

Rheumatic fever recurrences in New Zealand 2010–14

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ABSTRACT

AIM: To describe the epidemiology and clinical characteristics of recurrences of acute rheumatic fever (ARF) in New Zealand 2010–14.

METHOD: Retrospective hospital chart review for ARF with repeat hospital admissions from 2010–14, to identify recurrences of ARF. Definitions of recurrence as per NZ Heart Foundation Guidelines.

RESULTS: There were 65 episodes of recurrent ARF among 60 patients. Māori 51%, Pacific 49%. Arthritis and carditis were the most common major manifestations. Median age at recurrence 21.6 years, (8–42 years), with 83% patients over 15 years. There were 841 first episodes of ARF in New Zealand in 2010–4. Overall New Zealand ARF recurrence rate was 7.2% (CI 5.5–8.9%). The recurrence rate was 4% for those under 16 years, 16% for those aged 16–20 and 25% for those >20 years ($p < 0.05$). Seventy-three percent of recurrences occurred in the Auckland region. Recurrences of ARF were strongly associated with RHD progression.

CONCLUSION: The risk of recurrence of ARF in New Zealand is low for children. In contrast, recurrences of ARF in New Zealand occur predominantly after age 15, and disproportionately in the Auckland DHBs. Current medical systems and registers may not be meeting the needs of adolescents and adults requiring secondary prophylaxis.

Acute rheumatic fever (ARF) is an uncommon autoimmune disease following a group A streptococcal (GAS) infection. Following an episode of ARF, individuals are at high risk of ARF recurrence, preventable by secondary prophylaxis with intramuscular benzathine penicillin.¹ The New Zealand guideline for penicillin prophylaxis for those with no or mild rheumatic heart disease is to discontinue this at the age of 21, or after 10 years, *whichever is the longer*.¹ Penicillin prophylaxis is continued to age 30 or 40 for those with moderate or severe rheumatic heart disease (RHD) when reassessed at aged 21.¹

New Zealand has a strong track record of penicillin prophylaxis delivery to prevent ARF recurrence via regional rheumatic fever (RF) registers and public health nurse administration of penicillin.^{1–6} Adherence rates are high in Northland, Auckland, Waikato, Lakes, Tairāwhiti, Hawkes Bay and

Wellington, where registers are active. The landmark study by Spinetto and colleagues⁴ showed that the failure rate of four-weekly intramuscular benzathine penicillin was very low at 0.07/100 patient years. There is anecdotal and published evidence that ARF recurrence for individuals on these registers is acceptably low: in Auckland in the 1990s⁴ and Waikato in 1998–2004² with recurrence rates of 5% and 10% respectively. Much less is known about penicillin prophylaxis adherence and ARF recurrence for individuals who are not on a register.

In New Zealand, reporting of first episodes of ARF and ARF recurrences to the Medical Officer of Health is mandatory.¹ The Institute of Environmental Science and Research (ESR) monitors disease incidence on behalf of the Ministry of Health (MOH). When it was noted that there were approximately five times more *repeat* hospitalisations for ARF coded by ICD discharge data, compared

with the numbers of ARF recurrences reported, the MOH initiated an audit: repeat hospitalisations for ARF and ‘unexpected’ hospitalisations for RHD using the National Minimum Data Set (NMDS) were examined to ascertain the true burden of ARF recurrence in New Zealand, for 2010–2014 inclusive. That audit was undertaken by Technical Advisory Services (TAS) Limited who provided audit reports to each district health board (DHB) and produced a confidential national report to the MOH.

The aim of this audit was to define the epidemiology and clinical characteristics of ARF recurrences in New Zealand for 2010–14.

Methods

The MOH data set included ICD 9 and ICD 10 coding for ARF, RHD and valvular heart disease. A hospital chart review of the 375 repeat admissions for ARF, greater than six months apart, for 2010–14 was initially undertaken by TAS. A database of these repeat admissions was created detailing patient characteristics, hospital admission and follow-up data. The MOH engaged an experienced RF clinician (NW) to advise on the audit. Due to the nuances of ARF, it was apparent that an accurate evaluation of ARF recurrence would entail further review of the data by experienced RF clinicians. Such an expert panel was established (BP, EW, AL, MW, SB, NW). The TAS database, and clinical notes as required, were reviewed by the panel and episodes were classified as ARF recurrence or not. Evidence of a prior first episode of ARF was required for a diagnosis of recurrent ARF. Repeat admissions that were not an ARF recurrence were excluded. Finally, for consistency, two investigators (AD, NW) reviewed the data for classification and medical manifestations of ARF recurrence. Neither patients nor their primary healthcare providers were contacted. The public healthcare records of penicillin prophylaxis delivery and adherence were not accessed. The MOH Health Legal team approved the audit.

