Project: Ghana Emergency Medicine Collaborative

Document Title: Myasthenia Gravis (Case of the Week)

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CASE OF THE WEEK

BY CHRIS K. OPPONG,

BSc HUMAN BIOLOGY, MBChB

EMERGENCY MEDICINE RESIDENT-KATH

CASE OF THE WEEK

- A 17 year old female presented to KATH ED with a 3 day history of difficulty in swallowing , drooling ,dysphasia and shortness of breath.
- Differential diagnosis??

- PmHx: mother claims she has been treated for chronic tonsillitis recently and has been having non-specific recurrent illnesses which has been managed on OPD basis
- Drug hx: iv ceftriazone 2g, iv amoksiklav 1.2g
- Social hx: SHS 3 , boarding house

O/E

- Lethargic
- Weak respiratory effort
- Drooling
- Afebrile

- Vital signs:Bp-130/95, pulse-105bpmRGV, RR-30cpm, temp.-36.8oC, Spo2-62% room air. GCS m-6, v-5, e-3. any concerns??

Admission Day 1

UPPER AIRWAY OBSTRUCTION ?cause

ABC’s

- Normal throat examination :tonsils , soft palate
- Consult to ENT
- CBC, ABG’s, LFT ,RFT, pregnancy test
- Chest x-ray, lateral neck x-ray, ECG

Lab results

- Wbc-15, Hb-10.1, ESR-18
- ABG- pH-7.1, pCo2-42.9, HCO3- 15.8, pO2-29, Na-149.4, Cl-111.4
- AST 275, ALT-294
- UREA-6.02,CRT-67, BUN /CRT-42

DAY 2

- ENT consult : acute laryngitis
- Patient transferred to ENT ward

DAY 3

- Improvement in patients condition on the ward.
- Feeding again
- Mother expressed concern to doctors that her condition keeps fluctuating, worse in the evening???hysteria
- Ward cover doctor called to see patient who had become restless.

Day 4

- Better in the morning
- c/o diffiulty in swallowing
- Ward cover doctor called in the evening to see patient who had become restless again

Day 5

- 15:35 GMT , doctor called to see patient who had become unresponsive with a GCS of 8/15
- Physician consult; epiglotitis with sepsis+ adrenal insufficiency, requested head CT-scan
- 21:30 GMT, patient rushed to RED by ENT ward nurses with no cardio respiratory activity and brownish secretions from mouth and nostrils

