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# Rheumatic Fever and Rheumatic Heart Disease:

# A National Paediatric Cardiology Centre Study Over Two Decades

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**Abstract**

*Aims*

Rheumatic fever and rheumatic heart disease remain the commonest cause of acquired heart disease in children in the developing world, but the epidemiology in Ireland is unknown. To describe the epidemiology of rheumatic fever and rheumatic heart disease over the last 16 years presenting to the National Paediatric Cardiology Centre.

*Methods*

Retrospective chart review of all children with a diagnosis of rheumatic fever and/or rheumatic heart disease presenting to the National Centre for Paediatric Cardiology, Childrens Health Ireland at Crumlin between 2004 and 2020. Evaluation of echocardiograms, laboratory investigations and clinical course of carditis.

*Results*

Seventeen cases of rheumatic fever and/or rheumatic heart disease were identified during the study period. Median age at presentation was 10 years (range, 4 to 15 years). Girls (11, 65%) were more commonly affected than boys. Carditis (88%) (mitral valve involvement) and chorea (76%) were the most common manifestations at presentation. Six of the 15 children (40%) had additional valvular disease (tricuspid, 4 and aortic, 2). Median time from symptom onset to diagnosis was 3 weeks (range, 1-20). All cases of carditis responded to medical management alone.

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*Discussion*

Rheumatic fever and rheumatic heart disease remain uncommon in Ireland but the potential for significant cardiac sequelae emphasises the importance of continued vigilance and maintenance of a high index of suspicion. In the current era, improved education is required to improve physician awareness of the clinical manifestations of rheumatic fever to ensure early cardiology referral and prompt treatment.

**Introduction**

Rheumatic heart disease (RHD) is the most common cause of acquired heart disease in children in the developing world[1]. In 2015, the estimated annual incidence was 33.4 million cases with 10.5 million disability-adjusted life years and 319,400 deaths worldwide[2]. Acute rheumatic fever (ARF), the cause of RHD, is largely a disease of the poor, usually occurring in association with overcrowding and poor sanitation[3, 4]. It is now relatively rare in developed industrialized countries, with the exception of disadvantaged populations such as indigenous peoples of Australia and New Zealand and immigrants from countries with high prevalence[4-6]. Early diagnosis and treatment are essential to prevent significant morbidity and mortality. We describe our experience of ARF and RHD in two-tertiary paediatric hospitals in Ireland.

**Methods**

Retrospective review of the paediatric infectious disease and cardiology electronic databases in Children's Health Ireland at Crumlin and Temple Street, identified children diagnosed with ARF between from January 2004 to December 2020. Diagnosis of ARF was based on the Jones criteria[7, 8]. Demographic, microbiological, biochemical, haematological and cardiac data were collected using a standardised data collection tool. This study was approved by the Ethics Committee at Children's Health Ireland at Crumlin.

**Results**

A total of 17 cases of ARF were identified over the 16-year study period (Table 1). Two-thirds (11) of the cases were females. Median age at presentation was 10 years (range, 4 to 15 years). Median time to diagnosis was 3 weeks (range 1-20 weeks). Fifteen (88%) of the cases had RHD with mitral valve involvement, isolated in nine or combined with tricuspid (4) or aortic valve (2) involvement. Two children presented with severe mitral regurgitation and were acutely unwell. None required surgical intervention.

Sydenham's chorea was the next most common presenting feature (13 children, 76%). Neurological manifestations consisted of characteristic purposeless, involuntary, non-stereotypical movements of the trunk or extremities with an associated deterioration in balance and co-ordination. Three

children also had a marked deterioration in handwriting in the weeks prior to presentation. All cases had elevated Anti-Streptolysin O and anti-DNase B titres at presentation.

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*Table 1. Acute rheumatic fever cases diagnosed between 2004-2020*

| Case | Year of presentation | Age (years) | Gender | Duration of symptoms (weeks) | ECHO findings | Chorea | WCC | CRP |
|---|---|---|---|---|---|---|---|---|
| 1 | 2005 | 6 | M | 1 | Mild-mod MR, trivial AR | No | Normal | NR |
| 2 | 2009 | 9 | M | 1.5 | Mild MR | Yes | Normal | NR |
| 3 | 2010 | 10 | F | 2 | Normal | Yes | Normal | NR |
| 4 | 2012 | 11 | F | 5 | Mild MR, mild TR | Yes | Normal | Normal |
| 5 | 2012 | 5 | F | 3 | Severe MR, LAD, mild TR | No | Normal | ↑ |
| 6 | 2012 | 8 | F | 8 | Mild MR | Yes | Normal | Normal |
| 7 | 2012 | 11 | F | 3 | Mild MR | Yes | ↑ | Normal |
| 8 | 2013 | 11 | F | 2 | Trivial MR | Yes | Normal | Normal |
| 9 | 2013 | 12 | F | 20 | Normal | Yes | Normal | NR |
| 10 | 2014 | 15 | M | 2 | Mild MR | Yes | Normal | ↑ |
| 11 | 2014 | 10 | F | 1.5 | Mild MR | No | Normal | Normal |
| 12 | 2014 | 11 | M | 1.5 | Mild MR | Yes | Normal | Normal |
| 13 | 2016 | 4 | F | 3 | Mild MR, trivial TR | Yes | Normal | Normal |
| 14 | 2016 | 10 | M | 3 | Mild MR, mild AR | Yes | Normal | ↑ |
| 15 | 2017 | 7 | F | 1 | Trivial MR | Yes | Normal | Normal |
| 16 | 2018 | 6 | M | 12 | Mild MR | Yes | Normal | Normal |
| 17 | 2020 | 11 | F | 3 | Severe MR, mild TR | No | Normal | Normal |