Definitions of recurrent and initial ARF were as per the 2006 New Zealand RF/RHD Guideline as available in the years 2010–14.³

Definite recurrence: in a patient with previous ARF or RHD, a recurrence required

two major manifestations **or** one major and two minor manifestations **or** several minor manifestations, **plus** evidence of a preceding GAS infection. New Zealand guidelines also allow the WHO⁷ definition of recurrence for an individual with established RHD and two minor manifestations **plus** evidence of a preceding GAS infection. Elevated or rising streptococcal titres were accepted as evidence of GAS infection. Where the only evidence of GAS infection was a positive throat swab, the case was demoted to probable or possible recurrence as per the New Zealand guidelines.¹ New onset Sydenham’s chorea and indolent carditis without evidence of a preceding GAS infection were accepted as definite ARF recurrence in individuals with previous ARF or RHD.

Probable recurrence: one major and two minor manifestations with the inclusion of evidence of a preceding GAS infection as a minor manifestation.^{8,9}

Possible recurrence: when there was strong clinical suspicion of ARF recurrence, but there were insufficient symptoms and signs to meet the definite or probable definitions.

Excluded cases: Repeat hospital admissions of patients with ARF or RHD for any medical reason other than an ARF recurrence.

First episodes of ARF include indolent carditis and Sydenham’s chorea.¹ The onset and duration of these forms of ARF is often uncertain with normalisation of inflammatory markers by time of diagnosis. These were assigned to the category of first episode of ARF unless there was a clear evidence of previous ARF or RHD.

The echocardiographic term ‘acute on chronic RHD’ may be used at the time of first diagnosis of ARF, for example, when there is a degree of mitral stenosis. These cases were also not included as an ARF recurrence unless there was clear evidence of previous ARF or RHD.

First episodes of ARF 2010–14

Data for the numbers of first episodes of ARF, for 2010–14 were as notified to ESR (http://surv.esr.cri.nz/surveillance/annual_surveillance.php). Age and DHB data for these episodes was also provided on request. ESR also records the number of ARF recurrences notified.

The overall New Zealand ARF recurrence rate was calculated by the formula:

$$\frac{\text{ARF recurrences}}{\text{ARF recurrences + first episodes of ARF}}$$

ARF recurrences + first episodes of ARF

Progression of RHD severity related to the ARF recurrence was based on the comparison of any known pre-existing RHD severity with the severity at the time of ARF recurrence. Severity of RHD was based on available echocardiographic reports; echocardiographic images were not reviewed. Progression of valve disease was defined as an increase of one or more grades (eg, mild to moderate mitral regurgitation), or the need for cardiac intervention.

Statistics: Chi-squared test was used to determine differences in proportions between groups.

Results

There were 375 admissions with an ICD primary or secondary diagnosis coded as ARF, RHD or valvular heart disease with a previous first episode of ARF in the NMDS. After the review by TAS, 78 were deemed an ARF recurrence. (TAS report to the MOH, unpublished).¹⁰

The 375 admissions were reviewed by the expert panel who assessed that there were 65 episodes of ARF recurrence. These form the study cohort.

Demographics

The 65 episodes of ARF recurrence in the years 2010–2014 occurred in 60 patients. Three patients had two recurrences and a single patient had three recurrences. Fifty-three percent (32/60) were female. All patients were of Māori (51%) or Pacific (49%) ethnicity. The median age at recurrence was 21.6 (range 8.2–41.8) years. Most (83%) of the recurrences occurred after aged 15.

Epidemiology of ARF recurrences in New Zealand 2010–14

There were 841 initial (first) episodes of ARF recorded by ESR in the years 2010–14. The New Zealand ARF recurrence rate was thus calculated as $65/65+841=7.2\%$ (CI 5.5–8.9%). There was a marked difference in recurrence rate by age bracket; for those aged under 16 years the recurrence rate was 4% (CI=2.8–6.0%), for those aged 16–20 years the recurrence rate was 16% (CI=9.3–22.9%) and for those aged over 20 years the recurrence rate was 25% (CI=18.2–32.5%), ($p<0.05$).

