Rheumatic Fever
Getting to the heart of the matter

Andrew Kelly, WCH
• Highlight the importance of RF/RHD as a health issue, especially in our indigenous populations

• Gain understanding of the pathogenesis of the disease

• Understand the importance of accurate diagnosis

• Ensure awareness of current Australian guidelines

• Know the requirements to avoid missed diagnosis of RF
ARF Incidence (NT data)

Incidence of ARF by age in Aboriginal people (NT) 2002 - 2008
• Acute rheumatic fever (ARF) and rheumatic heart disease (RHD) occur at very high rates among Aboriginal and Torres Strait Islander people.

• In contrast, ARF is now rare in other population groups in Australia, and RHD in these groups occurs predominantly in the elderly.
### Table 4.2: Deaths from main cardiovascular conditions for Aboriginal and Torres Strait Islander peoples (a), by sex, 2002–2005(b)

<table>
<thead>
<tr>
<th>Cardiovascular condition</th>
<th>Indigenous males</th>
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<th>Indigenous females</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>No. of deaths(c)</td>
<td>SMR(d)</td>
<td>No. of deaths(c)</td>
<td>SMR(d)</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td>141</td>
<td>3.3</td>
<td>83</td>
<td>2.8</td>
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<tr>
<td>Cerebrovascular disease</td>
<td>28</td>
<td>2.1</td>
<td>33</td>
<td>1.8</td>
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<tr>
<td>Heart failure</td>
<td>4</td>
<td>2.0</td>
<td>7</td>
<td>2.4</td>
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<tr>
<td>Rheumatic fever and rheumatic heart disease</td>
<td>5</td>
<td>15.1</td>
<td>13</td>
<td>23.0</td>
</tr>
<tr>
<td>Other cardiovascular conditions</td>
<td>38</td>
<td>3.0</td>
<td>35</td>
<td>3.1</td>
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<tr>
<td>Total cardiovascular disease(e)</td>
<td>217</td>
<td>3.1</td>
<td>170</td>
<td>2.7</td>
</tr>
</tbody>
</table>

(a) Data are for Indigenous deaths for usual residents of Queensland, Western Australia, South Australia and Northern Territory.
(b) Deaths are based on year of occurrence of death for 2002–2004 and year of registration of death for 2005.
(c) Number of deaths has been averaged over the period 2002–2005.
(d) SMR (standardised mortality ratio) is the ratio of the observed number of deaths to the number of expected deaths if Indigenous Australians had experienced the same age–sex-specific death rates as non-Indigenous Australians.
(e) Components do not equal total due to rounding of averages.

*Note: All standardised mortality ratios are statistically significantly different from non-Indigenous Australians.*

*Source: AIHW National Mortality Database.*
GAS infection

ARF

Often prolonged asymptomatic period of RHD (→ screening)

RHD

Cardiac surgery

Stroke, endocarditis

Death

Primordial prevention

Primary prevention
- sore throat Rx
- ? vaccine
- ? skin sore Rx

Secondary prevention
- regular penicillin

Tertiary prevention
- heart failure meds
- surgery
- anticoagulation
‘Secondary prevention of rheumatic fever is defined as the continuous administration of specific antibiotics to patients with a previous attack of rheumatic fever, or well-documented rheumatic heart disease. The purpose is to prevent colonization or infection of the upper respiratory tract with group A beta-hemolytic streptococci and the development of recurrent attacks of rheumatic fever’.

World Health Organization, 2001
• Nearly half diagnosed with RHD - no prior history Rheumatic Fever

• Some diagnoses missed because ARF may be sub-clinical or mild

• Most misdiagnosed cases have sufficient clinical features to suggest ARF

• So, in most cases the earlier episodes were misdiagnosed
  – Reduced awareness by health workers
  – Lack of organisational memory
  – High staff turnover
  – Etc..

• Consequence of missed diagnosis – failure to deliver Penicillin prophylaxis for prevention of further episodes of RF, which may prevent subsequent development of RHD
Girl age 8Y - Pt Augusta, SA

3 days
  – Feeling unwell
  – Lethargy
  – Fever
  – Loss of appetite
  – Sore throat
  – Chest and neck pain

Examination
  – Reddened throat
  – Lymphadenopathy
  – School sores
  – Normal cardiac and respiratory examination
  – No arthritis
CXR unremarkable
ECG first degree heart block

Fevers, Arthralgia
CRP 180, wcc 22, Neut 18
Troponin NEG
Strep serology and throat swab sent
Echocardiogram done
• Streptococcal serology POSITIVE

