Foundation of New Zealand website (http://www.heartfoundation.org.nz).\textsuperscript{148} Some of these recommendations are also outlined on a wallet card to be carried by cases (Appendix D). See page 48 for details on antibacterial prophylaxis for dental procedures.

**Indications for Cardiac Surgery**

In general it is only those with severe valve lesions that will need cardiac surgery.

Recommendations for cardiac surgery for adults are abridged from the AHA/ACC guidelines based on all relevant data internationally.\textsuperscript{233} There is much less data upon which to base surgical decision making in the young. The experience and outcomes from the Greenlane and Starship Hospitals forms the basis for recommendations in those under 20 years of age.\textsuperscript{78,132,234,235,236,237}
**Mitral Regurgitation in Adults**

Referral for cardiac surgery is indicated in adults with mitral regurgitation, as detailed in Table 30.

**Table 30: Indications for Referral for Cardiac Surgery in Adults with Mitral Regurgitation**

| A. Severe MR with symptoms (NYHA class 2-4); or |
| B. Asymptomatic MR and one of the following: |
|   • LVESD ≥40mm in adults |
|   • Impaired LV function LVEF <60% |
|   • Pulmonary hypertension >50mmHg |
|   • New onset atrial fibrillation |
|   • If the valve is judged to have a high chance of repair, surgery can be recommended with moderate to severe MR with normal LV size and function |

Mitral valve repair is the operation of choice for MR because of lower mortality and morbidity. In adults mitral valve repair has a higher reoperation rate than replacement. Most patients (if asked) would presumably prefer to be alive with a need for a second operation than dead or suffering the effects of thromboembolism with a prosthetic valve.

If the mitral valve is not suitable for repair, the option is valve replacement with either a mechanical valve prosthesis or a bioprosthetic valve.

If a rheumatic mitral valve is not repairable, women in the childbearing age planning a pregnancy should be offered a bioprosthetic valve rather than a prosthetic valve even though the reoperation rate will be higher. The risk of warfarin to the fetus or risk to the patient on heparin type regimens remain high (see also section on pregnancy and childbirth).

New Zealand data shows that for those under 20 years of age the re-operation rate for mitral valve repair is the same as for mitral valve replacement so mitral valve repair should always be aimed for if technically feasible.

**Mitral Regurgitation in Children**

Referral for cardiac surgery is indicated in children with mitral regurgitation, as detailed in Table 31.

**Table 31: Indications for Referral for Cardiac Surgery in Children with Mitral Regurgitation**

| A. Severe MR with symptoms of breathlessness; or |
| B. Asymptomatic MR and one of the following: |
|   • Impaired LV function <60% |
|   • LVESV z-score >2 |
|   • Pulmonary hypertension >50mmHg |

**Mitral Stenosis in Adults and Children**

Referral for cardiac surgery is indicated in adults and children with mitral stenosis, as detailed in Table 32.

**Table 32: Indications for Referral for Cardiac Surgery or Balloon Valvuloplasty**

| A. Severe Mitral Stenosis with symptoms (NYHA class 2-4); or |
| B. Asymptomatic severe Mitral Stenosis and one of the following: |
|   • Paroxysmal atrial fibrillation |
|   • Mitral valve area <1.5cm2 |
|   • Pulmonary hypertension >50mmHg |
|   • Thromboembolism |

An exercise test can help define if ‘asymptomatic’ patients do in fact have restricted capacity.
Consider early referral in younger patients as they have the better chance of successful mitral valvuloplasty.

**Aortic Regurgitation in Adults**

Referral for cardiac surgery or valvuloplasty is indicated in adults with aortic regurgitation, as detailed in Table 33.

<table>
<thead>
<tr>
<th>Table 33: Indications for Referral for Cardiac Surgery in Adults with Aortic Regurgitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Severe AR with symptoms NYHA class 2-4; or</td>
</tr>
<tr>
<td>B. Asymptomatic severe AR and one of the following:</td>
</tr>
<tr>
<td>● LVESD $\geq$50 mm (55 mm in AHA/ACC guidelines prior to 2014)</td>
</tr>
<tr>
<td>● Impaired LV function LVEF &lt; 50%</td>
</tr>
<tr>
<td>● LVEDD $&gt;$65 mm (70 mm in AHA/ACC guidelines prior to 2014)</td>
</tr>
</tbody>
</table>

**Aortic Regurgitation in Children**

Referral for cardiac surgery or valvuloplasty is indicated in children with aortic regurgitation, as detailed in Table 34.

<table>
<thead>
<tr>
<th>Table 34: Indications for Referral for Cardiac Surgery in Children with Aortic Regurgitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Severe AR with symptoms and breathlessness; or</td>
</tr>
<tr>
<td>B. Asymptomatic severe AR and one of the following:</td>
</tr>
<tr>
<td>● LVESV z-score &gt;4</td>
</tr>
<tr>
<td>● Impaired LV function LVEF &lt;50%</td>
</tr>
</tbody>
</table>

**Mitral and Aortic Regurgitation in Children**

New Zealand data shows that combined severe MR and severe AR is the most deleterious to long term ventricular function and such patients should be considered early for surgery.\(^{234}\)

**Case Finding and Surveillance**

**Surveillance**

Passive surveillance of ARF usually depends on case identification from health care providers. In New Zealand, ARF and recurrent ARF are notifiable conditions.\(^{26}\) In New Zealand reporting of ARF cases to ensure free nurse led secondary prophylaxis (along with health care worker education) has led to an efficient prophylaxis service and reasonable epidemiological data for ongoing planning and evaluation of service delivery in many centres.\(^{26,30}\) Historically internationally however, reliance on notification has under-estimated the burden of disease due to inaccuracies and incompleteness.\(^{241}\) In under-resourced settings, the deficiencies of passive surveillance are exacerbated by high turnover of hospital and primary care staff and lack of awareness of ARF by many health care providers.

Ideally, regular audits i.e. active surveillance using all available sources should be used to augment passive surveillance (Grade D).\(^{242}\) This entails establishing mechanisms to identify new cases of ARF and to update information about existing cases. This could include:

- Mechanisms allowing access to hospital coding data
- Echocardiography reports
- Specialist review correspondence
- Primary health care information.

Where possible, these processes should be automated (including regular downloads of information regarding cases admitted to hospital with a diagnosis of ARF). This would have to be compliant with
the Health Information Privacy Code 1994.243 This is happening in most areas of the North Island where ARF is prevalent and builds on a process started in the 1980’s.39,190,196,244,245,246

RHD (in the absence of acute features) is not a notifiable condition; relying only on ARF notification does not identify a number of Māori and Pacific people with RHD. It is known that there are 600-800 admission with RHD and 150-200 deaths per year.247,248 Such data is based on discharge classification which will have variable accuracy. Until population-based epidemiological studies of RHD are performed in New Zealand, the extent of morbidity of RHD will remain unknown. Furthermore, there is great potential for RHD notification to improve outcomes for people with RHD because, unlike for most notifiable diseases, there is a simple, cheap and proven intervention; secondary prophylaxis.

**Suggested Indicators for Evaluation**

Control programmes for ARF/RHD should be evaluated on criteria for routine care and key epidemiological objectives. These include measurement of individual and community adherence to secondary prophylaxis, indicators of satisfactory care specified in best practice guidelines and rates of disease occurrence, recurrence and mortality.

Further consideration should be given to:

- Assessing the delivery of specialist cardiology services
- Availability and accessibility of echocardiography
- Referral practices and structures
- Transportation for cases
- Support structures and appropriate follow-up processes.

As has been highlighted throughout the developing world, the availability of and support for routine health care is essential to controlling ARF/RHD. Indicators used to evaluate ARF/RHD control programmes should be relevant, structured, measurable, routinely available and affordable. In particular, they should not overburden health care providers and should lead to improved clinical results. A list of suggested indicators is provided in Table 35 (Grade D).

**Table 35: Proposed Indicators for Evaluating ARF/RHD Control Programmes**

<table>
<thead>
<tr>
<th>Secondary Prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>• The proportion of scheduled benzathine penicillin injections delivered in the recommended time period</td>
</tr>
<tr>
<td>• Individual, community and regional figures, expressed as:</td>
</tr>
<tr>
<td>• Median percentage of doses delivered</td>
</tr>
<tr>
<td>• Proportion who receive 80% or less of scheduled doses</td>
</tr>
<tr>
<td>• Proportion who receive 50% or less of scheduled doses</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Medical Review</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Proportion of registered individuals who are more than 3 months overdue for specialist or other medical review, as defined by local guidelines</td>
</tr>
<tr>
<td>• Proportion of individuals who have echocardiography performed within 3 months of scheduled timing</td>
</tr>
<tr>
<td>• Median time elapsed between recommendation and performance of valvular surgery</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Epidemiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Yearly (or other appropriate time frame) age-specific incidence rates of ARF</td>
</tr>
<tr>
<td>• Proportion of ARF episodes in the register classified as recurrences</td>
</tr>
<tr>
<td>• Rates of ARF recurrence per 100 patient-years</td>
</tr>
<tr>
<td>• Number of deaths and age-standardised rates of mortality due to ARF/RHD in the previous 12 months (or other appropriate time frame)</td>
</tr>
<tr>
<td>• Yearly age-specific and overall point prevalence of RHD</td>
</tr>
<tr>
<td>• Proportion of ARF cases notified to and recorded by public health authorities in the previous 12 months (or other appropriate time frame)</td>
</tr>
<tr>
<td>• Proportion of newly registered individuals with an initial diagnosis being established of RHD (rather than ARF).</td>
</tr>
</tbody>
</table>
Screening for Rheumatic Heart Disease

Early activities in New Zealand in the control of ARF and RHD, at the time of the first Rheumatic Fever Working Party reflected the directions of current WHO directions. The first epidemiological surveys led to the establishment of a prophylaxis programme in the Gisborne area. It was considered at the time that with a reasonable primary and secondary health care system that RHD prevalence did not require a specific survey and ARF with reasonable practitioner awareness would be detected and referred for hospital evaluation. Thus, from hospital inpatient and outpatient records registers were set up where required.