Recurrences by district health board

The number of ARF recurrences and first episodes of ARF by DHB for 2010–14 were as follows, Northland (five recurrences: 82 first episodes of ARF), Waitemata (2: 52), Auckland (11: 68), Counties Manukau (35: 300), Waikato (2: 85), Lakes (1: 27), Bay of Plenty (1: 39), Taraiwhiti (2: 40), Hawkes

Figure 1: Recurrences of ARF by age group, 2010–14.

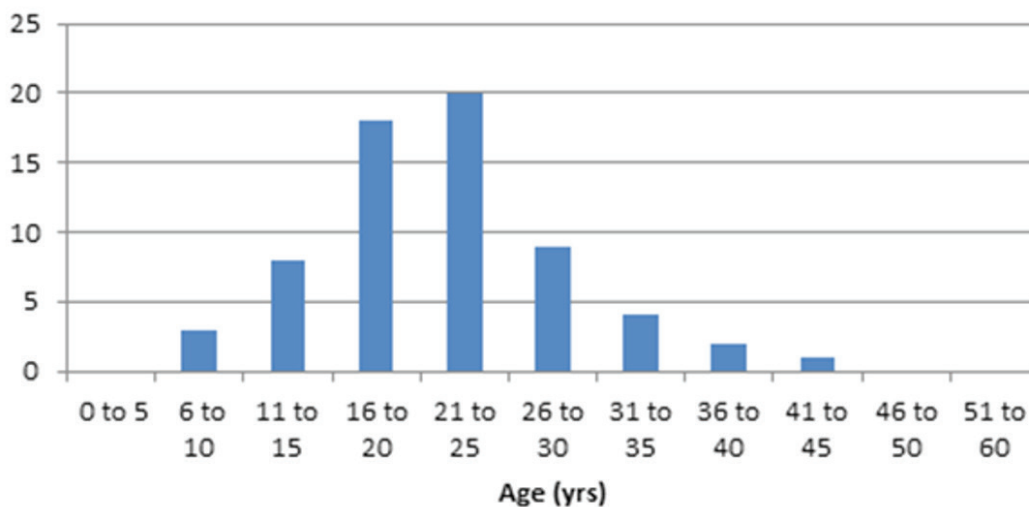
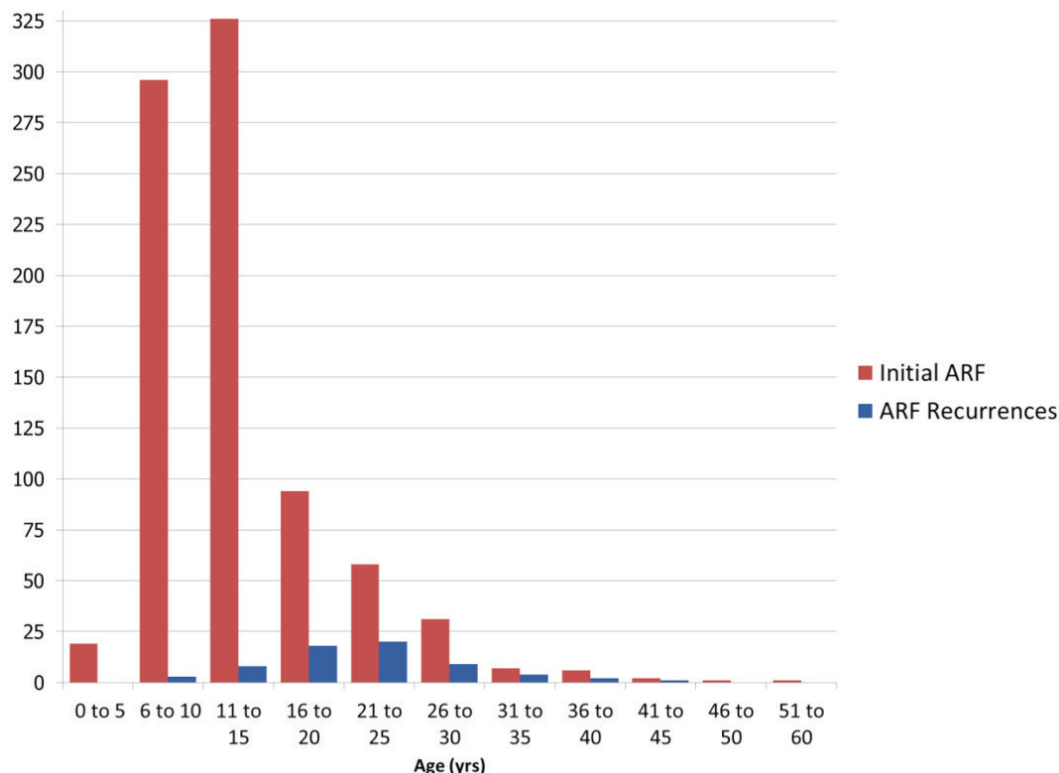