• ARF & RHD diagnosed
  – Treatment with Penicillin
  – Patient and family education commenced
  – First dose IM Penicillin
  – Appropriate community health FU
  – Cardiology FU
  – RHD Register
  – Infective endocarditis prevention
Girl age 13Y - Oodnadatta, SA

New presentation, Jan 2014

- Heart failure
- Myocardial ischemia (ECG, Troponin elevation)
- Shock
- Acute Liver failure
Other Ix

- Lactate 8.9
- Troponin 175 -> 359
- GGT 130
- AST 561 -> 9356
- ALT 221 -> 2954
- INR 7.1
- Heart failure, shock and multi-organ failure
- Severe valvular heart disease
- Rheumatic, acute on chronic

- Managed in Intensive care WCH
- Transferred to Royal Children’s Hospital in Melbourne for cardiac surgery
- Mitral and aortic valve repair
3 Yrs ago

Fever & migratory arthritis

- Workup revealed no clear cause for this
- CRP 100
- ASOT 300, anti-DNAseB 400 (borderline)
- Diagnosed was Idiopathic juvenile arthritis
Opportunities for diagnosis of RHD

• During episode of ARF
• Detection of incidental murmur
• Presentation with heart failure symptoms
• Screening program or study
• Incidental finding on echo
• High index of suspicion in high risk populations and regions
Acute Rheumatic Fever

- GAS is a common infective agent in children that causes a wide range of clinical disease
- ARF: GAS -> autoimmune response against cardiac, synovial, subcutaneous, epidermal, neuronal tissues
- Multi-system disease
- Multiple different ways of presenting
- No diagnostic laboratory test for ARF
- Largely still a clinical diagnosis
Approaches to diagnosis

Jones criteria – 1944

Major manifestations
  Carditis
  Polyarthritis
  Sydenham’s chorea
  Erythema marginatum
  Subcutaneous nodules

Minor manifestations
  Fever
  Arthralgia
  Elevated acute phase reactants
  Prolonged PR interval
Variations with 1992 Jones criteria, 2003 WHO criteria and previous Australian guidelines

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<tbody>
<tr>
<td>Carditis</td>
<td>Major</td>
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<tr>
<td>Subclinical carditis</td>
<td>n/a</td>
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<td>Prolonged P-R interval</td>
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<td>Polyarthritis</td>
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<td>Polyarthralgia</td>
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<td>Aseptic mono-arthritis</td>
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<td>Monoarthralgia</td>
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<td>Subcutaneous nodules</td>
<td>Major</td>
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<td>Sydenham’s chorea</td>
<td>Major</td>
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<td>Erythema marginatum</td>
<td>Major</td>
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<td>Fever</td>
<td>Minor</td>
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<td>Inflammatory markers</td>
<td>Minor</td>
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<td>Evidence of recent streptococcal infection</td>
<td>Required</td>
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<td>Changes from previous guidelines (in red)</td>
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<td><strong>Definite initial episode of ARF</strong></td>
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<td>2 major or 1 major and 2 minor manifestations</td>
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<td>plus</td>
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<td>evidence of a preceding GAS infection†</td>
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<tr>
<td><strong>Definite recurrent attack of ARF in a patient with known past ARF or RHD</strong></td>
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<td>2 major or 1 major and 1 minor or 3 minor manifestations</td>
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<td><strong>Probable ARF (first episode or recurrence)</strong></td>
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<td>A clinical presentation that falls short by either one major or one minor manifestation, or in the absence of streptococcal serology results, but one in which ARF is considered the most likely diagnosis. Such cases should be further categorised according to the level of confidence with which the diagnosis is made:</td>
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<tr>
<td>• highly-suspected ARF</td>
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<td>• uncertain ARF</td>
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<td><strong>Major manifestations</strong></td>
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<td>Carditis (including evidence of rheumatic valvulitis on echocardiogram)</td>
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<td>Polychondritis or aseptic mono-arthritis or polyarthritis‡</td>
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<td>Chorea¥</td>
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<td>Erythema marginatum§</td>
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<td>Mono-artralgia</td>
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<td>Fever†</td>
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<td>ESR ≥30 mm/h or CRP ≥30 mg/L</td>
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<td>Prolonged P-R interval on ECG⁰</td>
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</table>
Diagnosis of ARF

- **Evidence for recent Strep infection**
  - Positive culture of GAS from throat
  - Increase in Streptococcal antibody

- Clinical assx of tonsillitis lacks sensitivity and specificity
- Other causes of tonsillitis, eg viruses
- When ARF first suspected only 25% positive throat culture for GAS
- 3 wk latent period