ARF and RHD fell off the WHO agenda after the 1990’s but with a new tool, echocardiography, interest has resurfaced.

The WHO now recommends school-based screening for RHD as a tool for estimating the disease burden, and also for identifying cases in areas with a high prevalence of RHD. WHO Global Programme on RHD undertook auscultatory screening of over one million children. In some regions, this was augmented by echocardiography to confirm the diagnosis of RHD. The sensitivity of cardiac auscultation is highly dependent on the skill of the operator, and the specificity of auscultation for rheumatic carditis is low.

Since the original New Zealand Rheumatic Fever guidelines in 2006 there has been considerable study in New Zealand and internationally of the use of echocardiographic screening for RHD. It has been established that:

- Echocardiography is more accurate than auscultation for screening.
- By using portable echocardiography it is feasible to screen for RHD in school based programmes.
- Echocardiography is acceptable to populations at risk.
- The WHO and WHO-NIH criteria resulted in over-diagnosis of RHD.
- An international group of researchers (led from New Zealand and Australia) achieved standardisation of criteria for the minimal diagnosis of RHD (endorsed and published as the WHF guidelines 2012) using the best available evidence (echocardiographic, surgical and pathological descriptions of what does or does not constitute RHD).

However the natural history of echocardiographically detected RHD is unknown i.e. it is not known whether the finding of mild RHD detected by echocardiography carries the same risk of progression of RHD following a typical cases of ARF. For the latter there is 25-75% chance of ARF recurrence and secondary prophylaxis is justified. Milder valve lesions, which are often asymptomatic and thus the most common lesions that have been detected with screening, are more likely to resolve in those who adhere to secondary prophylaxis than more severe.

Currently in New Zealand it is recommended that those with ‘borderline RHD’ be followed and those with ‘definite RHD’ be started on secondary prophylaxis. (Grade D) As secondary compliance is low in almost every country outside New Zealand, an RCT of penicillin versus no penicillin is impractical. International collaboration has led to a registry of outcomes for those with echocardiographically detected RHD which has the best chance of defining the natural history.

New Zealand criteria for assessing screening programmes are as follows (Table 36):

Table 36: Recommended Elements of a Screening Programme in New Zealand

- The condition is a suitable candidate for screening. The condition should be an important health problem from both an individual and a community perspective. The epidemiology and natural history of the condition, including development from latent to declared disease, should be adequately understood and there should be a detectable risk factor or disease marker and a latent period or pre-symptomatic stage.
- There is a suitable test: safe, simple, reliable, accurate, sensitive, and specific.
- There is an effective and accessible treatment or intervention for the condition identified through early detection. There should be evidence that early treatment leads to better outcomes than late treatment.
- There is high quality evidence, ideally from randomised controlled trials, that a screening programme is effective in reducing mortality or morbidity.
- The potential benefit from the screening programme should outweigh the potential physical and psychological harm (caused by the test, diagnostic procedures and treatment).
- The health care system will be capable of supporting all necessary elements of the screening pathway, including diagnosis, follow-up and programme evaluation.
There is consideration of social and ethical issues. There should be evidence that the complete screening programme (identification and invitation, test, diagnostic procedures and treatment/intervention) is clinically, socially and ethically understood and acceptable to health professionals and the wider public.

There is consideration of cost-benefit issues.

When considering and evaluating a prospective screening programme, it is important to consider the direct benefit to participants and any public good benefits that may result.

Screening programmes need to specifically consider and respond to Māori, if they are to ensure participation by Māori, which is crucial to reducing inequalities in morbidity and mortality in New Zealand.

Source: National Advisory Committee on Health and Disability (2003)

In the Māori and Pacific populations in New Zealand, RHD fulfils some of these properties:

- RHD is an important health problem in these populations, with significant mortality, morbidity, social and economic burden. The natural history of RHD following ARF is well understood (thanks to classic studies of the 20th Century), with a latent or early symptomatic stage.
- Good adherence to secondary prophylaxis prevents the development or worsening of RHD and leads to disease resolution in many cases.

In New Zealand screening for RHD would have to target high-risk populations in order to improve the pre-test probability. (Grade D).

In the meantime individuals continue to be diagnosed by echocardiography following a number of clinical scenarios: evaluation of a cardiac murmur, history suggestive of ARF in the past, chance finding on echocardiography for other indications etc. The WHF guidelines can be used for diagnosis of RHD in these situations (Tables 37,38,39,40).

**Table 37: 2012 WHF Criteria for Echocardiographic Diagnosis of RHD**

<table>
<thead>
<tr>
<th>Definite RHD (either A, B, C or D):</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Pathological MR and at least two morphological features of RHD of the MV</td>
</tr>
<tr>
<td>B. MS mean gradient ≥4 mmHg*</td>
</tr>
<tr>
<td>C. Pathological AR and at least two morphological features of RHD of the AV†</td>
</tr>
<tr>
<td>D. Borderline disease of both the AV and MV‡</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Borderline RHD (either A, B or C):</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. At least two morphological features of RHD of the MV without pathological MR or MS</td>
</tr>
<tr>
<td>B. Pathological MR</td>
</tr>
<tr>
<td>C. Pathological AR</td>
</tr>
</tbody>
</table>

**Echocardiographic Criteria for Individuals Aged ≤20 Years**

<table>
<thead>
<tr>
<th>Definite RHD (either A, B, C or D):</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Pathological MR and at least two morphological features of RHD of the MV</td>
</tr>
<tr>
<td>B. MS mean gradient ≥4 mmHg*</td>
</tr>
<tr>
<td>C. Pathological AR and at least two morphological features of RHD of the AV, only in individuals aged &lt;35 years†</td>
</tr>
<tr>
<td>D. Pathological AR and at least two morphological features of RHD of the MV</td>
</tr>
</tbody>
</table>

**Abbreviations:** AR, aortic regurgitation; AV, aortic valve; MR, mitral regurgitation; MS, mitral stenosis; MV, mitral valve; RHD, rheumatic heart disease; WHF, World Heart Federation.

*Congenital MV anomalies must be excluded. Furthermore, inflow obstruction due to non-rheumatic mitral annular calcification must be excluded in adults.*
† Bicuspid AV, dilated aortic root, and hypertension must be excluded.
‡ Combined AR and MR in high prevalence regions and in the absence of congenital heart disease is regarded as rheumatic.

Table 38: WHF Criteria for Pathological Regurgitation

<table>
<thead>
<tr>
<th>Pathological Mitral Regurgitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>(All four Doppler echocardiographic criteria must be met)</td>
</tr>
<tr>
<td>• Seen in two views</td>
</tr>
<tr>
<td>• In at least one view, jet length ≥2 cm*</td>
</tr>
<tr>
<td>• Velocity ≥3 m/s for one complete envelope</td>
</tr>
<tr>
<td>• Pan-systolic jet in at least one envelope</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pathological Aortic Regurgitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>(All four Doppler echocardiographic criteria must be met)</td>
</tr>
<tr>
<td>• Seen in two views</td>
</tr>
<tr>
<td>• In at least one view, jet length ≥1 cm*</td>
</tr>
<tr>
<td>• Velocity ≥3 m/s in early diastole</td>
</tr>
<tr>
<td>• Pan-systolic jet in at least one envelope</td>
</tr>
</tbody>
</table>

* A regurgitant jet length should be measured from the vena contracta to the last pixel of regurgitant colour (blue or red).

Table 39: WHF Criteria for Morphological Features of RHD

<table>
<thead>
<tr>
<th>Features in the Mitral Valve</th>
</tr>
</thead>
<tbody>
<tr>
<td>• AMVL thickening* ≥3 mm (age-specific) †</td>
</tr>
<tr>
<td>• Chordal thickening</td>
</tr>
<tr>
<td>• Restricted leaflet motion‡</td>
</tr>
<tr>
<td>• Excessive leaflet tip motion during systole§</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Features in the Aortic Valve</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Irregular or focal thickening III</td>
</tr>
<tr>
<td>• Coaptation defect</td>
</tr>
<tr>
<td>• Restricted leaflet motion</td>
</tr>
<tr>
<td>• Prolapse</td>
</tr>
</tbody>
</table>

AMVL = anterior mitral valve leaflet

Important considerations
* AMVL thickness should be measured during diastole at full excursion. Measurement should be taken at the thickest portion of the leaflet, including focal thickening, beading, and nodularity. Measurement should be performed on a frame with maximal separation of chordae from the leaflet tissue. Valve thickness can only be assessed if the images were acquired at optimal gain settings without harmonics and with a frequency ≥2.0 MHz.
† Abnormal thickening of the AMVL is age-specific and defined as follows: ≥3 mm for individuals aged ≤20 years; ≥4 mm for individuals aged 21-40 years; ≥5 mm for individuals aged >40 years. Valve thickness measurements obtained using harmonic imaging should be cautiously interpreted and a thickness up to 4 mm should be considered normal in those aged ≤20 years.
‡ Restricted leaflet motion of either the anterior or the posterior MV leaflet is usually the result of chordal shortening or fusion, commissural fusion, or leaflet thickening.
§ Excessive leaflet tip motion is the result of elongation of the primary chords, and is defined as displacement of the tip or edge of an involved leaflet towards the left atrium resulting in abnormal coaptation and regurgitation. Excessive leaflet tip motion does not need to meet the standard echocardiographic definition of MV prolapse disease, as that refers to a different disease process. This feature applies to only those aged <35 years. In the presence of a flail MV leaflet in the young (≤20 years), this single morphological feature is sufficient to meet the morphological criteria for RHD (that is, where the criteria state “at least two morphological features of RHD of the MV” a flail leaflet in a person aged ≤20 years is sufficient).
In the parasternal short axis view, the right and noncoronary aortic cusp closure line often appears echogenic (thickened) in healthy individuals and this should be considered as normal.

