New Developments in Pediatric Myasthenia Gravis

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Disclosures

- None relevant

- No currently FDA approved therapies approved for children with MG

Overview

1. Myasthenia gravis (MG)
2. Neonatal (acquired) MG
3. Congenital MG

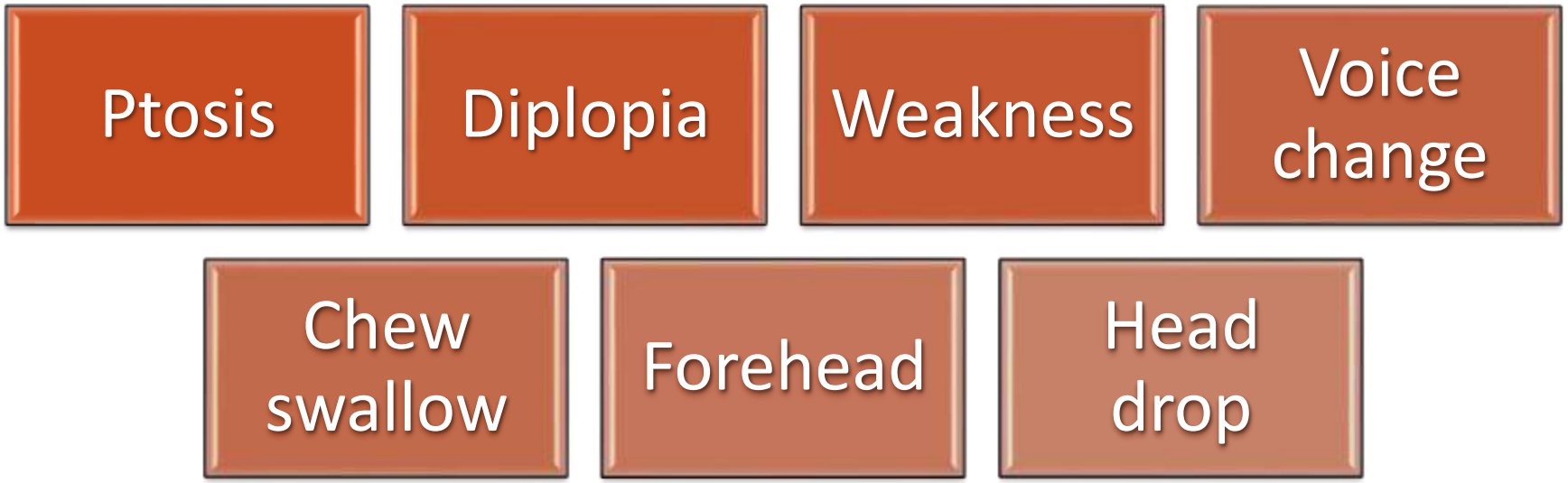
Case in point

- You see a 12-year-old girl in your office. Her mother reports that she has recently been having drooping eyelids and double vision. She is also complaining of increased fatigue. On warm days, she also notes a little bit of difficulty going up and down the stairs.

Myasthenia Gravis

- An acquired disorder moreso in younger children (when looking at just under 18), but occurs at any age