Figure 2: Number of initial episodes of ARF (red bars) and number of ARF recurrences (blue bars) by five year age groups, 2010–14.



Bay (0: 28), Taranaki (0: 5), Whanganui (2: 7), Capital Coast (2: 41), Hutt Valley (1: 30), South Island DHBs (1: 19). Overall, 73% (48/65) of ARF recurrences occurred in the three Auckland region DHBs. There were a significantly increased *proportion* of ARF recurrences compared to first episodes of ARF in the Auckland, Counties Manukau and Whanganui DHBs ($p < 0.05$). Most (82%) patients with ARF recurrence lived in areas of greater neighbourhood deprivation (NZDep Index decile 8, 9 or 10).

Category of ARF recurrence

75% (49/65) ARF recurrences were definite, 11% (7/65) were probable and 14% (9/65) were possible, as per the New Zealand RF/RHD Guideline in place in the years 2010–14 (Table 1).³ The hospital clinicians, as distinct from the audit review panel, made the diagnosis of definite recurrence in 60/65 (92%) episodes, and probable or possible recurrence in 5/65 (8%) episodes. The frequency of major and minor manifestations are shown in Table 2.

Figure 3: ARF recurrences by DHB.

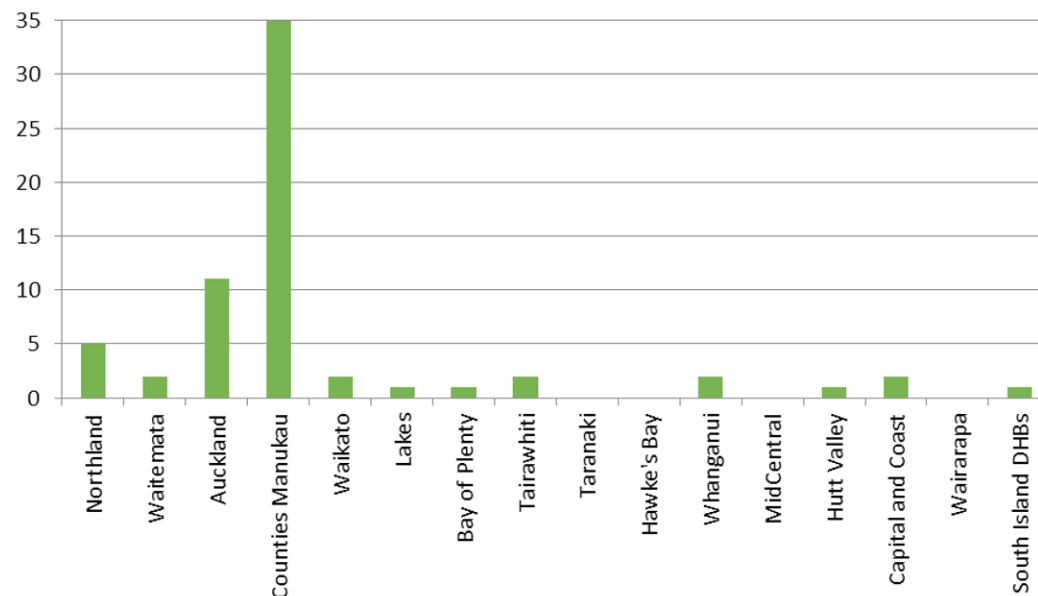


Table 1: Classification and clinical manifestations of ARF recurrences.