Table 40: Echocardiography Machine Settings

- Nyquist limits for color-Doppler echocardiography should be set on maximum to avoid overestimation of jet length
- Images for assessment of valvular and chordal thickness should be acquired with harmonics turned off and probes with variable frequency set on ≥2.0 MHz; low frequency settings and harmonics exaggerate valve and chordal thickness
- Gain settings should be adjusted to achieve optimal resolution; images acquired with an excessive gain setting will not be suitable for objective valve thickness measurements
- All other settings (including depth, sector size, and focus) should also be optimized to achieve maximal frame rate (ideally 30–60 frames per second) and resolution
Guideline Implementation

There are a number of driving forces that will assist the implementation of this guideline. There is a need for standardisation of the diagnosis of ARF in order to minimise over- and under-diagnosis and ensure that the high-risk populations receive appropriate care. There is also demand for effective and cost effective management and avoidance of ARF recurrence and subsequent disabling RHD. Restraining forces that have the potential to hinder the implementation of this guideline include: reduced access of cases to diagnostic tests and specialist services, limited resources available, reluctance of practitioners to change current practice, incomplete understanding of ARF amongst primary and secondary care professionals and inconsistent access to certain treatments including benzathine penicillin.

Suggested Implementation Strategies Include:

Streamlined Processes for the Diagnosis, Management and Prevention of ARF
- Ensure awareness of paediatric and adult services of the need to diagnose correctly ARF/RHD and refer for prophylaxis
- Consistent New Zealand standards for ARF diagnosis
- Consistent standards for streptococcal serology methodology, reporting and assay between laboratories.

Provision of Streamlined Specialist Services
- Where possible, regions have the opportunity for regular specialist rheumatic fever clinics (potentially involving both paediatric and medical input, in close association with available cardiology services). These should coordinate with rheumatic fever registers, the community services involved in benzathine penicillin delivery and with primary care providers (particularly Māori and Pacific). This has the potential for reducing cases that are lost to follow-up and to secondary prophylaxis and therefore reduce rheumatic fever recurrence, hospitalisations and RHD.

Ensure Funding for Training
- Maintain echocardiography standards for ARF and training of echo technicians in all main centres of ARF prevalence.

Education
- Professional education targeting both primary and secondary care providers, doctors, nurses, dentists, pharmacy, medical and nursing students
- Increased understanding in primary care of early management, and the need for hospitalisation in ARF.

Community Awareness and Health Promotion
- Raise awareness, especially in families and communities at high risk, of the “sore throats do matter” message and of the signs and symptoms of ARF.

Ensure Regular Supply of Benzathine Penicillin
- The supply of benzathine penicillin has been inconsistent, with occasional periods where no benzathine penicillin was available. These guidelines provide the evidence for the need for PHARMAC to ensure an uninterrupted supply of benzathine penicillin, including the possibility of having an alternative supplier.
- Discussions with hospitals pharmacies on storing back-up supplies of benzathine penicillin could ensure a contingency plan should supplies run out.

Resource and Support for a Local ARF Register in Each Area
- Professional leadership
- Adequate administrative support.
Case Follow-up

- Because a number of ARF cases (particularly in Auckland) involve Pacific people, there is opportunity for greater links to be forged between New Zealand and the Pacific Islands. Key contacts on each Pacific Island need to be identified. They should be able to access information on New Zealand registers and provide reciprocal information to the New Zealand registers. This will improve the continuity of prophylaxis therapy and care for cases that travel between these countries.

- In addition, there should be continued support for the outreach capacity of primary care providers in order to reduce the number of cases that are non-compliant or do not present for prophylaxis.

Dissemination of Guidelines

It is hoped that this guideline will be used widely. The following are suggestions for dissemination of this guideline:

- The Heart Foundation of New Zealand through printed resources, including this guideline and web-based information
- The Cardiac Society of Australia and New Zealand (CSANZ)
- District Health Boards
- Dissemination by members of the writing group, reviewers and contributors
- Production and distribution of an additional resource consisting of the algorithms from this and future guidelines
- Published articles
- Health promotion initiatives and discussion of this guideline in regions of relatively high prevalence of ARF
- Update of healthcare pathways in general practice (where these are available).
Algorithm 1: Guide for the use of echocardiography in acute rheumatic fever (ARF)

Any person with suspected ARF including cases of chorea, should have an echocardiogram shortly after admission to hospital.

- **Equivocal**
- **Normal**
  - Repeat at 2-4 weeks
  - Pursue alternative diagnoses for mono/polyarthritis
    - Notes 3 & 4
- **Abnormal**
  - Notes 1 & 2
  - **Second echocardiogram** at 2-4 weeks if no other alternative diagnosis. A second echo is usually unnecessary with a presentation of chorea.
    - Normal
    - Abnormal
      - Notes 1 & 2
  - **Second echocardiogram** at 4-6 weeks if:
    - Signs progress
    - Medication commenced
    - Recommended by cardiologist

Footnote:

* The diagnosis of ARF can still be made in the absence of abnormal echo change.
**Note 1**

Minimal Echocardiographic Criteria to Allow a Diagnosis of Pathological Valvular Regurgitation

### Mitral Regurgitation
- Seen in 2 views
- In at least 1 view jet length >2cm
- Peak velocity > 3m/sec
- Pan-systolic jet in at least one envelope

### Aortic Regurgitation
- Seen in 2 views
- In at least one view jet length >1cm
- Peak velocity >3m/sec
- Pan-diastolic jet in at least one envelope

These criteria can usually readily distinguish a small colour jet of physiological regurgitation in a normal child from pathological regurgitation in a child with ARF or RHD. The proportion of children with physiological valve regurgitation in a New Zealand population was 15% and this proportion increases in later decades. 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 excessive leaflet motion of the tip of anterior mitral valve leaflet (often referred to as prolapse) is the commonest mechanism of mitral regurgitation. Anterior leaflet prolapse is more common than posterior valve prolapse
- Multiple jets of mitral regurgitation
- The presence of morphological or anatomical changes consistent with chronic RHD are:
  - Excessive leaflet motion of the tips of the AMVL or PMVL
  - Restrictive leaflet motion (including subchordal thickening)
  - Definite thickening of anterior mitral valve leaflets > 3mm
  - Mitral stenosis with a mean valve gradient > 4mmHg

These features of RHD take time to develop but may be present in ARF on presentation indicating an acute on chronic presentation.

**Source:** Adapted with permission from Wilson, N.J. & Neutze, J.M. 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 and subsequently the 2014 WHF guidelines.

* 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 occurs in the first weeks of acute rheumatic carditis (Level IV)

† 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. Although none of these morphological features is unique to ARF, the experienced echocardiographic operator can use their presence as supportive evidence of a rheumatic aetiology of valvulitis

‡ It is recommended that descriptive terms such as ‘elbow’ or ‘dog leg’ or ‘hockey stick’ deformity of anterior mitral valve leaflet be avoided: such appearances are due to the combination of valve thickening and restrictive valve motion.
## Note 2

### Severity of ARF Carditis

#### Mild Carditis*
- Mild mitral or aortic regurgitation clinically and/or on echocardiography (fulfilling the minimal echocardiographic standards in Note 1) without heart failure, without cardiac chamber enlargement on CXR, ECG or echocardiography

#### Moderate Carditis
- Any valve lesion of moderate severity on clinical examination or
- Cardiac chamber enlargement seen on echocardiogram or
- Any valve lesion graded as moderate on echocardiogram†
  - Regurgitation is considered moderate if there is a broad high-intensity proximal jet filling half the left atrium i.e. Mitral or a lesser volume high-intensity jet producing prominent blunting of pulmonary venous inflow
  - 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

#### Severe Carditis
- Any impending or previous cardiac surgery for RHD, or
- Any valve lesion associated with significant cardiomegaly or heart failure, or graded as severe on clinical examination
- Any valve lesion graded as severe on echocardiogram:
  - An abnormal regurgitant colour and Doppler flow patterns in pulmonary veins is a prerequisite for severe mitral regurgitation in children
  - Doppler reversal in lower descending aorta is required for the diagnosis of severe aortic regurgitation in children
  - In adults, Doppler flow reversal in the pulmonary veins (for severe MR) or abdominal aorta (for severe AR) is specific if present, but can be more difficult to detect; their absence does not exclude severe regurgitation if not detected.

* 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

† 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.
### Differential Diagnoses of Common Major Manifestations of ARF

ARF is still an uncommon condition and all potential cases should be discussed with an expert to aid diagnosis and management.

