Congenital Myasthenia: Overview

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Congenital Myasthenic Syndromes

• Greek – “Myasthenia,” “Muscle weakness”

• Fatiguability- Weakness worsens during period of activity

• Fluctuation- Good days & Bad days
• **Rare:** Prevalence: 3.8 per million in UK

• Inherited disorders

• >20 genes

• >300 Mutations (Mutation = Change in a gene)
CMS: Sweets

Genes: M&Ms

Mutation: Variety
Neuromuscular Junction

PRESYNAPTIC

SYNAPTIC

POSTSYNAPTIC
Signal ‘Traffic’ at the NMJ
Presynaptic

- CHAT: Impaired Ach synthesis
- Ach Deficiency
- Breathing Difficulties
- Poor Swallow.
- Usually apparent from birth
- Pyridostigmine and 3, 4-DAP
Synaptic

- COLQ: Loss of AChE
- Prolonged lifetime of Ach
- Too Much Stimulation
- Weakness from birth/infancy
- Breathing difficulties
- Weakness of muscles that move eyes
- Salbutamol or Ephedrine
Postsynaptic

- AChR deficiency
- Usually ε subunit
- Presents at Birth or infancy
- Feeding problems
- Drooping of eyes
- Eye Muscles
- Pyridostigmine +/- 3,4 DAP
Postsynaptic continued...

- **DOK7, MUSK, AGRIN**

- AchR clustering & folding of the muscle surface

- Deterioration in walking

- Limb girdle weakness

- Worsened by Pyridostigmine

- Salbutamol or ephedrine
Postsynaptic continued....

- Rapsyn
- AChR Clustering protein
- Onset at birth
- Respiratory crises
- Poor Feeding, Joint contractures
- Pyridostigmine +/- 3,4 DAP
Postsynaptic continued...

- Slow channel syndrome
- Prolonged AChR Channel opening
- ‘Signal overload’
- Age of onset variable
- Neck flexion weakness
- Difficulty running
- Fluoxetine or Quinidine
Fast channel syndrome

- **Severe**, onset at birth
- Resp Crises, poor feeding
- Droopy eyes & eye muscles weak
- Breathing difficulties
- Pyridostigmine +/- 3,4 DAP
Glycosylation Defects
Glycosylation Defects = Assembly Defect
Glycosylation CMS: Clinical Features

- Delayed/Later onset
- Limb-girdle muscle weakness
- No weakness muscles that move eyes
- No swallowing problems
- Lack of exacerbations
- Clinical course stable
No ‘one size fits all’ Treatment.

- Patient-tailored approach
- Pyridostigmine
- 3,4 DAP
- Salbutamol
- Ephedrine
- Quinidine/Fluoxetine
Treatments continued: Multidisciplinary

- Physiotherapy
- Respiratory Care eg. NIV, Prophylactic antibiotics.
- Dietary modifications
- Speech & Language therapy
- Orthopaedic
- Education re: practical issues
- Ophthalmological interventions
- Pre Op precautions
Thank You!