Superficial Consults

Infectious Diseases

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Infectious Diseases Fellow
**M. ulcerans**

- Bairnsdale, Buruli, Daintree Ulcer
- Victoria – Changing epidemiology – Westward march
  - Bairnsdale & Phillip Island
  - Queenscliff & Point Lonsdale
  - Frankston & Mornington Peninsula
- 157 cases in 2011-2012
- In Victoria
  - Epidemiological link to possums
  - *M. ulcerans* isolated from mosquitos
- Long incubation period
**M. ulcerans - Clinical**

- **Location:** exposed limbs
  - Lower limb > upper limbs
- **Starts as a small papule**
  - Nodular, ulcerative and oedematous forms
  - Ulceration and surrounding erythema
  - Undermined edge
  - Rarely invades deep structures, bones
- **Diagnosis**
  - Ulcer – PCR highly sensitivity
  - Biopsy not often required, useful if papules
• **Shift from surgical excision to antibiotics**
  – Avoids need for extensive grafting
• **Rifampicin + clarithromycin at least 8 weeks**
• **Paradoxical Reactions** in 20%
  – Do not represent a failure of treatment
  – Prednisolone for severe reactions
• **Surgery**
  – Not required for cure
  – Previous trend to excise ulcer and surrounding erythematous area
  – Indicated when Abx declined or not tolerated
  – Risk of relapse when surgery is performed without adjuvant antibiotics
Clinical Bottom Line: Sheath the Scalpel

• Think of M ulcerans in chronic non-healing skin lesions
  – Undermined edge
  – Usually solitary, on exposed limbs
  – Test surface PCR

• Treatment - Antibiotics
Diagnostic tests for EBV - Monospot

- **Monospot**: Heterophile antibody test
  - Serum -> Horse blood -> agglutination
- Sensitivity 70%, varies with age:
  - 90% of adolescents/adults
  - <50% in children less than 4 years
- Specificity >95%
  - False positive – CMV, toxoplasmosis, rubella, leukaemia, lymphoma
- May not be detectable until 2nd week of illness
- Persistence 1-2 months but up to one year
  - May not always indicate acute EBV infection
- Poor negative predictive value
- Good positive predictive value in older children and adolescents
Diagnostic Tests for EBV - serology

VCA IgM
• Fall at 3-4 weeks

VCA IgG
• As early as 2 weeks
• Persistent

• IgM Cross reactivity
  • Eg CMV

Specific serology: useful if monospot negative and clinical picture not consistent with typical acute EBV infection
Further Investigations

- FBE - WC 10, Lymphocytes 4.5 (<3.6)
  - Platelets - NORMAL
- Blood Film WC 10, Lymphocytes 4.5 (<3.6)
- Hepatitis ALT 396 ALP 221 GGT 105
- Urinalysis - NORMAL
- Skin Biopsy
  - Lichenoid Lymphocytic Vasculitis
  - No eosinophils, or neutrophilic infiltrate
  - IgA staining negative
  - “drug or viral reaction “
EBV + Rashes

• Rash in 5-10%
  – Macular, petechial, scarlatiniform, urticaria, EM
  – Spares extremities
  – 1-6 days

• Rash with EBV and amino-penicillins 90-100%
  – More severe and generalised
  – Torso, face extremities
  – 7-10 days after medication given
Genesis - EBV + amoxicillin = rash as a “diagnostic test”
Is rash with EBV + Abx really that common?

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Total Treated</th>
<th>Antibiotic-Induced Rash</th>
<th>Rate, %</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td>35</td>
<td>3</td>
<td>8.57</td>
<td>1.80–23.06</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>61</td>
<td>18</td>
<td>29.51</td>
<td>18.52–42.57</td>
</tr>
<tr>
<td>Amoxicillin + clavulanate</td>
<td>45</td>
<td>7</td>
<td>15.56</td>
<td>6.49–29.46</td>
</tr>
<tr>
<td>Cephalosporins</td>
<td>65</td>
<td>10</td>
<td>15.38</td>
<td>7.63–26.48</td>
</tr>
<tr>
<td>Macrolides</td>
<td>33</td>
<td>3</td>
<td>9.09</td>
<td>1.92–24.33</td>
</tr>
</tbody>
</table>

EBV + no antibiotics → Rash 23%
EBV + amoxicillin → Rash 29%

*Antibiotic induced rash far less common than previously thought*
Other complications of EBV

**Immune thrombocytopenic purpura**
- Associated with EBV
- May be slower to resolve if EBV associated

**Henoch Schnolein Purpura**
- Describe as association with EBV
- Typically preceded by URTI
The spectrum of EBV associated disease

Although the associations of EBV with many of the putative complications are intriguing both individually and in toto, for many complications, the small numbers of cases studied, the limitations of the methodologies and analyses employed, and, in some instances, reports of contradictory findings, often result in inconclusive evidence to confirm a causal relation to EBV. There