*AR, aortic regurgitation; CRP, C-reactive protein; LAD, Left Atrial Dilatation; MR, mitral regurgitation; NR, not recorded; TR, tricuspid regurgitation; WCC, white cell count.*

**Discussion**

Acute rheumatic fever occurs as a delayed non-suppurative complication of Group A streptococcal (GAS) pharyngitis. Signs and symptoms usually manifest an average of 18 days (range, 10 days to 5 weeks) following an episode of pharyngitis[9]. In keeping with a delayed presentation, our ARF cohort were afebrile, had elevated antistreptococcal antibody titres, and the majority had normal white cell count (16/17, 94%) and CRP (10/13, 76%) at diagnosis. All children in our study responded well to medical treatment with none requiring surgical or catheter intervention.

The true incidence of ARF in Ireland is unknown as it is not a notifiable disease. However, the present study suggests that ARF and RHD are uncommon in Ireland, with only 17 cases presenting to the National Paediatric Cardiology Centre over the 16-year study period up to 2020. As such, Irish children appear to be a low-risk population for ARF and RHD (defined as an incidence of ≤ 2 /100,000 school-aged children per year)[7].

While the average number of cases of ARF and RHD per year in Ireland is low, the frequency of ARF increased in some years (Table 1). Nine of the 17 cases (53%) presented in the three-year period from 2012-2014, with the highest number of cases presenting in 2012. 2012-2013 saw the highest annual incidence of invasive GAS disease over the 16 year study period[10]. The incidence of invasive GAS disease increased from 0.4-1.65/per 100,000 population in 2004-2011 to 2.65/100,000 in 2012 and 3.66-3.37/100,000 population in 2013-14. The largest increase and highest age-specific incidence was observed in children under the age of four years and the elderly. Interestingly, 2012 and 2013 saw significantly increased prevalence of more rheumatogenic (more likely to lead to ARF) emm1 and emm3 GAS sequence types in Ireland, the UK and Scandinavia[10-12]. Temporal changes in incidence of ARF have previously been linked to changes in the epidemiology of GAS types[13].

In the present study, carditis was the most common manifestation at presentation (15/17, 88%) followed by chorea (70%). The mitral valve was affected in all 15 cases and more than one valve was affected in six (40%). Frequency of chorea at presentation (76%) was higher than reported elsewhere (10% to 30%) and cases of large joint arthritis or arthralgia, the most common clinical presentation of ARF reported worldwide, (35%-66% of cases) were notably absent[7,14,15]. In our cohort, median time from symptom onset to diagnosis was three weeks (range, 1-20 weeks) and was more than 8 weeks in 3 children, suggesting a need for improved primary (diagnosis and treatment of GAS infection) and secondary prevention (improved medical student and healthcare professional education). An example of a comprehensive RHD control programme adapted for a population at low risk for RHD is shown in Figure 2[16].

There is no single confirmatory test for ARF; clinical diagnosis is made using the Jones Criteria (first developed in 1944) and by excluding other conditions[7]. The most recent revision of the Jones Criteria (2015) continues to require presence of two major and one minor or one major and two minor criteria and evidence of preceding GAS infection for diagnosis of ARF (Table 2). In recognition

of the disparity in global distribution of ARF and RHD, the revised Jones Criteria aims to improve specificity in low-risk populations and sensitivity in high-risk populations.

The past century has seen a dramatic reduction in the incidence of ARF in the United States and western Europe, where attention has focused on the emergence of suppurative manifestations of invasive GAS disease (necrotising fasciitis, pleural empyema and toxic shock syndrome)[13, 17-19]. The resultant lack of familiarity with ARF has led to concern that the prevalence and morbidity of RHD may be underestimated in high resource settings[2, 4]. While clinical manifestations of ARF may vary in different patient populations, the relative paucity of cases with arthritis in our cohort suggests that cases without cardiac involvement are possibly being overlooked or diagnosed later after carditis has developed[7]. In populations at low risk for ARF, such as Ireland, general practitioners and paediatricians require a high index of suspicion and knowledge of common clinical presentations of ARF (Table 3) to ensure early diagnosis, appropriate treatment, and prompt referral to paediatric cardiology.