#### Presentation

<table>
<thead>
<tr>
<th><strong>Polyarthritis and fever</strong></th>
<th><strong>Carditis</strong></th>
<th><strong>Chorea</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Other infections* (including gonococcal)</td>
<td>• Innocent murmur</td>
<td>• Systemic lupus erythematosus†</td>
</tr>
<tr>
<td>• Connective tissue and other auto-immune disease†</td>
<td>• Mitral valve prolapse</td>
<td>• Drug ingestion (extrapyramidal syndrome)§</td>
</tr>
<tr>
<td>• Reactive arthropathy</td>
<td>• Congenital heart disease</td>
<td>• Wilson’s disease (usually adult onset)</td>
</tr>
<tr>
<td>• Sickle cell anaemia</td>
<td>• Infective endocarditis</td>
<td>• Tic disorder (see guideline)</td>
</tr>
<tr>
<td>• Infective endocarditis</td>
<td>• Hypertrophic cardiomyopathy</td>
<td>• Congenital, e.g. hyperbilirubinaemia</td>
</tr>
<tr>
<td>• Leukaemia or lymphoma</td>
<td>• Myocarditis - viral or idiopathic</td>
<td>• Choreoathetoid cerebral palsy</td>
</tr>
<tr>
<td>• Gout and pseudogout</td>
<td>• Pericarditis - viral or idiopathic</td>
<td>• Encephalitis</td>
</tr>
<tr>
<td>• Henoch-Schonlein purpura</td>
<td></td>
<td>• Familial chorea (including Huntington’s)</td>
</tr>
<tr>
<td>• Post-streptococcal reactive arthritis‡</td>
<td></td>
<td>• Intracranial tumour</td>
</tr>
<tr>
<td>• Other, e.g. HIV/AIDS, leukaemia</td>
<td></td>
<td>• Hormonal ‡</td>
</tr>
</tbody>
</table>

* Includes septic arthritis (e.g. Staphylococcus aureus, Neisseria gonorrhoea), and reactive arthritis from e.g. cytomegalovirus, Epstein-Barr Virus, mycoplasma, rubella (also post-vaccination), hepatitis B, parvovirus, and Yersinia species and other gastrointestinal pathogens

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

‡ Some patients present with arthritis not typical of ARF, but with evidence of recent streptococcal infection and are said to have poststreptococcal reactive arthritis. 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. These patients are said not to be at risk of carditis, and therefore do not require secondary prophylaxis. However, some patients diagnosed with post-streptococcal reactive arthritis have developed later episodes of ARF, indicating that the initial diagnosis should have been atypical ARF (Level IV)

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

‡ Some cases of chorea are mild or atypical and may be confused with motor tics or the involuntary jerks of Tourette’s syndrome. There may therefore be confusion between Sydenham’s chorea and these conditions. The term PANDAS (Pediatric Auto-immune Neuropsychiatric Disorder Associated with Streptococcal infection) refers to a subgroup of children with tic or obsessive-compulsive disorders (OCD), whose symptoms may develop or worsen following GAS infection.

Five criteria have been used to define the PANDAS subgroup:

- The presence of a Tic disorder and/or OCD
- Pre-pubertal age of onset (usually between 3 and 12 years of age)
- Abrupt symptom onset and/or episodic course of symptom severity
- Temporal association between symptom exacerbations and streptococcal infection (approx 7-14 days)
- Presence of neurologic abnormalities during periods of symptom exacerbation (typically adventitious movements or motoric hyperactivity)

---

**Note 3**

*Include other infections* (including septic arthritis, gonococcal), and reactive arthritis from e.g. cytomegalovirus, Epstein-Barr Virus, mycoplasma, rubella (also post-vaccination), hepatitis B, parvovirus, and Yersinia species and other gastrointestinal pathogens

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

‡ Some patients present with arthritis not typical of ARF, but with evidence of recent streptococcal infection and are said to have poststreptococcal reactive arthritis. 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. These patients are said not to be at risk of carditis, and therefore do not require secondary prophylaxis. However, some patients diagnosed with post-streptococcal reactive arthritis have developed later episodes of ARF, indicating that the initial diagnosis should have been atypical ARF (Level IV).

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). Patients so diagnosed should receive secondary prophylaxis for at least 5 years (Grade D). Echocardiography (see algorithm 2) should be used to confirm the absence of valvular damage in all of these cases before discontinuing secondary prophylaxis (Grade D).

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

‡ Some cases of chorea are mild or atypical and may be confused with motor tics or the involuntary jerks of Tourette’s syndrome. There may therefore be confusion between Sydenham’s chorea and these conditions. The term PANDAS (Pediatric Auto-immune Neuropsychiatric Disorder Associated with Streptococcal infection) refers to a subgroup of children with tic or obsessive-compulsive disorders (OCD), whose symptoms may develop or worsen following GAS infection.

Five criteria have been used to define the PANDAS subgroup:

- The presence of a Tic disorder and/or OCD
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- Abrupt symptom onset and/or episodic course of symptom severity
- Temporal association between symptom exacerbations and streptococcal infection (approx 7-14 days)
- Presence of neurologic abnormalities during periods of symptom exacerbation (typically adventitious movements or motoric hyperactivity)
However, the evidence supporting PANDAS as a distinct disease entity has been questioned. Hence, in New Zealand populations with a high prevalence of ARF, clinicians should rarely (if ever) make a diagnosis of PANDAS, and should rather err on the side of over-diagnosis of ARF and secondary prophylaxis (Grade D). If ARF is excluded, secondary prophylaxis is not needed, but such cases should be carefully followed up to ensure that they do not develop carditis in the long term.

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

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 1st test not confirmatory)

**Tests for Alternative Diagnoses, Depending on Clinical Features**

- Serology or reactive arthritis
- Anti Nuclear Antibody (ANA) for autoimmune arthritis
- 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.

* Occasionally, when the diagnosis has already been confirmed and the patient is not unwell (e.g. mild recurrent chorea in a child with no other symptoms or signs), outpatient management may be appropriate. In such patients health staff must ensure that investigations, treatment, health education, registration (where available) and notification are all completed and prophylaxis commenced

† Controlled studies have failed to show that treating ARF with large doses of penicillin affects the outcome of rheumatic valvular lesions one year later. Despite this, most authorities recommend a course of penicillin, even if throat cultures are negative, to ensure eradication of streptococci that may persist in the upper respiratory tract (Grade D)

‡ Most people labeled as being allergic to penicillin are not. Because penicillin is the best antibiotic choice for secondary prophylaxis it is recommended that those with stated penicillin allergy be investigated carefully, preferably with the help of an allergist, before being accepted as truly allergic (Grade D).

Neuroimaging is not necessary and should be reserved for patients who have an atypical presentation, such as hemichorea.
Algorithm 2: Guide for the duration of secondary prophylaxis in acute rheumatic fever (ARF)

New Zealand standard recommendations are for 4-weekly (28-day) IM BPG prophylaxis. A 21-day prophylaxis schedule is recommended only for those who have had confirmed recurrent ARF despite full adherence to 4-weekly prophylaxis. Note 1

Established RHD

Definite or probable ARF
Note 2

Possible ARF
Note 2

No or mild carditis
Note 3

Moderate carditis
Note 3

Severe carditis
Note 3

Prophylaxis

– individualise, see Note 4

Prophylaxis for 10 years or until age 30 (whichever is longer), then

Low-risk environment
Note 5

Ongoing exposure to high-risk GAS environment Note 5

Stop prophylaxis

Consider continuation of prophylaxis

Prophylaxis for 10 years or until 30 (whichever is longer), then review severity of disease, GAS exposure (Note 5) and discuss continued prophylaxis (probably lifelong)

Prophylaxis for 10 years or until 21 (whichever is longer)

Possible to consider 5 years prophylaxis

Prophylaxis for 10 years or until 21 (whichever is longer)

Age over 21

Age under 21

Possible to consider 5 years prophylaxis

Age over 21

Age under 21

Note 1

Note 2

Note 3

Note 4

Note 5

Abbreviations:
ARF = acute rheumatic fever
GAS = group A streptococcus
IM = intramuscular
RHD = rheumatic heart disease
Note 1
Antibiotic Regimens for Secondary Prevention of Acute Rheumatic Fever/Rheumatic Heart Disease

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dose</th>
<th>Route</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First line</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benzathine penicillin*</td>
<td>Children &lt;30kg: 450mg (600,000 U)</td>
<td>Most effectively given as a deep intramuscular injection†</td>
<td>4-weekly (28 days), or 3-weekly for those who have had confirmed recurrent ARF despite full adherence to 4-weekly benzathine penicillin‡</td>
</tr>
<tr>
<td></td>
<td>Children &amp; Adults ≥30kg: 900mg (1,200,000 U)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Second line (if intramuscular route is not possible or refused)</strong>‡</td>
<td>Penicillin V</td>
<td>Children &lt;20kg: 250mg</td>
<td>Oral</td>
</tr>
<tr>
<td></td>
<td>Adolescents &amp; Adults ≥20kg: 500mg</td>
<td>Oral</td>
<td>Two or three times daily</td>
</tr>
<tr>
<td><strong>Following documented penicillin allergy§</strong></td>
<td>Erythromycin ethyl succinate (EES)</td>
<td>Children &amp; Adults: 40mg/kg per day</td>
<td>Oral</td>
</tr>
</tbody>
</table>

