Myasthenia Gravis Testing
Reliance on Pathology as Proof

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Immunopathology Track
MG

• Acetyl-choline receptor is major target
  – Associated proteins intracellularly
  – MuSK, LRP-4, agrin

  – Thymoma associated antibodies
    • Skeletal muscle
      – Ryanodine receptor
      – Titin
      – Kv1.4
AChR Abs

• Looked on as proof of MG

• RSR used as default antigen source
• Mix of epsilon (adult) and gamma (foetal) AChR

• Data Sheet 98% specificity (blood donors)
• Sensitivity: ~80%, higher if generalised disease and better clinicians
Background

RIA:
-slow (takes a working day)
-can work on 2 other assays for that day
-not a job for junior scientists

- 400 requests per week

- An level of automation would be useful
2010

• ELISA -1 was evaluated

• Initial evaluation promising
  – Overnight incubation
  – Sensitivity 100% cf AChR
  – Specificity 95%

• BUT
The new lot arrived

- High background
- Negative control failed
- QC failed
- Lack of repeatability
- High results unexplained

- Manufacturer blamed us.
• We has almost three months without testing
• We are referral lab for all of Sonic, also QH for AChR
Five Years Later

- ELISA-2 Different manufacturer

- Re-evaluated

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<th>ACR Ab</th>
<th>True Results</th>
<th>False Results</th>
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<td>Positive</td>
<td>Negative</td>
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<td>Ria</td>
<td>45</td>
<td>124</td>
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<tr>
<td>ELISA</td>
<td>45</td>
<td>121</td>
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- Some samples re-evaluated indeterminable which was correct answer: excluded but in retrospect may have been incorrect
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• ELISA assay rolled out
• Letters to all neurologists and referring labs
• Letters to interstate referring labs just went to other labs not referrers
9 months later

- A gestation that lead to a monster

- Discussion with a learned colleague (and research collaborator, and friend)

- Seeing referrals for ?MG
  - Treated as MG on basis of test despite low clinical suspicion
• Assay results
• Slight increase in numbers of high positive (>8) results over time
• No pattern

• All samples re-tested RIA all neg
• Clinically patients had no MG
Samples sent overseas: manufacturer

• Samples negative

• Repeatedly positive here

• ?Transport issue
Had changed back

- Back log of tests
- Repeated all positives
- Letters to neurologists and referrers affected
- Communication to referrers
- Reputational risk management
Issue not resolved

- Manufacturer admits issue is ongoing
- They don’t know the basis
- Performs well in UKNEQAS
Points

• Clinicians think differently to you

• No test is proof

• Contact referrers before (and after if there is one)

• Admit fault and rectify
  – Risk Management