Delay in diagnosis and referral to paediatric cardiology may result in life-altering or life-limiting chronic cardiac sequelae. Diagnosis and adequate antibiotic treatment of GAS pharyngitis is the primary means of preventing ARF[20]. Inadequate or lack of antibiotic treatment of streptococcal pharyngitis increases the risk of someone developing ARF. Thereafter, individuals with a history of ARF have an increased risk of recurrence with subsequent streptococcal pharyngeal infections[20, 21]. So children with RHD require long term cardiology follow up and antibiotic prophylaxis to prevent recurrent episodes of ARF and progression or worsening of existing RHD.

Given the current dramatic surge in suppurative complications of invasive GAS disease, in Ireland and the UK, parents, general practitioners and paediatricians should also remain vigilant and aware of the possibility of an associated increase in non-suppurative complications of GAS such as ARF[22]. Finally, the All-Island Congenital Heart Disease Network offers the opportunity to establish a patient registry and to gather prospective data across centres to further enhance understanding of the epidemiology of ARF and RHD on the island of Ireland.

*Table 2. The Jones Criteria 2015 for diagnosis of rheumatic fever in low risk populations*

| **Criteria** | **Patient population *** | **Manifestations** |
|---|---|---|
| Major | Low risk * | • Carditis<br>• Arthritis (polyarthritis only)<br>• Chorea **<br>• Erythema marginatum<br>• Subcutaneous nodules |
| Minor | | |

| | | |
|---|---|---|
| | | • Polyarthralgia<br>• Fever (>38.5°C)<br>• ESR>30mm/hr or CRP 3mg/dL<br>• Prolonged PR interval |

* Annual ARF incidence of ≤2 per 100,00 school-aged children or all-age prevalence of ≤1 per 1,000 person per years.

** Presence of chorea is an exception and is considered sufficient evidence alone for diagnosis of ARF

*Table 3: Most common clinical presentations of acute rheumatic fever **

| |
|---|
| • Large joint arthritis and/or arthralgia, usually with fever, and sometimes with pansystolic murmur of mitral regurgitation<br>• Acute fever, tiredness and breathlessness from cardiac failure, with or without joint pain and/or swelling and pansystolic murmur of mitral regurgitation<br>• Choreiform movements, commonly with behavioural disturbance but often without other manifestations<br>• Gradual onset of tiredness and breathlessness and pansystolic murmur of mitral regurgitation (indicative of cardiac failure and insidious onset of carditis) without fever or other manifestations |

* Skin manifestations (erythema marginatum and subcutaneous nodules) are less common features.

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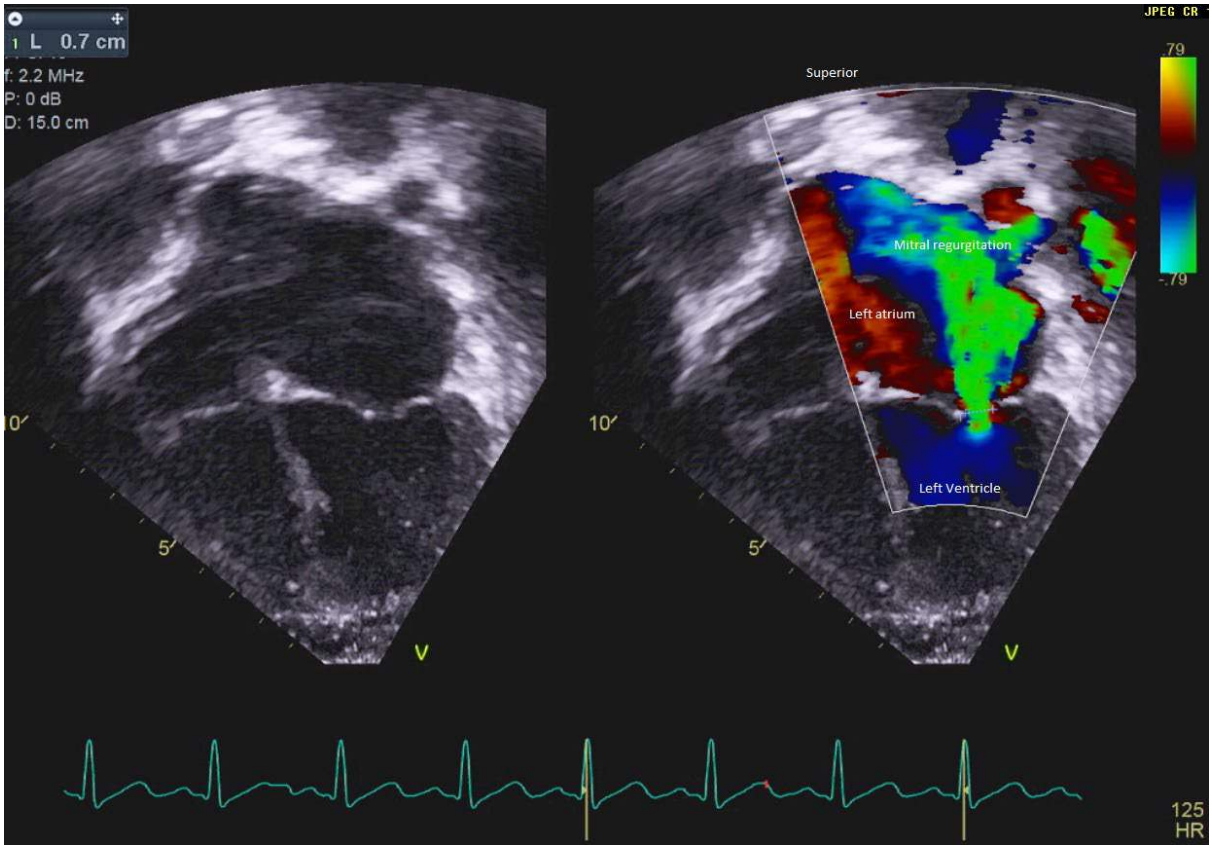


