Other Neuromuscular Transmission Disorders

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Congenital Myasthenias

* incidence << incidence of MG.
* *not autoimmune*!

**Pathogenetic Classification** – see [p. Mus1 >>](http://www.neurosurgeryresident.net/Mus.%20Muscular%2C%20Neuromuscular%20disorders%5CMus1.%20Myasthenia%20Gravis.pdf)

Clinical Features

**myasthenic symptoms after neonatal period** (“floppy baby”) + **family history** (autosomal recessive inheritance is most common)

N.B. may present later in life and, in some cases, without family history – diagnosed as serologically-negative autoimmune myasthenia.

* difficulty with feeding, delayed motor milestones, persistent or sometimes progressive limb weakness.
* skeletal abnormalities can result from weakness.
* some syndromes lack ocular involvement!

Diagnosis

* positive **AChR antibody test** excludes congenital myasthenia (negative test is less helpful).
* positive\* **edrophonium (Tensilon) test** confirms myasthenic syndrome but does not differentiate congenital myasthenia from MG.

\*may be negative in deficiency of acetylcholinesterase.

* **repetitive nerve stimulation**\*\* → decrement in CMAP.

\*\*at 10 Hz (vs. MG – at 3 Hz).

* **single-fiber EMG** – as in MG.

**Differential Diagnosis**

* 1. mitochondrial myopathy
	2. myasthenia gravis / neonatal myasthenia (passive placental transfer of AChR antibodies).

Treatment

* **respiratory & bulbar** supportive measures.
* some patients respond to **anticholinesterases**; if not – try 3,4,-diaminopyridine.

Eaton-Lambert Syndrome

- autoantibodies against **voltage-gated Ca2+-channels** in peripheral nerves → reduced acetylcholine release\* (at *neuromuscular* and *autonomic* synapses).

\*number↓ of released ACh quanta.

Disorder of **presynaptic cholinergic cell**

1. 66% **paraneoplastic disorder** (60% patients, esp. men, have small cell lung cancer) - antibodies arise in reaction to tumor.

Syndrome may predate tumor detection by up to 3 years!

1. 33% associated with **other autoimmune disorders** (thyroid disease, pernicious anemia, vitiligo, type I diabetes mellitus).

N.B. botulism also affects Acch release!

Clinical Features

Skeletal muscles: **proximal & limb girdle muscle weakness + hyporeflexia** (esp. knee and ankle) are hallmarks.

respiratory, bulbar\*, ocular muscles spared

\*pharyngeal weakness (dysphagia) is only cranial weakness regularly encountered.

* + lower limbs > upper limbs.

**proximal muscles of lower limbs!**

* + myalgia may occur.
	+ general fatigue (precedes weakness).
	+ gait dysfunction (follows weakness on standing).

N.B. ***repetitive / sustained*** *contraction can improve muscle strength for few seconds*!!! (warming-up phenomenon) – opposite of fatigability!; with continued use muscle fatigability returns.

Autonomic cholinergic (nicotinic & muscarinic) dysfunction: xerostomia, loss of taste, impotence.

* + orthostatic hypotension, sluggish pupillary responses, peripheral paresthesias are rare.

Diagnosis

* negative **edrophonium test**.
* abnormally small CMAP amplitude on **EMG**.
* **repetitive nerve stimulation**: see [p. D20 >>](http://www.neurosurgeryresident.net/D.%20Diagnostics%5CD20-29.%20Electrophysiology%20%28EEG%2C%20evoked%20potentials%2C%20MEG%2C%20EMG%2C%20nerve%20conduction%29%5CD20.%20EMG.pdf), [p. D22 >>](http://www.neurosurgeryresident.net/D.%20Diagnostics%5CD20-29.%20Electrophysiology%20%28EEG%2C%20evoked%20potentials%2C%20MEG%2C%20EMG%2C%20nerve%20conduction%29%5CD22.%20Nerve%20Conduction%20Studies.pdf)

at > 10 Hz\* → CMAP increment (2 to 20 times original)!!! – that is the opposite of myasthenia gravis!!!

\* facilitates calcium accumulation in nerve terminal

at 2 Hz → CMAP decrement.

* search for malignancy: chest X-ray, mammography, pelvic ultrasound.

Treatment

- directed to concomitant tumor.

* amifampridine phosphate (Firdapse) tablets – FDA approved (11/28/2018).
* to **facilitate ACh release** - combination pyridostigmine + 3-4-diaminopyridine.
* other drugs that facilitate ACh release have had adverse effects:

guanidine - bone marrow depression, cerebellar syndrome.

4-amino pyridine - convulsions.

* **IVIG, plasmapheresis** effects are transient.
* **cytotoxic drugs** should be used cautiously.
* optimal treatment of non-neoplastic cases - modest doses of alternate-day prednisone.

Bibliography for ch. “Neuromuscular, Muscular Disorders” → follow this [link >>](http://www.neurosurgeryresident.net/Mus.%20Muscular%2C%20Neuromuscular%20disorders%5CMus.%20Bibliography.pdf)

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