- **Fatiguing** (or fluctuating) weakness



Features

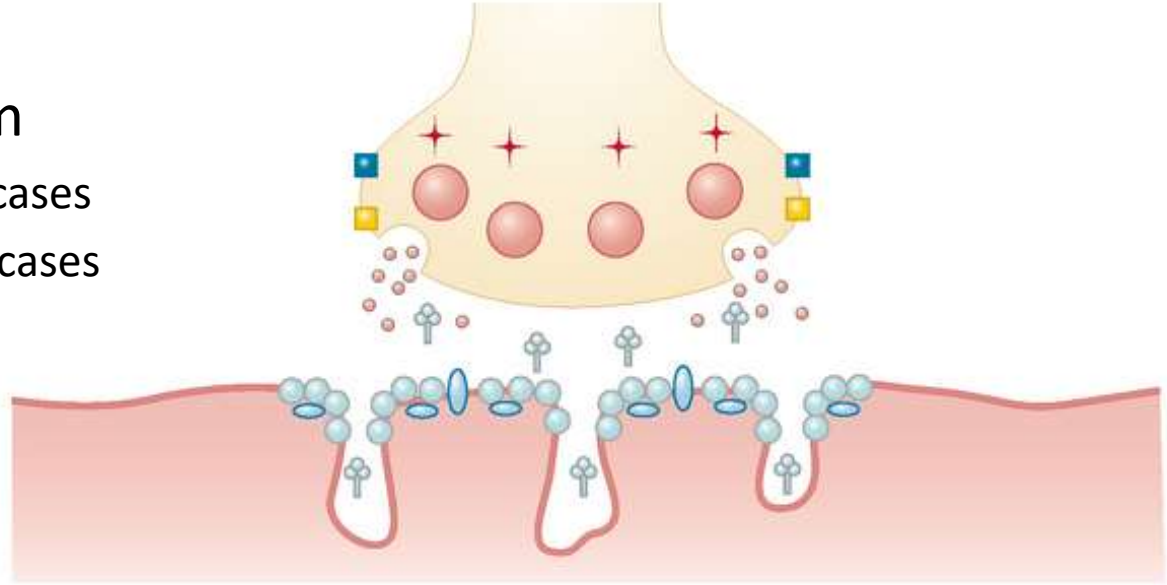
- Affects ~ 1/10,000 individuals, ~ 1 per million under age 18
- Peak ages 30 years (F>M) and 50 (M=F) [bimodal]
- Juvenile: prepubertal > pubertal, F>M
- More common ocular presentation

Dedicated Neuromuscular Physical examination

- Eyes
  - Full range of motion
  - Cogan's sign
  - facilitated ptosis
  - *pupils never involved* - not nicotinic receptors
- Face
  - Puff cheeks, hold air
  - Count 1-50 in a single breath
- proximal weaker than distal muscles
- specific muscles: triceps (can't do push-ups), neck extensors (head drop), diaphragm
- standing from a seated position without using hands
- give-away quality to weakness

Pathophysiology

- action potential triggers synaptic vesicle to release ACh into synaptic space
- ACh binds acetylcholine receptor
- requires multiple miniature end plate potentials (EPP) to depolarize post-synaptic membrane
- one quanta (7-10,000 molecules of ACh) elicits one EPP
- AChR antibody prevents ACh binding
- humoral immune-mediated mechanism
  - acetylcholine receptor antibody in up to 90% of cases
  - muscle specific kinase (MuSK) antibody in 1% of cases
  - titin antibody
  - lipoprotein-related protein 4 (LRP4)
  - clustered AChR in 3.8% cases



