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PATHOLOGY



# 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

ACR Ab	True Results		False Results	
	Positive	Negative	Positive	Negative
Ria	45	124	0	0
ELISA	45	121	3	0

- Some samples re-evaluated indeterminable which was correct answer: excluded but in retrospect may have been incorrect



ACR Ab	True Results		False Results	
	Positive	Negative	Positive	Negative
Ria	45	124	0	0
ELISA	45	121	3	0

- 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