- Increase in ASOT in >80% patients with GAS tonsillitis
- Adding anti-DNaseB titre improves sensitivity to ~95%
- Streptococcal antibody tests are preferred to throat culture
ARTHRITIS
A swollen and hot joint with pain on movement

• Most common presenting symptom

• Usually asymmetrical & migratory

• Large joints - knees, ankles, elbows and wrists most frequently

• Extremely painful

• Very responsive to Aspirin/NSAIDs

• Virtually never results in permanent joint deformity
ARTHRITIS

• ARF should always be considered in patients presenting with arthritis in high risk populations

• Patients with sterile joint aspirates should never be treated speculatively for septic arthritis without further investigation

• Simple falls and minor trauma rarely cause joint effusions

• In high-risk populations in Australia mono-arthritis or polyarthralgia are a common manifestation of ARF, and are often associated with carditis
CARDITIS

- Inflammation of myocardium, endocardium and pericardium
- Predominantly inflammation of heart valves
- MV in 90%
- Mitral regurgitation predominant lesion
- Mitral stenosis in ~25% in adolescence/adulthood
- Associated with increased mortality
- Aortic valve involvement also common
- Right-sided heart valves are rarely affected
- Variable severity and timing
- Chronic valve damage
  - Most likely when first attack severe and in young patient
  - With recurrent ARF
• Clinical findings of carditis
  – significant murmur
  – cardiac enlargement
  – cardiac decompensation
  – pericardial friction rub or effusion

• Sub-clinical evidence of valvulitis on echocardiogram is considered a manifestation of carditis in Australia
  ie. carditis that is silent on auscultation, but detectable by echocardiography

• Less common presentation of rheumatic carditis is the so-called ‘insidious onset’ or ‘indolent’ carditis. subacute illness of several weeks in children aged less than 6 years with mild or no fever, few joint symptoms and relatively severe cardiac involvement
Echocardiography

- Highly sensitive - detect any valvular lesion
- More sensitive and specific than auscultation
- Ability to diagnose subclinical RHD
- It is recommended that all patients with suspected or definite ARF should undergo echocardiography
- Serial echo for diagnosis or follow up
- Change in severity of valve lesions, chamber dimensions, left ventricular function
- Assessment of LV systolic function
- Timing of intervention
Access to echocardiography

- All RHD patients in Australia should have access regardless of location
- Portable echo has improved access enormously
- Possible role for handheld echo – even smaller and cheaper
- Still requires training and expert interpretation
Table 3.9 Minimal echocardiographic criteria to allow a diagnosis of pathological valvular regurgitation (from WHF guidelines\textsuperscript{198})

<table>
<thead>
<tr>
<th>Pathological MR (all four Doppler criteria must be met)</th>
<th>Pathological AR (all four Doppler criteria must be met)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Seen in 2 views</td>
<td>1. Seen in 2 views</td>
</tr>
<tr>
<td>2. In at least one view jet length 2 cm\textsuperscript{*}</td>
<td>2. In at least one view jet length \geq 1 cm\textsuperscript{*}</td>
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<tr>
<td>3. Peak velocity \geq 3 m/sec</td>
<td>3. Peak velocity \geq 3 m/sec</td>
</tr>
<tr>
<td>4. Pan-systolic jet in at least one envelope</td>
<td>4. Pan-diastolic jet in at least one envelope</td>
</tr>
</tbody>
</table>

\textsuperscript{*}A regurgitant jet length should be measured from the vena contracta to the last pixel of regurgitant colour (blue or red) on non-magnified (non-zoomed) images.

AR, aortic regurgitation; MR, mitral regurgitation.
Screening??

World Heart Federation criteria for echocardiographic diagnosis of rheumatic heart disease—an evidence-based guideline

Bo Reményi, Nigel Wilson, Andrew Steer, Beatriz Ferreira, Joseph Kado, Krishna Kumar, John Lawrenson, Graeme Maguire, Eloi Marijon, Mariana Mirabel, Ana Olga Mocumbi, Cleonice Mota, John Paar, Anita Saxena, Janet Scheel, John Stirling, Satupaitea Vialli, Vijayalakshmi I. Balekundi, Gavin Wheaton, Liesl Zühlke and Jonathan Carapeti

The NEW ENGLAND JOURNAL of MEDICINE

Prevalence of Rheumatic Heart Disease Detected by Echocardiographic Screening

Eloi Marijon, M.D., Phalla Ou, M.D., David S. Celermajer, Ph.D., F.R.A.C.P., Beatriz Ferreira, M.D., Ph.D., Ana Olga Mocumbi, M.D., Dinesh Jani, M.D., Christophe Paquet, M.D., M.P.H., Sophie Jacob, Ph.D., Daniel Sidi, M.D., Ph.D., and Xavier Jouven, M.D., Ph.D.
Echocardiographic Screening for Rheumatic Heart Disease in High and Low Risk Australian Children