* Benzathine penicillin can be given with lignocaine to reduce injection site pain
† The timing of administration may be advanced to aid compliance for extenuating circumstances such as tangi leave, overseas travel, school holidays etc. For people on a 28 day regimen it can be advanced as much as 14 days, and for those on a 21 days regime, up to 7 days.
‡ Oral penicillin is less efficacious than benzathine penicillin in preventing GAS infections and subsequent recurrences of ARF. Twice-daily oral regimens are also likely to result in poorer rates of adherence over long periods of time and less predictable serum penicillin concentrations, when compared to intramuscular benzathine penicillin. In addition, oral penicillin V incurs a cost to the patient, while IM benzathine penicillin is free when provided through an ARF prevention programme. Oral penicillin should be reserved for cases who refuse intramuscular benzathine penicillin (Level II, Grade B). If a patient is offered oral penicillin, the consequences of missed doses must be emphasised and adherence carefully monitored (Grade D).
§ The benefits of long-term benzathine penicillin administration outweigh the rare risk of serious allergic reactions to penicillin and fatality as a result of anaphylaxis. The rates of allergic and anaphylactic reactions to monthly benzathine penicillin are 3.2% and 0.2%, respectively, and fatal reactions are exceptionally rare. There is no increased risk with prolonged benzathine penicillin use. A prospective study of 1,790 ARF/RHD patients found similar rates of reactions in those receiving long-term penicillin therapy and those receiving short-term therapy for sexually transmitted diseases (Level III-2). Before commencing penicillin treatment, cases should be carefully questioned about known allergies to penicillin and other beta-lactam antibiotics. When patients state they are allergic to penicillin or when a non-specific reaction has been reported but there is no unequivocal evidence, they should be investigated for penicillin allergy, preferably in consultation with an immunologist/allergist. The options include skin testing or a supervised challenge test. Most of these patients are not truly allergic. Penicillin desensitisation is not applicable to these patients, even with a regimen of more frequent injections, as it would have to be repeated before each dose of benzathine penicillin. A RAST (RadioAllergoSorbent Test) may be used as a screening tool only. Because this is a specific but not very sensitive test, a negative RAST test must be followed up in all cases with penicillin skin testing and/or consideration of a graded challenge if appropriate (Grade D).
### Note 2

**New Zealand Guidelines for the Diagnosis of ARF**

<table>
<thead>
<tr>
<th>Diagnostic Requirements</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial episode of ARF</td>
<td></td>
</tr>
<tr>
<td>2 major or 1 major and 2 minor manifestations Plus evidence of a preceding GAS infection*</td>
<td>Definite ARF</td>
</tr>
<tr>
<td>Initial episode of ARF</td>
<td></td>
</tr>
<tr>
<td>1 major and 2 minor with the inclusion of evidence of a preceding GAS infection* as a minor manifestation (Jones, 1956)(^2)</td>
<td>Probable ARF</td>
</tr>
<tr>
<td>Initial episode of ARF</td>
<td></td>
</tr>
<tr>
<td>Strong clinical suspicion of ARF, but insufficient signs and symptoms to fulfil diagnosis of definite or probable ARF</td>
<td>Possible ARF</td>
</tr>
<tr>
<td>Recurrent attack of ARF in a case with known past ARF or RHD</td>
<td></td>
</tr>
<tr>
<td>2 major or 1 major and 2 minor or several(^\dagger) minor plus evidence of a preceding GAS infection* (Jones, 1992)(^4)</td>
<td>Recurrent ARF</td>
</tr>
<tr>
<td>Major manifestations: modified(^8) from Jones 1992 (see Table 4 for key points in identifying major manifestations)</td>
<td></td>
</tr>
<tr>
<td>Carditis (including evidence of subclinical rheumatic valve disease on echocardiogram)(^8)</td>
<td></td>
</tr>
<tr>
<td>Polyarthritis(^8) or aseptic monoarthritis (with or without a history of NSAID use)*</td>
<td></td>
</tr>
<tr>
<td>Chorea (can be stand-alone for ARF diagnosis)</td>
<td></td>
</tr>
<tr>
<td>Erythema marginatum</td>
<td></td>
</tr>
<tr>
<td>Subcutaneous nodules</td>
<td></td>
</tr>
<tr>
<td>Minor manifestations: (see Table 4 for key points in identifying minor manifestations)</td>
<td></td>
</tr>
<tr>
<td>Fever</td>
<td></td>
</tr>
<tr>
<td>Raised ESR or CRP</td>
<td></td>
</tr>
<tr>
<td>Polyarthralgia(^8)</td>
<td></td>
</tr>
<tr>
<td>Prolonged P-R interval on ECG</td>
<td></td>
</tr>
</tbody>
</table>

Categories of Definite, Probable and Possible ARF can be determined by the application of the New Zealand criteria to each case (Table 4 and 5).

All categories assume that other more likely diagnoses have been excluded. Please see additional tables for details about specific manifestations.

CRP=C-reactive protein; ECG=electrocardiogram; ESR=erythrocyte sedimentation rate; GAS=group A streptococcus; RHD=rheumatic heart disease

* Elevated or rising antistreptolysin O or other streptococcal antibody (Table 6), is sufficient for a diagnosis of definite ARF. A positive throat culture or rapid antigen test for GAS alone is less secure as 50% of those with a positive throat culture will be carriers only. Therefore, a positive culture alone demotes a case to probable or possible ARF.

\† Most cases of recurrence fulfil the New Zealand criteria. However in some cases (such as new carditis on previous RHD) it may not be clear. Therefore in order to avoid under-diagnosis, a presumptive diagnosis of rheumatic recurrence may be made where there are several minor manifestations and evidence of a preceding GAS infection in a person with a reliable history of previous ARF or established RHD. In addition, WHO (2004) recommendations state that where there is established RHD, a recurrent attack can be diagnosed by the presence of two minor manifestations plus evidence of a preceding group A streptococcal infection.\(^5\)

\‡ Acceptance of echocardiographic evidence of carditis as a major criterion was the New Zealand modification to the Jones (1992) update

\§ When carditis is present as a major manifestation (clinical and/or echocardiographic), a prolonged P-R interval cannot be considered an additional minor manifestation in the same person

\¶ Other causes of arthritis/arthritis should be carefully excluded, particularly in the case of monoarthritis e.g. septic arthritis (including disseminated gonococcal infection), infective or reactive arthritis and auto-immune arthropathy e.g. juvenile chronic arthritis, inflammatory bowel disease, systemic lupus erythematosus, or other systemic vasculitis and sarcoidosis. Note that if polyarthritis or monoarthritis is present as a major manifestation, polyarthralgia cannot be considered an additional minor manifestation in the same person.

Special consideration should be given to high-risk population groups such as Māori and Pacific people, and those residing in poor socio-economic circumstances. In these cases, it may be important to err on the side of diagnosis and prophylaxis.
**Note 3**

**Severity of ARF Carditis**

<table>
<thead>
<tr>
<th>Mild Carditis*</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Mild mitral or aortic regurgitation clinically and/or on echocardiography (fulfilling the minimal echocardiographic standards in Table 7) without heart failure, without cardiac chamber enlargement on CXR, ECG or echocardiography</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Moderate Carditis</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Any valve lesion of moderate severity on clinical examination or</td>
<td></td>
</tr>
<tr>
<td>• Cardiac chamber enlargement seen on echocardiogram or</td>
<td></td>
</tr>
<tr>
<td>• Any valve lesion graded as moderate on echocardiogram†</td>
<td></td>
</tr>
<tr>
<td>• Regurgitation is considered moderate if there is a broad high-intensity proximal jet filling half the left atrium i.e. Mitral or a lesser volume high-intensity jet producing prominent blunting of pulmonary venous inflow72</td>
<td></td>
</tr>
<tr>
<td>• 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 aorta72</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Severe Carditis</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Any impending or previous cardiac surgery for RHD, or</td>
<td></td>
</tr>
<tr>
<td>• Any valve lesion associated with significant cardiomegaly or heart failure, or graded as severe on clinical examination</td>
<td></td>
</tr>
<tr>
<td>• Any valve lesion graded as severe on echocardiogram:</td>
<td></td>
</tr>
<tr>
<td>• An abnormal regurgitant colour and Doppler flow patterns in pulmonary veins is a prerequisite for severe mitral regurgitation in children72</td>
<td></td>
</tr>
<tr>
<td>• Doppler reversal in lower descending aorta is required for the diagnosis of severe aortic regurgitation in children.72</td>
<td></td>
</tr>
<tr>
<td>• In adults, Doppler flow reversal in the pulmonary veins (for severe MR) or abdominal aorta (for severe AR) is specific if present, but can be more difficult to detect; their absence does not exclude severe regurgitation if not detected.</td>
<td></td>
</tr>
</tbody>
</table>

* 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 Zealand72

† When there is both mitral and aortic regurgitation, one 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 4**

For those presenting with RHD for whom no initial episode of ARF can be identified, the decision to commence penicillin prophylaxis should be taken on an individual basis with regard to the age of the patient, severity of the disease, possible age of first attack and risk of exposure to GAS. See also page 46.

It is recommended that cases with established valvular disease have regular dental care and follow the guidelines for endocarditis prophylaxis.

**Note 5**

Individuals working or living with children, or in a living situation where there is overcrowding or close proximity to others (such as boarding schools, barracks and hostels), have a higher risk of exposure to GAS and subsequent development of ARF. In these cases, consideration should be given to extending the duration of prophylaxis.
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Appendices

Appendix A: Guideline Development Process

In 2006:

- Relevant literature regarding ARF was identified primarily using computerised Medline, CINAHL, ProQuest and other databases. Publications were limited to those in the English language. Articles found through this methodology were then searched for relevant information and further articles identified through bibliographic references. A substantial physical library of ARF references held at the School of Population Health was also reviewed for key articles. In addition to journal article searches, regular review and searches were made of internet sites such as the World Health Organisation, New Zealand Ministry of Health, New Zealand Environment Scientific Research (ESR) and the New Zealand Department of Statistics.