https://neupsykey.com/neuromuscular-junction-disorders/

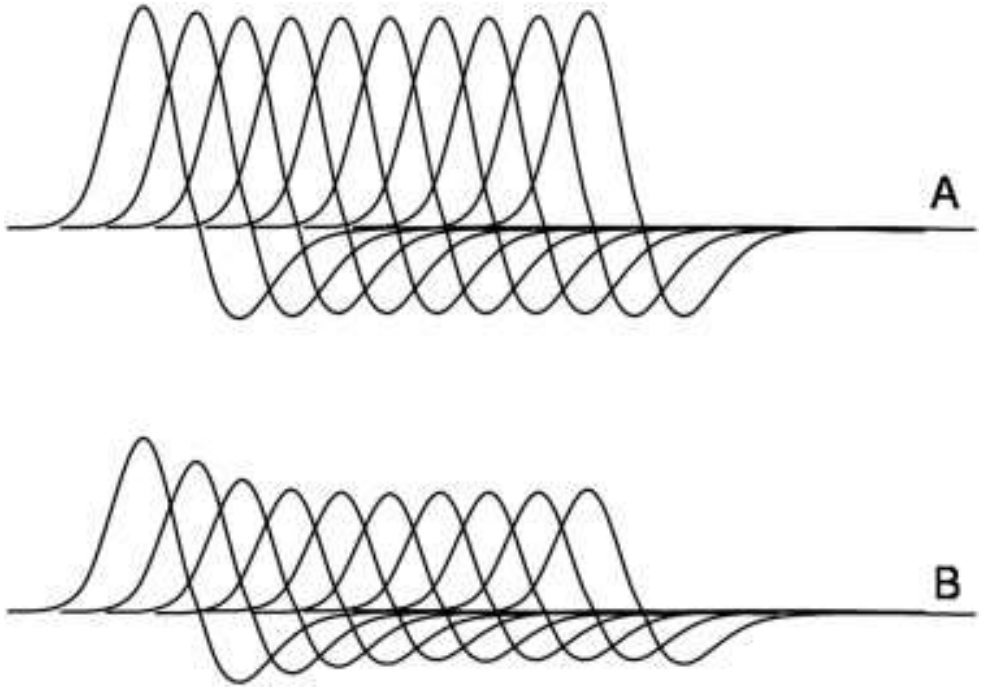
Diagnosis

- old days - hot bath test
- ice pack test 2 minutes - cold improves ptosis
- Tensilon test (IV edrophonium)
- Acetylcholine receptor antibody
- MuSK, LRP4, and titin antibody
- EMG/NCS with repetitive stimulation
- Chest XR, chest CT

EMG/NCS

- repetitive stimulation
  - >10% decrement at low frequency (2-3 Hz)
- needle EMG – unstable motor potentials
- single fiber EMG - “jitter”
  - 99% sensitive
- nerve conductions normal

EMG repetitive stimulation



https://obgynkey.com/neuromuscular-junction-disorders/

Treatments

- pyridostigmine
- prednisone
- IVIg/SQIg
- PLEX
- mycophenolate*
- azathioprine
- cyclosporine
- tacrolimus*
- methotrexate*

*did not meet primary endpoints

- endoscopic thymectomy

Monoclonals (IV)

- rituximab
- eculizumab* – complement C5
- ravulizumab – complement C5
- efgartigimod – FcRN

Subcutaneous

- rozanolixizumab - FcRN
- zilucoplan – C5 inhibitor

Outcomes

- Better prognosis compared to adults (e.g. spontaneous remission)
- Between 40% and 70% of patients with ocular MG will progress to generalized MG within 2 years of developing symptoms, especially if anti-AChR antibody positive (adult)
- Overall anticipate a normal life expectancy, and excellent prognosis with treatment
- Increased risk of developing other autoimmune diseases, mostly thyroid, SLE, and RA

General recommendations

- Regular exercise with rest is encouraged; try Tai Chi or yoga
- Avoid high temperatures
- Watch carefully for fatigue, dyspnea, snoring
- Caution when ill, postpartum, stressed, or overheated
- Transient worsening with steroids
- Consider medications you select
  - High risk: botulinum toxin, immune checkpoint inhibitors, magnesium, penicillamine, telithromycin
  - Moderate: aminoglycoside antibiotics, macrolide antibiotics
  - Low: beta-blockers, chloroquine, hydroxychloroquine, interferon alpha, iodinated contrast agent, quinine, statins