Kathryn Roberts, MBBS, BmedSci, FRACP, MPH&TM; Graeme Maguire, BMedSc, MBBS, FRACP, MPH&TM, PhD; Alex Brown, BMed, MPH, FCSANZ, FRACP (hon), PhD; David Atkinson, MBBS, MPH; Bo Reményi, MBBS, FRACP; Gavin Wheaton, MBBS, FRACP, FCSANZ; Andrew Kelly, MBBS, FRACP, FCSANZ; Raman K. Kumar, MD, DM; Jiunn-Yih Su, MB, MPH; Jonathan R. Carapetis, MBBS, FRACP, FAFPHM, PhD

(Circulation. 2014;129:1953-1961.)
Sydenham’s chorea

• Involuntary, jerky, uncoordinated movements

• Especially affecting the hands, feet, tongue and face

• Useful signs
  – the ‘milkmaid’s grip’
  – ‘spooning’
  – the ‘pronator sign’
  – inability to maintain protrusion of the tongue

• Relatively common in Australia

• May occur after a prolonged latent period following GAS infection

• The vast majority of cases resolve within 6 months

• Higher prevalence of attention-deficit hyperactivity disorder, anxiety, depression and cognitive dysfunction
Subcutaneous nodules

- Very rare
- 0.5 to 2 cm in diameter
- Painless, firm, movable
- Crops of up to 12
- Elbows, wrists, knees, ankles, Achilles tendon, occiput, posterior spinal processes of vertebrae
- They tend to appear 1–2 weeks after the onset of other symptoms, last only 1–2 weeks (rarely more than 1 month)
- Usually associated with severe carditis
Erythema marginatum

- Rare
- Bright pink macules or papules
- Blanch under pressure and spread outwards in circular or serpiginous pattern
- Difficult to detect in dark-skinned people
- Not itchy or painful
- Occur on the trunk and proximal extremities
- May be induced by application of heat, after showering
Minor manifestations

• Arthralgia.

• Fever

• Elevated acute phase reactants

• Prolonged PR interval & other rhythm disturbances
Current Australian guideline (2012)

www.rhdaustralia.org.au

Online and phone app versions available
Current Australian guideline (2012)

- Overview of ARF and RHD
- Primordial and primary prevention
- Diagnosis & management of ARF
- Guidelines for secondary prevention
  - What to do during preg
  - Factors that affect the duration of sec proph
  - Advice on how to improve adherence
  - How to decrease the pain of the needles...
  - Recommended routine review and structured care planning
  - Organisational approaches to secondary prevention
- Diagnosis and management of RHD
Getting to the heart of the matter

• Acute rheumatic fever (ARF) and rheumatic heart disease (RHD) occur at very high rates among Aboriginal and Torres Strait Islander people

• Importance of accurate diagnosis is clear

  Overdiagnosis -> unnecessary BPG over many yrs

  Underdiagnosis -> further attacks of ARF, cardiac damage, morbidity, premature death
Requirements to avoid a missed diagnosis of RF

• Awareness of the persistence of the disease in the Aboriginal population

• Awareness of current diagnostic criteria

• Knowledge of the revised Jones criteria

• Important that health staff receive appropriate education about ARF before remote postings

• Knowledge of the need to obtain evidence of Streptococcal infection

• Streptococcal antibody tests are preferred to throat culture

• All patients with suspected ARF should be admitted to a hospital for specialist paediatric review and echocardiography
Thank you
GAS infection

ARF

RHD

Cardiac surgery

Stroke, endocarditis

Death
June 2013

Transferred from Pt Augusta Hospital to Adelaide
?appendicitis

- Abdominal pain, fever
- Normal CVS exam and CXR normal
- Abdo u/s normal
- Improved following day: “physical exam, bloods & u/s did not suggest a surgical cause”
- Diagnosis: “non-specific abdominal pain and fever”
- Discharged

- CRP 300??
GAS infection

ARF

RHD

Cardiac surgery

Stroke, endocarditis

Death
Rheumatic Fever

Autoimmune disease precipitated by infection with the group A Streptococcus (GAS) bacterium
Group A Streptococcus

Common infective agent in children

- Superficial infection
- Invasive infections
- Toxin-mediated disease
- Post infectious - rheumatic fever