- In 2005, a steering group which arose out of the New Zealand members of the writing group for the Australian guidelines met and agreed to develop the New Zealand version of guidelines for the diagnosis, management and prevention of ARF

- A writing group comprising experts in the area reviewed the Australian draft and reached consensus on areas of disagreement

- Selected individuals re-wrote the Australian guidelines for the New Zealand context, and according to the outline recommended by the New Zealand Guidelines Group (NZGG)

- Members of the writing group with experience in ARF/RHD diagnosis, management, and prevention then reviewed each chapter and their suggestions were incorporated into a second draft

- The revised draft was widely distributed to a range of stakeholders, who were then invited to comment

- The stakeholders reviewed the draft and reached consensus on areas of disagreement

- The comments were then incorporated into a final draft, which was endorsed by the stakeholders.

In 2013:

- The Guideline Update was Co-Chaired by Professor Diana Lennon and Dr Nigel Wilson. Rachel Liddel was project manager.

- The Lead Authors identified the relevant sections that required updating and the Co-Chairs based on relevant literature and evidence

- The Lead Authors prepared an updated version of the guideline which incorporated new evidence and a new section on rheumatic heart disease

- An Advisory Group consisting of experts from cardiology, paediatrics, general practice, public health and nursing considered the evidence and recommendations

- Following Advisory Group consultation a number of changes were made to the draft guideline

- The draft guideline was sent to various organisations for endorsement. Further recommendations were considered by the Lead Authors.
Appendix B: Evolution of the Jones Criteria for the Diagnosis of ARF

It is recommended that the New Zealand criteria is used for the diagnosis of ARF in New Zealand (page 14) not the Jones criteria

The Jones criteria for the diagnosis of ARF were introduced in 1944. There is no single symptom, sign, or laboratory test that is diagnostic for ARF. The Jones criteria were introduced in 1944. Major manifestations (least likely to lead to an incorrect diagnosis) at that time included carditis, joint symptoms, subcutaneous nodules and chorea. Historical evidence of ARF or RHD was also a major manifestation. Minor manifestations (suggestive, but not sufficient for the diagnosis) included clinical signs such as fever, erythema marginatum, and abdominal pain and laboratory markers of inflammation such as ESR and leukocytosis. Since a previous history of ARF was considered a major criterion, cases only needed minor manifestations in order to fulfil the diagnosis (one major and two minor).

In order to improve specificity, in 1956 arthritis replaced joint symptoms as a major manifestation, and erythema marginatum was reconsidered as a major manifestation. A preceding ARF or RHD was reclassified as a minor manifestation, and other minor manifestations of arthralgia, and evidence of a preceding GAS infection were added. In subsequent revisions in 1965 and 1984, evidence of a GAS infection was considered essential.


PR = PR interval in the electrocardiogram; WBC = leukocytosis; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein.
The Jones criteria have been periodically modified and updated. The 1992 update is the most recently published version. The current Jones Criteria (1992) are designed to establish the diagnosis of the initial attack of ARF and a previous history of ARF or RHD is excluded from the list of minor manifestations. The sensitivity of ARF arthritis to NSAIDs and salicylates, and therefore the potential for the use of these medications to aid in diagnosis, is described. In addition, the 1992 criteria define three circumstances in which the diagnosis of ARF can be made without strictly adhering to the Jones criteria.

A review of the Criteria in 2002 did produce any further changes. This revision introduced or reiterated important circumstances where ARF can be diagnosed without strictly adhering to the Jones criteria: chorea as the only manifestation of ARF and indolent carditis (carditis of insidious onset and slow progression with evidence of inflammatory disease as distinguished from chronic RHD) as the only manifestation of ARF. Both these types of patients may have insufficient supporting historical, clinical or laboratory findings to fulfil the Jones criteria.

These are:
- Chorea occurring as the only manifestation of ARF
- Indolent carditis occurring as the only manifestation of ARF
- A presumptive diagnosis of rheumatic fever recurrence may be made when a single major or several minor manifestations are present in a patient with a reliable history of ARF or established RHD, provided there is evidence of a recent GAS infection.

The Jones criteria Working Group met again in 2000 to review the adequacy of existing guidelines for the diagnosis of the initial attack of ARF. The consensus opinion at this time was that no new version of the criteria was justified. It was reiterated that the epidemiological setting where diagnosis is being made is important, and that strict adherence to the Jones criteria in areas of high prevalence may result in under-diagnosis. This group determined that echocardiography is useful for confirming clinical findings, assessing severity of valvular disease, chamber size and ventricular function, and noting the presence and size of pericardial effusions. Echocardiography was also noted to be useful for the management of ARF, and to exclude ARF as a cause of murmur. However, the use of echocardiography in the diagnosis of ARF was determined by this working group to be too controversial to classify as a major or minor criterion. Controversy arose because of 'normal' valvular regurgitation (which increases with age), regurgitation with febrile illnesses unrelated to ARF, and the uncertainty over the long-term prognostic significance of echocardiography.

In the New Zealand setting, when the first registers and prophylaxis programmes were set up, to ensure accurate epidemiologic data the Jones criteria of 1965 and 1956 were honed to produce Definite and Probable categories of ARF diagnosis.

These definitions are now incorporated into the New Zealand RF Criteria. Definitions of raised temperature, ESR and CRP were used. However the criteria need not be rigidly adhered to when ARF is the most likely diagnosis i.e. a possible case of ARF.
Appendix C: Use of Echocardiography in ARF

Echocardiography is now recommended for all suspected cases of ARF. The uses of echocardiography in ARF are presented in Table 41.

Table 41: Uses of Echocardiography in ARF

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Echocardiographic evidence of subclinical carditis is sufficient as a major manifestation of ARF</th>
</tr>
</thead>
</table>
| Pericarditis | Confirming the presence of a pericardial effusion  
Revealing inaudible or subclinical valvular regurgitation in presence of a friction rub |
| Myocarditis and Congestive Heart Failure | Assess left ventricular function  
Assessing the severity of valvulitis (valvulitis is usually present in ARF with heart failure) |
| Valvulitis | Visualisation of anatomy of the valves, especially in mitral regurgitation. This is paramount in surgical decision-making  
Defining the severity of mitral, aortic and/or tricuspid regurgitation  
Defining the severity of mixed valve disease  
Identifying subclinical evidence of rheumatic valve damage. |

M-mode echocardiography used to evaluate chamber size and ventricular function. More complex formulae based on 2DE can also be used to calculate left ventricular function (e.g. single plane ellipse and Simpson’s methods of discs). Valvular regurgitation can be accurately graded with pulsed and colour Doppler echocardiography as absent, physiological, mild, moderate and severe for both rheumatic and non-rheumatic valve disease. Valvular regurgitation can be accurately graded with pulsed and colour Doppler echocardiography as absent, physiological, mild, moderate and severe for both rheumatic and non-rheumatic valve disease.269,270,271,272

Echocardiography and Physiological Valvular Regurgitation

Trivial valvular regurgitation is commonly detected on echocardiography as a normal finding. Regurgitant jets, albeit trivial in degree, may be observed in normal individuals of all ages. These extend beyond the valve coaptation point, but usually by only less than 1cm. They may have a high velocity component, but this is usually only for part of systole or diastole.

Trivial mitral tricuspid and pulmonary regurgitation is very common, but trivial aortic regurgitation is not, occurring in 0-1% of normal subjects, except in one study where closing volumes were included. The characteristic Doppler echocardiographic feature of trivial mitral regurgitation in normal subjects is an aliasing flow pattern in early systole, with a velocity usually <1m/s. One study reported holosystolic flow signals, but they were recorded only at the valve leaflets, and had a poorly defined spectral envelope. Sometimes a brief high velocity component may be detected.
Subclinical Evidence of Rheumatic Valve Damage

In those with suspected ARF and a murmur, reliance on clinical findings alone may result in misclassification of carditis.71,127,100 Some cases have been shown on echocardiography to have a physiological or flow murmur, or even congenital heart disease. The likelihood of misclassification has increased in recent years, as physicians’ auscultatory skills have become less proficient.127 There is convincing evidence that subclinical or silent rheumatic valve damage detected by echocardiography is part of the spectrum of rheumatic carditis and should not be ignored.127 This has been confirmed by investigators in many regions around the world with high rates of rheumatic fever, including New Zealand71,72,100 Australia, USA,92,277,278 Qatar,279,280 Brazil,281 Turkey, Chile,282 Tahiti,283 Nepal,284 Portugal,285 Egypt and India.286 A single report from India describing 28 patients with polyarthritis or chorea failed to detect any subclinical carditis.104 In experienced hands, subclinical rheumatic valve damage can usually be differentiated on echocardiography from physiological regurgitation.71,275,282 However, there are some authors who advocate against the concept of subclinical rheumatic valve damage.287

A World Health Organisation expert committee concurred that subclinical rheumatic valve damage exists.127 However, because the clinical significance of this finding is not yet known, they decided against recommending its inclusion in the Jones criteria. In the opinion of the authors of this review, echocardiographic diagnosis of subclinical valve damage can help experienced clinicians in making the diagnosis of ARF, or in confirming the presence of carditis in cases of ARF without an obviously pathological heart murmur. Therefore, it was recommended that echocardiographically suggested valve damage (subclinical or otherwise), diagnosed by a clinician with experience in echocardiography of patients with ARF/RHD, be included as a major manifestation in the 2006 New Zealand guidelines (Table 5) (Level IV, Grade C), endorsed by other countries.13 The American Heart Association Guidelines are currently under review.