Definite recurrence (n=49)	Manifestations/criteria of ARF	Notes
2 Major (12)	Polyarthrititis + carditis (8)	
	Monoarthrititis + carditis (4)	
1 Major + 2 Minor (17)	Carditis + 2 minor (14)	
	Polyarthrititis + 2 minor (1)	
	Monoarthrititis + 2 minor (2)	
Sydenham's chorea (3)		
Several minor (13)	3 minor manifestations	
WHO criteria (4)	Previous RHD + 2 minor	
Probable recurrence (7)		
2 Major (2)	Carditis + polyarthrititis	*+
1 Major and 2 minor (1)	Carditis, polyarthralgia + raised inflammatory markers	*+
1 Major and 1 minor (2)	Polyarthrititis + raised inflammatory markers	*+
Several minor (2)	Polyarthralgia, raised inflammatory markers + 1st degree heart block (1)	+
	Polyarthralgia, fever + raised inflammatory markers (1)	*
Possible recurrence (9)		
2 Major (1)	Carditis + monoarthrititis (1)	#
1 Major and 2 minor (7)	Carditis, polyarthralgia+ raised inflammatory markers (1)	+
	Carditis, polyarthralgia, fever+ raised inflammatory markers (1)	+
	Carditis, polyarthralgia, raised inflammatory markers (1)	+
	Carditis, fever + raised inflammatory markers (1)	#
	Monoarthrititis, raised inflammatory markers + 1st degree heart block (1)	+
	Monoarthrititis, fever, raised inflammatory markers + prolonged PR interval (1)	#
	Erythema marginatum (not accepted as sole major manifestation), Polyarthralgia, raised inflammatory markers(1)	
Several minor (1)	Polyarthralgia, raised inflammatory markers, and fever	#

*Positive throat swab, # Insufficient elevation of GAS serology to meet New Zealand guidelines criteria¹ or Australian criteria,¹¹ + met Australian GAS serology criteria.

Table 2: Frequency of major and minor manifestations of ARF recurrences.

Major criteria	Percentage
Carditis	52% (34/65)
Polyarthrititis	20% (13/65)
Monoarthrititis	13.8% (9/65)
Erythema marginatum	1.5% (9.2/65)
Subcutaneous nodules	0% (0/65)
Sydenham's chorea	4.65% (3/65)
Minor criteria	
Polyarthralgia	52% (34/65)
Fever	43% (28/65)
Raised inflammatory markers	100% (65/65)
Prolonged PR interval	45% (29/65)

Table 3: Miscellaneous reasons for failure of penicillin prophylaxis provision.

Patient	Age (years)	Reason for not initiating secondary antibiotic prevention	Explanation
1	18	Incomplete initial work up/ misdiagnosis	Initial presentation aged 13 with polyarthralgia, raised inflammatory and raised strep titres. No echo. Represented with polyarthrititis and carditis.
2	12	Misdiagnosis	Initial presentation age 10 with L) hip arthritis, raised inflammatory markers and GAS titres. Echo initially reported as normal. Presented two years later with severe carditis, and pericardial tamponade.
3	12	Health systems error	Known ARF patient on register adherent with prophylaxis. District nursing paper work misplaced and prophylaxis omitted for three months resulting in recurrence.
4	33	Health systems error	After RHD aortic valve surgery prophylaxis not recommenced at discharge. Recurrence three months later.
5	24	Multiple drug sensitivity	Not on prophylaxis due to multiple drug sensitivities
6	19	Miscommunication between health services/ health systems error	RHD diagnosed during hospitalisation for pregnancy related complication necessitating tertiary hospital transfer. Documented on transfer letter, but prophylaxis not commenced by referring DHB.

Echo: echocardiography; strep titres: group A streptococcal serology.

At the time of recurrence, 42 (65%) were non-adherent with penicillin prophylaxis. Eleven patients (17%) had stopped penicillin prophylaxis on medical recommendation (eight had completed a period of prophylaxis as per the New Zealand guidelines but three had not: one did not complete 10 years but was aged over 21 and two completed 10 years but not to age 21); five (8%) were receiving four-weekly penicillin prophylaxis, one was receiving three-weekly penicillin prophylaxis; and six (9%) had a recurrence for miscellaneous circumstances as detailed in Table 3. The median duration from diagnosis of first episode of ARF until ARF recurrence was 10.5 years (range seven months to 29.1 years). The median duration off penicillin prophylaxis in the 11 patients who were medically recommended to stop penicillin prophylaxis until ARF recurrence was two years (range three months to 16 years). The median duration off penicillin prophylaxis in those patients who were non-adherent (data available in 38/42) until ARF recurrence was two years (range six months to five years). The median age of those who were non-adherent with penicillin prophylaxis was 21.6 (range 13.2–38.6) years.