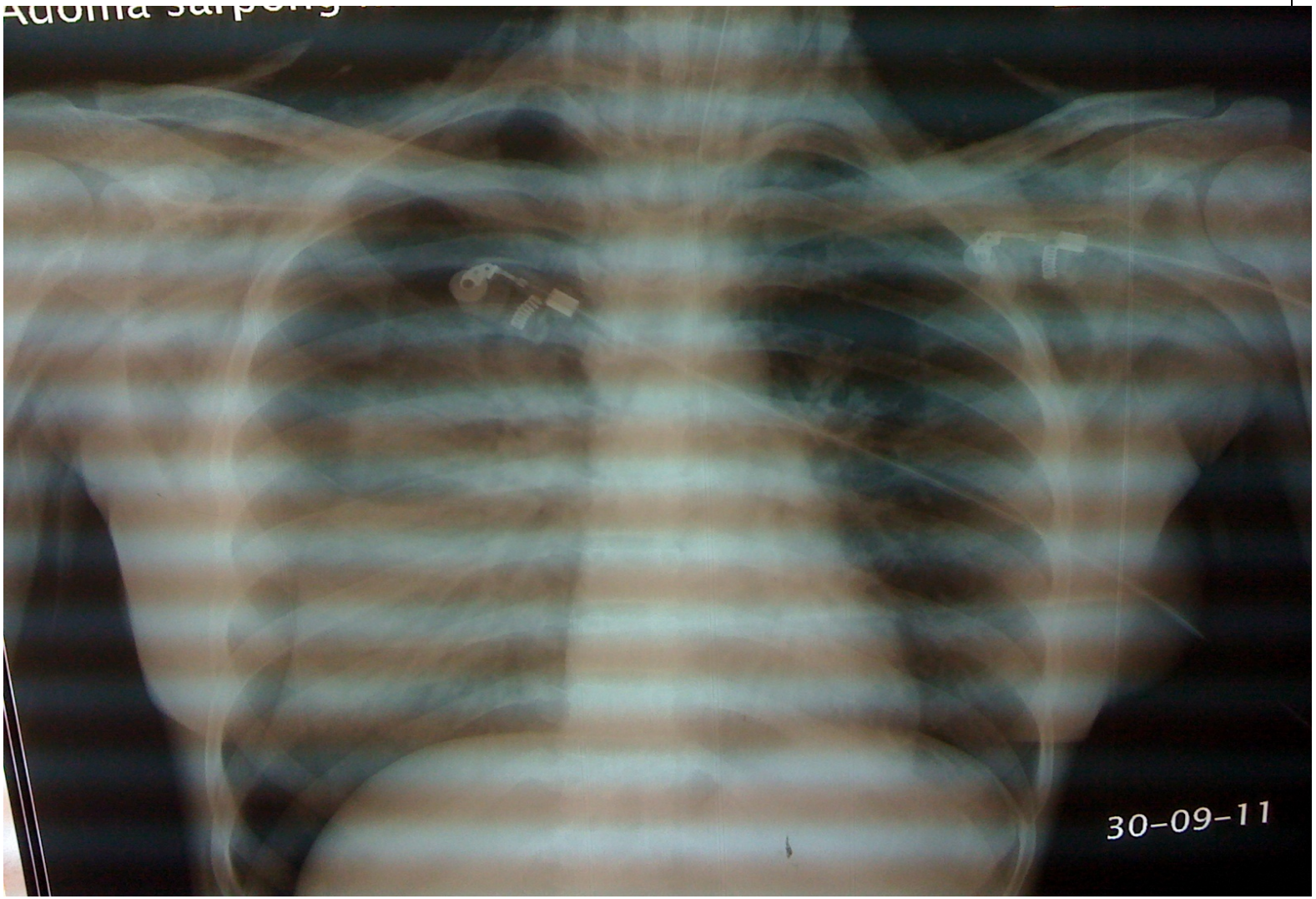
- CPR
- Patient revived after 3 cycles and intubated
- ICU ventilators were malfunctioning so patient was kept at RED on the transport ventilator
- CXR- aspiration

Day 6

- Patient transferred to ICU
- Physician consult; atypical pneumonia(mycoplasma pneumonia)
- Rapid HIV test ?positive
- ELISA-negative

Day 7

- Massive subcutaneous emphysema ?? barotrauma
- RT pneumothorax



Source Undetermined

Day 10

PD-INEL

Source Undetermined

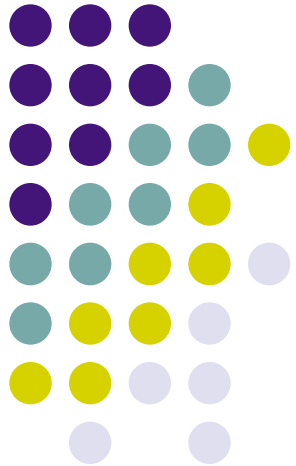
- Hypopyon
- Ophthalmology consult
- Ophthalmologist recognizes patient and discloses he had treated her for ocular myasthenia gravis
- MYASTHENIC CRISIS now the working diagnosis

Day 18 post admission

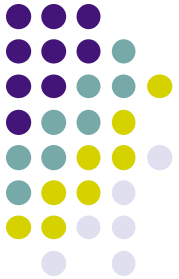
- Patient is still on a ventilator on CPAP
- Being treated with pyridostigmine, azathioprine and iv immunoglobulin
- Significant improvement, , GCS m-5, e-2

v-Intubated

Myasthenia Gravis



MYASTHENIC CRISIS



Outline

- Background
- Anatomy
- Pathophysiology
- Epidemiology
- Clinical Presentation
- Work-up
- Treatment
- Rehabilitation