Subclinical valve damage influences the diagnosis of ARF in relatively few individuals.104 Most cases have either migratory polyarthritis, or clinically overt carditis that can be confirmed by echocardiography. However, there are some cases in which the finding may help to confirm the diagnosis, and to reinforce in the minds of cases and their families the importance of adherence to a secondary prophylactic regimen (Table 27).

Table 42: Diagnostic and Clinical Utility of Subclinical Rheumatic Valve Damage in ARF

<table>
<thead>
<tr>
<th>Main ARF</th>
<th>Clinical Features of</th>
<th>Implications of a Finding of Subclinical Valve Damage</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Diagnostic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Helps to reinforce the importance of 2° prophylaxis</td>
</tr>
<tr>
<td>Polyarthritis</td>
<td>Usually none, as Jones criteria fulfilled, but can increase confidence in diagnosis of ARF</td>
<td></td>
</tr>
<tr>
<td>Monoarthritis or arthralgia</td>
<td>May confirm the diagnosis as ARF, as long as other causes of joint disease are excluded</td>
<td></td>
</tr>
<tr>
<td>Chorea</td>
<td>Confirms the diagnosis as ARF. Avoids the need to exclude other causes of chorea</td>
<td></td>
</tr>
<tr>
<td>Erythema marginatum</td>
<td>Nil, because clinical carditis or polyarthritis usually present</td>
<td></td>
</tr>
<tr>
<td>Subcutaneous nodules</td>
<td>Nil, because clinical carditis or polyarthritis usually present</td>
<td></td>
</tr>
<tr>
<td>Clinical carditis</td>
<td>Nil</td>
<td>Defines involvement of second valve if only 1 valve has clinical carditis</td>
</tr>
</tbody>
</table>
Appendix D: Wallet card for infective endocarditis prevention

For patients who have a penicillin allergy or who have taken a penicillin or cephalosporin-group antibiotic* more than once in the past four weeks:
- Clindamycin 600mg (child = 15mg/kg up to 600mg);
  - Orally, 1 hour before the procedure
  - IV, over at least 20 minutes, just before the procedure
  - IM, 30 minutes before the procedure
- Clarithromycin 500 mg (child = 15mg/kg up to 500mg) orally, 1 hour before the procedure.

Antibacterial agents may be given up to 2 hours after the procedure if inadvertently not given beforehand.

*Includes those on long-term penicillin prophylaxis for rheumatic fever

Antibacterial regimen for surgery and procedures at sites of established infection should include:

- Dental or upper respiratory tract infections:
  - Amoxycillin (clindamycin or clarithromycin if penicillin allergy)

- Gastrointestinal, hepatobiliary, genitourinary or obstetric/gynaecological infections:
  - Amoxycillin (vancomycin if penicillin allergy)

- Skin, skin-structure or musculoskeletal infections:
  - Flucloxacinil (a cephalosporin if mild penicillin allergy, clindamycin if severe penicillin allergy or suspected MRSA)

Heart Foundation
Printed September 2011

Advice to Prevent Infective Endocarditis

Name
NHI
Heart Condition
GP
Hospital Doctor

Please carry this card with you.

Information for patient, parents and guardians

Has a heart condition which requires antibacterial (antibiotic) protection before some dental and surgical procedures.

You must show this card to any dentist, dental therapist or doctor BEFORE treatment is started.

General Advice
2. Avoid sugary foods and drinks to reduce the need for dental surgery.
3. Have regular dental check-ups to help keep teeth and gums healthy.
4. Use a mouth guard for contact sports to help protect teeth.
5. Antibacterials (antibiotics) are not needed for natural loss of baby teeth.

Hospital medical check-ups
DO NOT replace visits to your local dentist or dental therapist.

Information for doctor, dentist and dental therapist

This patient is at risk of infective endocarditis and requires prophylaxis as detailed below.

Antibacterial prophylaxis is necessary for all dental procedures that involve manipulation of the gingival tissue or the periapical region of teeth or perforation of the oral mucosa.

Dental Procedures (plus Tonsillectomy and Adenoidectomy)
For patients who have not received a penicillin or cephalosporin-group antibiotic in the past four weeks:
- Amoxycillin 2g (child 50mg/kg up to 2g);
  - Orally, 1 hour before the procedure
  - IV, just before the procedure
  - IM, 30 minutes before the procedure.

Administer parenterally if unable to take orally. Administer IV if IV access is readily available.
Appendix E: Comparison of intramuscular penicillin and oral penicillin for secondary prevention

A search was conducted by Manyemba and Mayosi (2002). The search strategy included the Controlled Trials Register (Cochrane Library Issue 2, 2001), Medline (January 1996 to July 2000), Embase (January 1985 to July 2000), reference lists of articles and consultation with experts.

Randomised and quasi-randomised studies comparing: (i) oral with intramuscular penicillin; and (ii) two-weekly or three-weekly with four-weekly intramuscular penicillin in patients with previous ARF. Two reviewers independently assessed the trial quality and extracted the data of six included studies (1,707 patients).

Four trials (1,098 patients) compared IM with oral penicillin and all showed that IM penicillin was more effective than oral in reducing recurrence of ARF and streptococcal throat infections.

One trial compared two-weekly with four-weekly IM penicillin. Penicillin given every two weeks was better at reducing ARF recurrence (relative risk (RR) 0.52, 95% confidence interval (CI) 0.33-0.83) and streptococcal throat infections (RR 0.60, 95% CI 0.42-0.85).

One trial (249 patients) showed that three-weekly IM penicillin injections were more effective than four-weekly IM penicillin at reducing streptococcal throat infections (RR 0.67, 95% CI 0.48-0.92).

The conclusions made therefore were that IM penicillin seemed to be more effective than oral penicillin in preventing ARF recurrence and streptococcal throat infections. Two-weekly or three-weekly injections appeared to be more effective than four-weekly injections. However, the evidence was based on poor-quality trials and the use of outdated formulations of oral penicillin.
Appendix F: KidzFirst Guideline: Analgesia for IM Penicillin Injection (2011)

Guideline Summary

The use of BUZZY®* prior to AND during this painful uncomfortable procedure as well as the utilization of behavioral techniques will be initiated as indicated. *Buzzy® is a vibrating device which incorporates a cold pack, which should be frozen. The cold pack is inserted under the elastic band behind the Buzzy®.

2% Lignocaine 0.25ml will be mixed in with the Penicillin prior to the injection being given. The dose of Benzathine penicillin given will be based on the weight of the child, see below.

Advice on the use of analgesia can be given to families if the injection site is causing pain later that day and/or the next day. If there is any concern of a recurrence of ARF, then NSAIDs should be avoided until diagnosis is clarified.

Procedure

1. Preparation of Benzathine penicillin & Lignocaine 2%
   To prepare the injection immediately prior to administration.

   1. Draw the correct dose (as charted) of Penicillin from the premixed syringe into a 3ml syringe.
   2. With a needle draw 0.25ml of 2% Lignocaine (as charted) into a 1ml syringe.
   3. Add Lignocaine from 1ml syringe to Benzathine penicillin filled syringe
   4. Mix with gentle inverting of syringe
   5. Push plunger up so there is no air in the syringe
   6. Attach IM needle to syringe

2. Administering the IM injection
   If it is the patient’s first time with the BUZZY® let them feel it vibrating on their hand and explain that it will take some of the sting out of the injection.

   - Obtain BUZZY®, frozen cold pack and necessary equipment for procedure.
   - Warm injection in your hands
   - Insert frozen cold pack into Buzzy®.
   - Locate site on upper outer quadrant of the gluteus or the ventrogluteal site
   - Press Buzzy® directly on site where you will give the injection and activate vibration. This can be done by the nurse/caregiver or the child/young person themselves.
   - Leave the BUZZY® in place for **1 minute** before administering the injection.
   - When ready to administer injection slide Buzzy® 2-5 cm proximal to site (pressing on boney area directly above injection site) with wider end of Buzzy® closer to site. The patient or caregiver can hold this in place.
   - Use distraction while administering the injection (non-procedural talk/eye spy/breathing)
   - Clean site with alcohol wipe
   - Insert needle and inject the Benzathine penicillin slowly
   - Leave BUZZY® vibrating and in place until the needle is removed
   - Ask for a pain rating on faces scale 0-10
   - Document on patient record the use of BUZZY® and pain score
   - Clean BUZZY®, strap and cold pack with sani wipe.

Give advice (to caregiver or adolescent) on the use of paracetamol at home if the child or young person is experiencing pain later that day or the following day. If they do not have paracetamol at home then please arrange a prescription.

Refer to local policies for anaphylaxis management.

Source: KidzFirst Guideline: Analgesia for IM Penicillin Injection 2011 adapted with permission from Middlemore Hospital 2013.
Appendix G: Key Data Elements of ARF/RHD Registers

A possible dataset for ARF/RHD registers is outlined in Table 43. Registers are primarily for the efficient nurse coordinated delivery of free secondary prophylaxis using delegated authority by a registered medical practitioner to facilitate the process. In addition a minimum data set of epidemiological data enables measurement of the outcome of secondary and primary prevention programmes. Detailed clinical data is best sourced from electronic patient records now widely available in New Zealand.