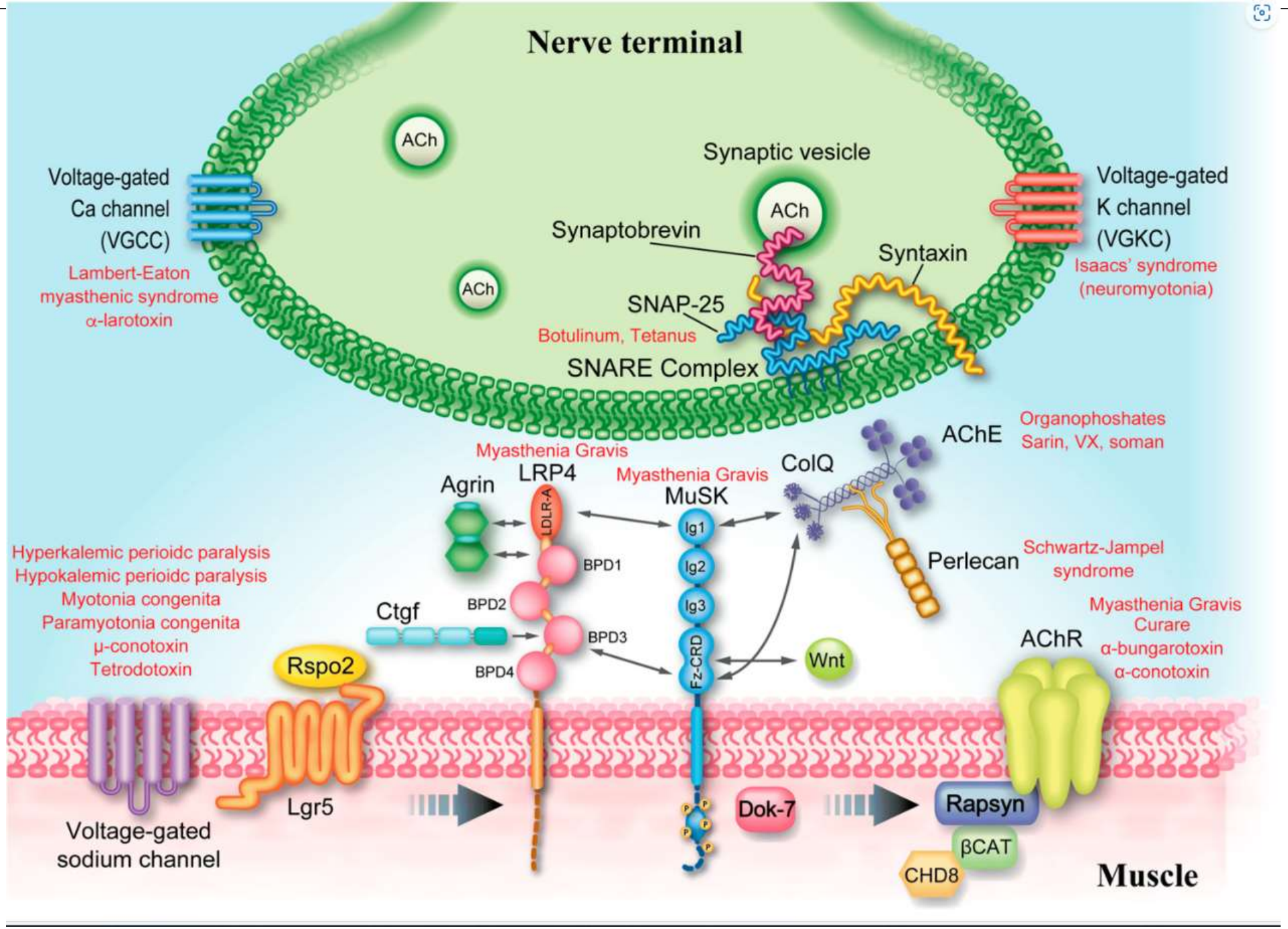
Neonatal myasthenia

1. Neonatal transient
   - poor suck, choking, respiratory distress
   - weak cry
   - examine mother for myasthenia
   - passive transfer of antibodies

2. Congenital

Non-autoimmune myasthenic syndrome

- (formerly known as congenital myasthenia)
  - Pre-synaptic
  - Synaptic
  - Post-synaptic
- Consider in cases of neonatal apnea
- Treatments variably include: pyridostigmine, 3,4-DAP, ephedrine, albuterol and other beta-agonists



Ohno et al, IJSMI 2023 24(4), 3730. https://www.mdpi.com/1422-0067/24/4/3730

Thank you!

Any questions?

Reach us at (732) 235-7875

Child Health Institute of NJ