PD-EXP

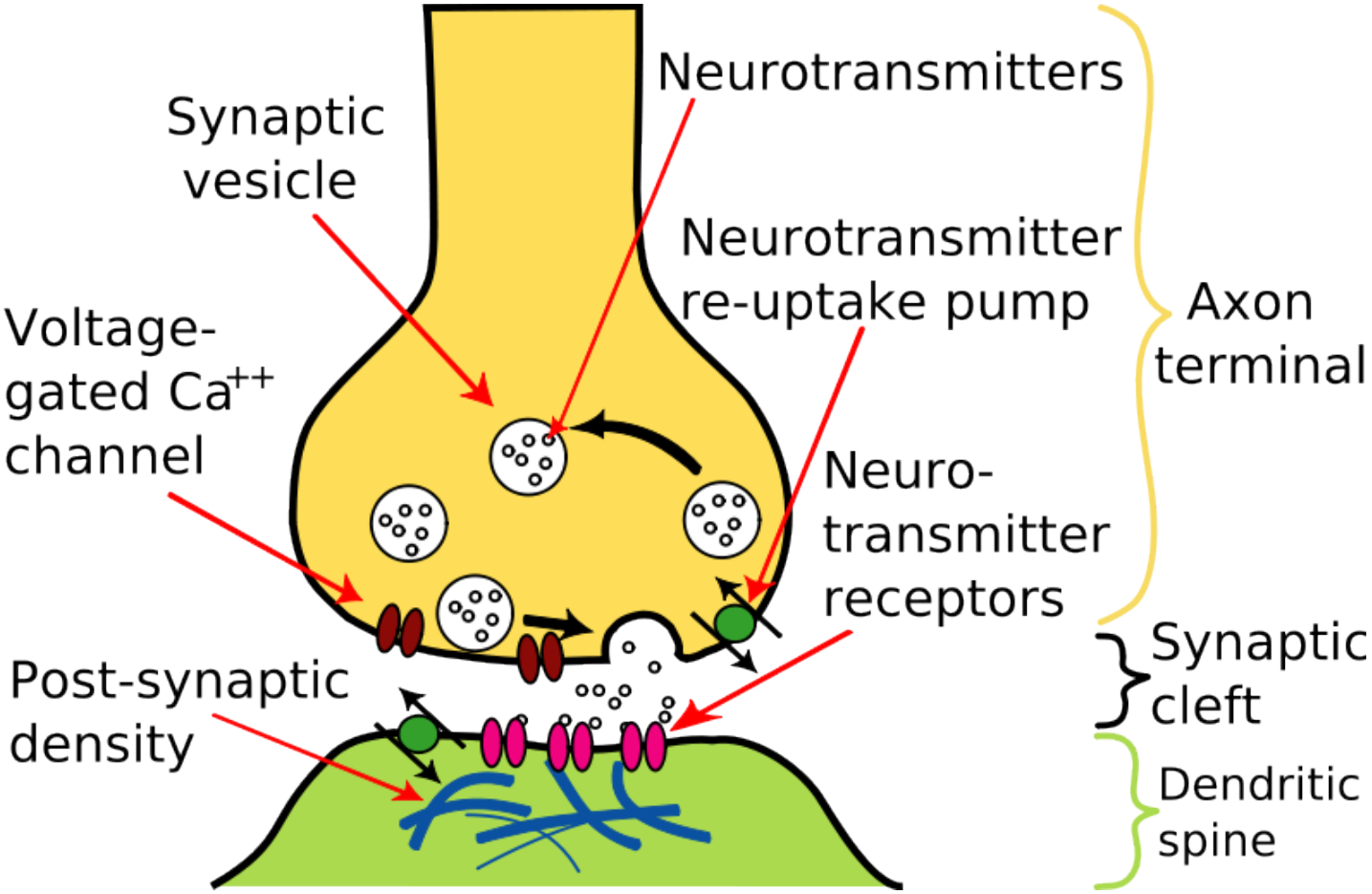
Posey & Spiller, Wikimedia Commons

Background

- Acquired autoimmune disorder
- Clinically characterized by:
  - Weakness of skeletal muscles
  - Fatigability on exertion.
- First clinical description in 1672 by Thomas Willis

Anatomy

- Neuromuscular Junction (NMJ)
  - Components:
    - Presynaptic membrane
    - Postsynaptic membrane
    - Synaptic cleft
  - Presynaptic membrane contains vesicles with Acetylcholine (ACh) which are released into synaptic cleft in a calcium dependent manner
  - ACh attaches to ACh receptors (AChR) on postsynaptic membrane



Nrets, Wikimedia Commons

Anatomy

- Neuromuscular Junction (NMJ)
  - The Acetylcholine receptor (AChR) is a sodium channel that opens when bound by ACh
    - There is a partial depolarization of the postsynaptic membrane and this causes an excitatory postsynaptic potential (EPSP)
    - If enough sodium channels open and a threshold potential is reached, a muscle action potential is generated in the postsynaptic membrane