*Figure 1: Transthoracic echocardiography apical four-chamber view demonstrating thickened rolled leaflets with severe mitral regurgitation in a child presenting with rheumatic fever. Left panel shows left atrial and left ventricular dilatation on the apical four-chamber view. The right panel shows colour flow representation severe mitral valve regurgitation secondary to carditis.*

**PRIMORDIAL PREVENTION** – Developing World

- Reduction in poverty, inequality and overcrowded living conditions
- Improved access to healthcare

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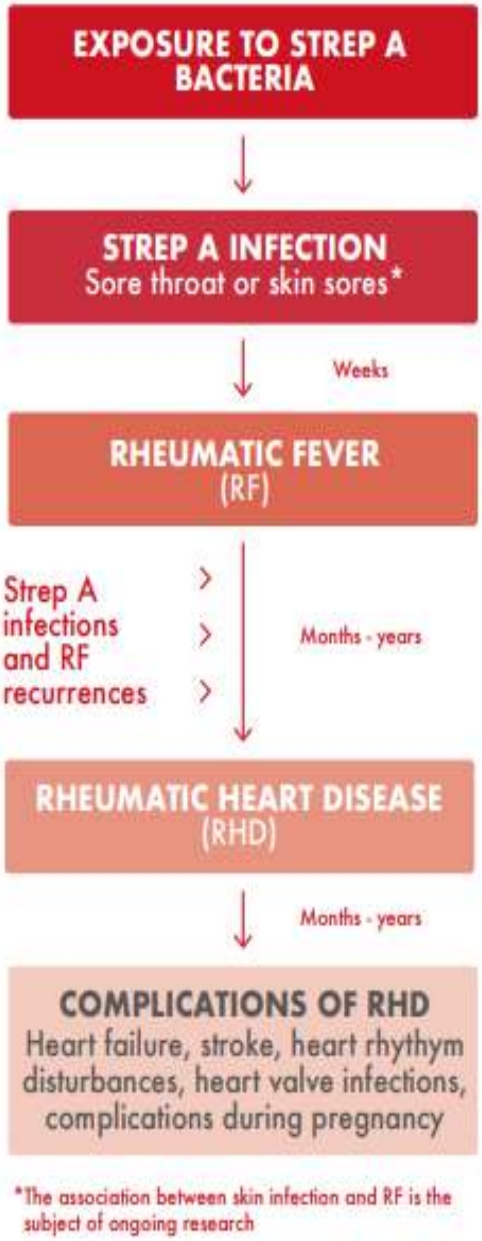


**PRIMARY PREVENTION**

- Diagnosis of GAS infection
- Appropriate antibiotic treatment
- Development of GAS vaccine

**SECONDARY PREVENTION**

- Physician and patient education to improve awareness and diagnosis of RF
- Urgent referral to paediatric cardiology
- RF and RHD patient registry
- Antibiotic prophylaxis for patients at risk of recurrent RF

**TERTIARY PREVENTION**

- Treatment of complications of RHD
- Anticoagulation
- Access to interventional cardiology and surgical intervention

*Figure 2: Opportunities for intervention in rheumatic fever and rheumatic heart disease (Adapted from Wyber et al 2014).*

**Declaration of Conflicts of Interest:**

None declared.

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