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**Table 1**

<table>
<thead>
<tr>
<th>Diseases</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLE</td>
<td></td>
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<tr>
<td>Antioabody production</td>
<td></td>
</tr>
<tr>
<td>Increased risk of EBV infection</td>
<td></td>
</tr>
<tr>
<td>JIA</td>
<td></td>
</tr>
<tr>
<td>Complications from medication</td>
<td></td>
</tr>
<tr>
<td>Henoch-Schönlein</td>
<td></td>
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<tr>
<td>Small-vessel</td>
<td></td>
</tr>
<tr>
<td>Polyarteritis</td>
<td></td>
</tr>
<tr>
<td>Kawasaki disease</td>
<td></td>
</tr>
<tr>
<td>Recurrent</td>
<td></td>
</tr>
<tr>
<td>Patients</td>
<td></td>
</tr>
<tr>
<td>ITP</td>
<td></td>
</tr>
<tr>
<td>Platelet</td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
</tr>
<tr>
<td>HLH</td>
<td></td>
</tr>
<tr>
<td>Renal involvement</td>
<td></td>
</tr>
<tr>
<td>Organ transplant</td>
<td></td>
</tr>
<tr>
<td>Skin manifestations</td>
<td></td>
</tr>
<tr>
<td>Treatment options</td>
<td></td>
</tr>
<tr>
<td>Genetics/Gene studies</td>
<td></td>
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<tr>
<td>T cell populations</td>
<td></td>
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<tr>
<td>Cytokines/Signaling pathways</td>
<td></td>
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<tr>
<td>Apoptosis</td>
<td></td>
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<tr>
<td>Perforin/Granzyne B</td>
<td></td>
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<tr>
<td>Macrophage activation syndrome</td>
<td></td>
</tr>
<tr>
<td>EBV = Epstein-Barr virus; HLH = Hemophagocytic lymphohistiocytosis; ITP = Immune thrombocytopenic purpura; JIA = Juvenile idiopathic arthritis; KD = Kawasaki disease; SLE = Systemic lupus erythematosus.</td>
<td></td>
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</table>
Clinical bottom line

• A florid presentation of a common condition
• EBV +/- amoxycillin
  – Although this is less common than previously thought
Melbourne
1936 -1942

→ 645 cases of ARF

“Its onset in the young may be insidious and it is frequently overlooked because of the vague and indefinite nature of the symptomatology”
## Jones Criteria 1992

<table>
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<tr>
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</tr>
<tr>
<td>Polyarthritis</td>
</tr>
<tr>
<td>Chorea</td>
</tr>
<tr>
<td>Subcutaneous nodules</td>
</tr>
<tr>
<td>Erythema marginatum</td>
</tr>
</tbody>
</table>

**Major Criteria:**
- Carditis
- Polyarthritis
- Chorea
- Subcutaneous nodules
- Erythema marginatum

**Minor Criteria:**
- Fever ≥39°C
- Positive throat swab or rapid test
- Polyarthralgia
- Elevated streptococcal antibody titres
- Elevated acute phase reactants
- Prolonged PR interval on ECG
- Erythema marginatum
Improving diagnosis

Adaptation of the guidelines for endemic regions

The Australian guideline for prevention, diagnosis and management of acute rheumatic fever and rheumatic heart disease (2nd edition)
### Improving diagnosis

**Adaptation of the guidelines for endemic regions**

<table>
<thead>
<tr>
<th>Major Symptoms</th>
<th>Additional Diagnoses</th>
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<tr>
<td>Carditis</td>
<td>&quot;Subclinical&quot; carditis (echocardiogram)</td>
</tr>
<tr>
<td>Polyarthritis</td>
<td>Mono-arthritis</td>
</tr>
<tr>
<td></td>
<td>Reported arthritis</td>
</tr>
<tr>
<td>Chorea</td>
<td></td>
</tr>
<tr>
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National Heart Foundation ARF RHD Guidelines 2012
Improving diagnosis

Adaptation of the guidelines for endemic regions

<table>
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<tr>
<th>MINOR</th>
<th>Fever ≥39°C</th>
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National Heart Foundation ARF RHD Guidelines 2012
The region as a hotspot for ARF

Incidence rheumatic fever per 100,000

Pacific Islanders 81
Maori 40
Other 2

Milne J Paed Child Health 2012
Parnaby J Paed Child Health 2010
National data 2007-2010 – 151 cases
-131 ATSI
-8 Pacific Islander
-10 Caucasian
There is “no doubt that ARF is more common outside the remote Indigenous populations than previously thought”

• *Non-Indigenous children* with ARF cf. high risk groups:
  • more likely to have highly specific features
  • Higher streptococcal titres in low risk children in urban areas

*However*

The clinical characteristics of ARF are in fact stable between different populations
Therefore

“When children preset with features of possible ARF in regions or from populations not normally at high risk of ARF, clinicians may be only diagnosing the most obvious cases and a probably missing milder or atypical cases”

Lost Opportunities for secondary prophylaxis against Rheumatic Heart Disease
Target Lesions

• Typical target lesions
  – dusky central area or blister,
  – dark red inflammatory zone surrounded by a pale ring of edema,
  – erythematous halo on the extreme periphery

• Atypical target lesions
  – raised, edematous, palpable lesions
  – two zones of color change and/or a poorly defined border
Recurrent Erythema Multiforme

No evidence of infectious trigger here but could still be infectious...

• Various causes, however 60-90% related to HSV

• Usually HSV PCRs negative at time of EM
A double-blind, placebo-controlled trial of continuous acyclovir therapy in recurrent erythema multiforme


Reduced recurrence of HSV associated Recurrent EM AND also when no evidence of preceding HSV

Idiopathic REM
• HSV-DNA in tissue from ~50% of idiopathic REM
• consider trial of suppressive antivirals
• Less promising response to antivirals in other retrospective cohorts
• Often requires immunosuppressive therapy
Dog Tape Worm
Dipylidium caninum
Dipylidium caninum

The life cycle of Dipylidium caninum involves infected fleas and can be transmitted from animal to human. The infected fleas contain cysticercoid larvae that can be ingested by humans, leading to infection. The adult worms reside in the small intestine, and gravid proglottids are passed intact in the feces or emerge from perianal region of either animal or human hosts.
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