Table 43: Dataset for ARF Register

<table>
<thead>
<tr>
<th>Domain</th>
<th>Data Elements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td>National Hospital Index and name(s)</td>
</tr>
<tr>
<td></td>
<td>Date of birth</td>
</tr>
<tr>
<td></td>
<td>Gender</td>
</tr>
<tr>
<td></td>
<td>Address and phone numbers (including cellphone for text message contacting), alternate address</td>
</tr>
<tr>
<td></td>
<td>Details of parents/caregivers</td>
</tr>
<tr>
<td></td>
<td>Ethnicity</td>
</tr>
<tr>
<td></td>
<td>GP details</td>
</tr>
<tr>
<td></td>
<td>School at diagnosis (where relevant)</td>
</tr>
<tr>
<td>Initial ARF diagnosis</td>
<td>Date and place of diagnosis and date of admission to hospital</td>
</tr>
<tr>
<td></td>
<td>Definite, probable or possible diagnosis</td>
</tr>
<tr>
<td></td>
<td>Medications taken prior to presentation/admission</td>
</tr>
<tr>
<td></td>
<td>Major criteria:</td>
</tr>
<tr>
<td></td>
<td>• Presence (and severity) of carditis</td>
</tr>
<tr>
<td></td>
<td>• Presence (and site) of arthritis</td>
</tr>
<tr>
<td></td>
<td>• Presence of chorea</td>
</tr>
<tr>
<td></td>
<td>• Presence of erythema marginatum and/or subcutaneous nodules</td>
</tr>
<tr>
<td></td>
<td>Minor criteria:</td>
</tr>
<tr>
<td></td>
<td>• Fever</td>
</tr>
<tr>
<td></td>
<td>• Acute phase reactants</td>
</tr>
<tr>
<td></td>
<td>• P-R interval</td>
</tr>
<tr>
<td></td>
<td>Evidence of a preceding GAS infection:</td>
</tr>
<tr>
<td></td>
<td>• History of sore throat</td>
</tr>
<tr>
<td></td>
<td>• Throat swab</td>
</tr>
<tr>
<td></td>
<td>• Titres</td>
</tr>
<tr>
<td>ARF recurrences†</td>
<td>Onset date</td>
</tr>
<tr>
<td></td>
<td>Presence and severity of carditis</td>
</tr>
<tr>
<td></td>
<td>Other symptoms and signs at each recurrence</td>
</tr>
<tr>
<td></td>
<td>Prophylaxis status at time of recurrence</td>
</tr>
<tr>
<td>RHD diagnosis</td>
<td>Onset date/date of diagnosis</td>
</tr>
<tr>
<td></td>
<td>Documented history of ARF</td>
</tr>
<tr>
<td></td>
<td>Severity of valve disease at time of diagnosis including assessment of ventricular function</td>
</tr>
<tr>
<td></td>
<td>Cardiac surgery</td>
</tr>
<tr>
<td></td>
<td>Dentist</td>
</tr>
<tr>
<td>Secondary prophylaxis</td>
<td>Antibiotic used</td>
</tr>
<tr>
<td></td>
<td>Dose and frequency</td>
</tr>
<tr>
<td></td>
<td>Date commenced on prophylaxis</td>
</tr>
<tr>
<td></td>
<td>Date of last dose</td>
</tr>
<tr>
<td></td>
<td>Date of next expected dose</td>
</tr>
<tr>
<td></td>
<td>Designated authority</td>
</tr>
<tr>
<td></td>
<td>Expected date of cessation</td>
</tr>
<tr>
<td></td>
<td>Annual adherence data</td>
</tr>
</tbody>
</table>
| Follow-up/recall | Date and place of last review  
|                 | Date and place of next scheduled review by each provider (cardiologist, paediatrician, physician, echocardiography)  
|                 | Recall system for missed BPG  
|                 | Recall system for missed appointment  
| Mortality       | Date and cause of death according to agreed criteria (e.g. due to RHD, not due to RHD).  

* This dataset is an amalgamation of systems currently in use in New Zealand. Some of the functions may be fulfilled elsewhere. Other information such as details of surgical procedures and medical management may also be included.  
† To facilitate the set-up of school-based primary prevention programmes  
‡ It is recommended that each ARF recurrence notified to the register is thoroughly investigated to determine if any changes in the system of prophylaxis delivery need to be made to prevent such recurrences from occurring in the future.
Appendix H: Protocol for follow up of non-adherent patients

Patient is non-adherent with injections on 3-4 concurrent occasions. All attempts at contact are clearly documented in the patients file. **These attempts should include the use of multiple modalities for contact including telephone calls, visits, texting and the use of the local knowledge of community health workers**

Discuss with primary care nurse and refer to community health worker, public health nurse or other community staff as fitting in the area for follow up. Note this opportunity to involve staff from Māori and Pacific primary health providers, if appropriate

Community health worker (or other community staff responsible) follows up patient (and family) to determine reason for non-adherence. Where necessary and appropriate, provides ongoing support, education and arrangers appointments for review at outpatient clinic as fitting in the area for follow up. Note this opportunity to involve staff from Māori and Pacific

If adherence is no longer a problem, continue routine secondary prophylaxis

If non-adherence continues, letter of planning to discharge is copied to the patient, patient file and all involved in the patient’s care (e.g. GP, paediatrician, internist, cardiologist) after discussion with primary nurse and community health worker (local policy may recommend discussion at case review)

Patient file goes "on hold" for up to six months (local area policy may suggest regular attempts at contact while patient is on hold)

At the end of the holding period, the primary nurse and community health worker review the patient and if considered appropriate a discharge letter to the patient file, GP, and rheumatic fever register (if available) (local policy may recommend a case review in consultation with clinicians prior to discharge from service)
**Key Definitions**

**Case control study:** A study which involves identifying with the outcome of interest (cases) and control patients who do not have the same outcome and looking back to see if they had an exposure of interest.²⁸⁸

**Group A streptococcus (GAS):** Also known as *Streptococcus pyogenes*. Gram positive cocci producing beta

**Penicillin (oral):** Oral penicillin is known by its ingredient name; phenoxymethylpenicillin, but is more commonly called ‘Penicillin V’.

**Penicillin (intramuscular):** IM Benzathine Benzylpenicillin (New Zealand Formulary) is more commonly known as benzathine penicillin (trade name: Bicillin® LA), and also known as Penicillin G Benzathine or Benzathine Penicillin G (BPG). Within this guideline IM Benzathine Benzylpenicillin is referred to as ‘Benzathine Penicillin’, so as not to confuse with benzylpenicillin (which has different pharmacokinetic properties and is not recommended for the treatment of GAS pharyngitis or for secondary prophylaxis).

**Pharyngitis:** Acute pharyngitis is an inflammatory syndrome of the pharynx caused by a variety of microorganisms. Most cases are of viral aetiology and occur as part of common colds and influenzal syndromes. The most important cause of bacterial pharyngitis is that due to group A beta haemolytic streptococci (*Streptococcus pyogenes*).²⁸⁹

**Rheumatic fever:** Acute rheumatic fever (ARF) is a disease characterised by non-suppurative inflammatory lesions involving primarily the heart, joints, central nervous system, the skin and subcutaneous tissues. Permanent sequelae may result from cardiac involvement. Current opinion holds that all cases of ARF follow a group A streptococcal (GAS) upper respiratory tract infection, although the exact mechanism is unclear. ARF is diagnosed using the Jones Criteria²⁹⁰ and adapted in New Zealand (and Australia) to permit echocardiography as a diagnostic criteria (see New Zealand Guidelines for Rheumatic Fever: 1. Diagnosis, Management and Secondary Prevention, available from: http://www.heartfoundation.org.nz ).
Glossary

ACE........................angiotensin-converting enzyme
AF..........................atrial fibrillation
Anti-Xa........................anti factor Xa
APTT........................activated partial thromboplastin time
AR..........................aortic regurgitation
ARF..........................acute rheumatic fever
AS..........................aortic stenosis
ASO..........................antistreptolysin O
BD..........................twice a day
CRP..........................C-reactive protein
CS..........................caesarian section
DHB..........................district health boards
EES..........................erythromycin ethyl succinate
ESR..........................erythrocyte sedimentation rate
GAS..........................group A streptococcal
IM..........................intramuscular
INR..........................international normalised ratio
IOL..........................induction of labour
IV..........................intravenous
LMWH........................low molecular weight heparin
LV..........................left ventricle
MS..........................mitral stenosis
MVA..........................mitral valve area
NSAIDs..........................non-steroidal anti-inflammatory drugs
NYHA..........................New York Heart Association
OD..........................once a day
PAS..........................pulmonary artery systolic
PBMV..........................percutaneous balloon mitral valvuloplasty
PTAV..........................percutaneous transluminal aortic valvuloplasty
PO..........................orally
QID..........................four times a day
RHD..........................rheumatic heart disease
TDS..........................three times a day
UFH..........................unfractionated heparin
WHF..........................World Heart Federation
WHO..........................World Health Organisation
We need your help
to keep Kiwi hearts beating

When you support the Heart Foundation you make a difference to the lives of thousands of New Zealanders.

There are 16 people today who will lose the fight against heart disease. People you may even know. And worse, many of these deaths are premature and preventable. For every one of these people, many more are affected – husbands, daughters, brothers, friends, me, you. So much lost potential, so many lost dreams.

Help us fight the disease that cuts short too many lives and too many stories before they’re told.

As an independent charity, we rely on the generosity of New Zealanders. Your donations are crucial to our ongoing work – funding vital research, helping people make healthy living choices, and running community programmes that encourage Kiwi heart health.

Every dollar you give helps another Kiwi live out and fulfil their lifetime.

Please take a moment to donate

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Phone us on 0800 830 100

Thank you for your support.

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