Clinical manifestations

Recorded clinical management

Given that the audit was based on ICD hospital discharge data all patients with episodes of ARF recurrence had been admitted to hospital. The median length of stay was four days (range 1–31 days). The hospital clinicians' categorisation of ARF recurrence showed close concordance with the expert panel: definite recurrence was diagnosed in 60/65 episodes, and probable or possible recurrence in five episodes. Ninety-six percent (62/65) of the episodes of ARF recurrence had documented commencement of penicillin prophylaxis at the time of discharge from hospital. However, in only 72% of these was the provider for penicillin prophylaxis copied into the discharge summary. Referral for clinic follow-up was documented in the discharge summary in 82% (53/65) of episodes.

Cardiac manifestations of the ARF recurrence

There were 34 episodes of carditis; 22 episodes complicating existing RHD and 12 episodes in patients without existing

RHD. The predominant valve lesion in pre-existing, and new cases of RHD was mitral regurgitation (MR), in 33/34 (97%) episodes. 20/34 (59%) episodes had aortic regurgitation (AR). Four patients, median age 19 years, all with pre-existing RHD, required cardiac intervention during the audit period: one had severe mixed mitral and aortic valve disease, one had severe AR and heart failure, one had severe AR and moderate MR, and the fourth patient with pre-existing severe aortic and mitral valve disease underwent a pericardiocentesis for symptomatic pericarditis that resulted from the ARF recurrence.

Progression of RHD could be ascertained in 18 of the 22 cases of carditis complicating existing RHD (where echocardiogram reports could be reviewed). MR progressed in 17/18 episodes (94%). There was mild to moderate, or moderate to severe progression in 13/18 episodes (72%), with the remaining five cases being new mild MR in patients with previous AR. AR progressed in 6/18 episodes (33%). There was mild to moderate or moderate to severe progression in three episodes with the remaining three cases being new AR in patients with previous MR.

In the 12 patients without pre-existing RHD, MR was the most common lesion, recorded in 11/12 episodes; mild MR (n=10) and moderate MR (n=1). AR occurred in 5/12 episodes, mild AR (n = 4) and moderate AR (n=1). Overall 46% (30/65) recurrent episodes resulted in progression of RHD.

Discussion

This audit found that the ARF recurrence rate for 20100–14 in New Zealand was 7.2%. This is within the range reported for the Auckland region in the 1990s,⁴ and Waikato region in 1998–2004.² The Waikato region reported the very low 3% rate for 2002–2011.¹² While these rates are lower than those reported in other countries^{13,14} (12–40% from 2002–8 in Northern Territory, Australia; 21% in a series from Brazil), they are not cause for complacency. The ARF recurrence rate is a strong indicator of the effectiveness of secondary prevention programmes.

A striking finding of the audit was the median age of ARF recurrence of 21.6 years. Most (83%) ARF recurrences occurred in those aged 16 and over. The ARF recurrence

rate for those under 16 was low at 4% despite this being the age group with the highest risk for initial ARF; this reflects high adherence to penicillin prophylaxis for children on regional RF registers receiving penicillin from community nurses.⁵ Other studies have reported that the risk of ARF recurrence is associated with younger age, the first year after ARF diagnosis, and the failure of penicillin prophylaxis delivery.^{11,14–18}

The strong message for healthcare professionals in New Zealand is that the relative risk of an ARF recurrence increases with age (highest for those over 20 years) despite the decreasing risk of first episode of ARF with age.⁴ This almost certainly reflects the lower adherence to penicillin prophylaxis in adolescents and young adults compared with the higher adherence in children.

The reasons for the unplanned discontinuation of penicillin prophylaxis in adolescents and young adults could not be ascertained by this audit. However, qualitative research by Anderson and colleagues^{19,20} gives new insights into the mismatch between health systems and the complexities of life for many Māori and Pacific families. Their research found that the transitioning of adolescents with RF/RHD to adult medical and nursing services needs to be addressed in more culturally appropriate ways and that the cost of medical and dental care is often a significant barrier for young adults. Similar personal, socioeconomic, cultural and system factors have been found to affect the delivery of penicillin prophylaxis in other countries.^{21–23} Patients are joining health professionals in the call for a national RF register in New Zealand which should help reduce recurrences due to residential mobility of families and young adults.^{19,20,24}

Malcolm and colleagues have described their holistic approach to RF/RHD control in the Bay of Plenty.²⁵ They recommend that a diagnosis of ARF recurrence should lead to “whole-hearted patient care and whānau follow-up” for these patients. This type of approach should help reduce the disease burden of ARF recurrence in New Zealand.

Guidelines and definitions of RF recurrences

There were no changes in the definitions of ARF recurrence comparing the 2006³ with the 2014 New Zealand RF/RHD

Guidelines.¹ However, the 2014 Guideline¹ more clearly emphasises that the decision to discontinue penicillin prophylaxis should be made not only on the completed duration of penicillin, but also on the individual’s current RHD status after 10 years or aged 21. This audit revealed that 17% of ARF recurrences occurred after medical recommendation to discontinue penicillin prophylaxis compared with 10% reported in an earlier New Zealand study.⁴ This data, as well as the finding that the median time to recurrence in such patients was two years, supports not reducing the New Zealand RF/RHD Guideline’s recommended duration of penicillin prophylaxis.

Another important finding of this audit is that the clinical manifestations of an ARF recurrence are similar to first episodes of ARF with the majority of ARF recurrences fulfilling the definite recurrence criteria. One could argue that an ARF recurrence should be easier to diagnose than a first episode of ARF, given that the patient already has a diagnosis of RF or RHD.

There were seven episodes where the category of recurrence was classified as probable or possible based on the New Zealand RF/RHD Guideline GAS serology criteria¹ that would have been classified as definite using the Australian Guideline criteria (Table 1). There have been recent calls to re-examine the New Zealand GAS criteria,²⁶ which the next edition of the New Zealand RF/RHD Guideline needs to address.

The 2014 New Zealand RF/RHD Guideline’s criteria for ARF diagnosis were adjusted to include monoarthritis as a major criterion to improve sensitivity of the diagnostic criteria in the New Zealand setting.^{1,27} The application of earlier versions of the Jones criteria in high-risk settings have previously resulted in false negative diagnoses.^{18,28,29} In this audit, articular manifestations were seen in 86% of recurrences, with polyarthralgia being most commonly seen. The AHA 2015 revised Jones criteria for initial ARF³⁰ have recommended polyarthralgia as a major criterion, and monoarthralgia as a minor criterion in high-risk groups. New Zealand data is needed for this to be adopted locally.

Severity of carditis in recurrences

It is well described that recurrences of rheumatic fever result in RHD progression.^{1,7,11} This was highlighted by our

audit with at least 46% patients either developing new RHD or developing progression of pre-existing RHD. This underscores the importance of addressing the barriers to penicillin prophylaxis in New Zealand to prevent progression of RHD.

ESR data

The number of ARF recurrences reported to ESR during the audit period was 70, similar to the 65 episodes identified by this audit. This confirms that ESR data on ARF recurrences appears to be reasonably robust and can be used to monitor future trends of New Zealand ARF recurrence rates without the need for detailed chart review. This is in contrast to previously reported discrepancies of ICD discharge data, ESR data and regional registers for initial episodes of ARF.^{31,32} In part, this reflects the much higher numbers of initial episodes of ARF than recurrences of ARF.

Limitations

Only those case notes with ICD codes of ARF or RHD were reviewed in the audit. Those presentations where the differential

of ARF was considered but not coded, or not considered, would not have been captured. The details of penicillin prophylaxis prescription and adherence were limited by the audit design. We were not able to ascertain whether transition to adult services or mobility between DHBs with or without RF registers were risk factors for penicillin prophylaxis non-adherence. The progression of RHD was graded by echocardiograms at the time of ARF recurrence, therefore immediate rather than long-term RHD outcomes have been reported.

Conclusion

This audit describes the epidemiology of ARF recurrences in New Zealand. Adolescents and young adults are significantly more likely to have recurrences than children. The audit confirms that ARF recurrences often lead to progression of RHD. Systems to improve adherence to penicillin prophylaxis need to be tailored in culturally appropriate ways, and inequities between DHB could be addressed by the development of a national RF/RHD register.

Competing interests:

Dr Galloway reports affiliation with Ministry of Health during the conduct of the study.

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