Pathophysiology

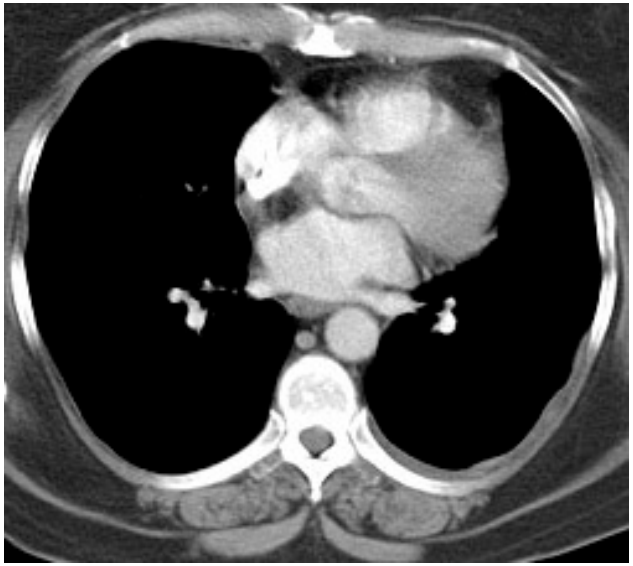
- In MG, antibodies are directed toward the acetylcholine receptor at the neuromuscular junction of skeletal muscles
- Results in:
  - Decreased number of nicotinic acetylcholine receptors at the motor end-plate
  - Reduced postsynaptic membrane folds
  - Widened synaptic cleft

Pathophysiology

- Anti-AChR antibody is found in 80-90% of patients with MG
- MG may be considered a B cell-mediated disease
  - Antibodies

Pathophysiology

- T-cell mediated immunity has some influence
  - Thymic hyperplasia and thymomas are recognized in myasthenic patients*



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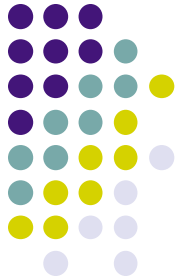
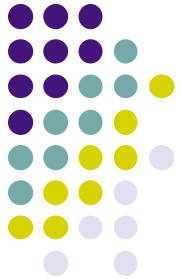
Epidemiology



- Frequency
  - Annual incidence in US- 2/1,000,000
  - Worldwide prevalence 1/10,000
- Mortality/morbidity
  - Recent decrease in mortality rate due to advances in treatment
    - 3-4% (as high as 30-40%)
  - Risk factors
    - Age > 40
    - Thymoma
- Sex
  - F-M (6:4)
  - Mean age of onset (M-42, F-28)
  - Incidence peaks- M- 6-7th decade F- 3rd decade

Clinical Presentation



- Fluctuating weakness increased by exertion
  - Weakness increases during the day and improves with rest
- Extraocular muscle weakness
  - Ptosis is present initially in 50% of patients and during the course of disease in 90% of patients
- Head extension and flexion weakness
  - Weakness may be worse in proximal muscles

Clinical presentation

- Progression of disease
  - Mild to more severe over weeks to months
    - Usually spreads from ocular to facial to bulbar to truncal and limb muscles
    - Often, symptoms may remain limited to EOM and eyelid muscles for years
    - The disease remains ocular in 16% of patients
- Remissions
  - Spontaneous remissions rare
  - Most remissions with treatment occur within the first three years

Clinical presentation

- Basic physical exam findings
  - Muscle strength testing
  - Recognize patients who may develop respiratory failure (i.e. difficult breathing)
  - Sensory examination and DTR’s are normal

Clinical presentation

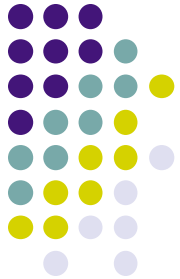
- Muscle strength
  - Facial muscle weakness
  - Bulbar muscle weakness
  - Limb muscle weakness
  - Respiratory weakness
  - Ocular muscle weakness

Clinical presentation

- Facial muscle weakness is almost always present
  - Ptosis and bilateral facial muscle weakness
  - Sclera below limbus may be exposed due to weak lower lids

Cumulus, Wikimedia Commons

Clinical presentation



- Bulbar muscle weakness
  - Palatal muscles
    - “Nasal voice”, nasal regurgitation
    - Chewing may become difficult
    - Severe jaw weakness may cause jaw to hang open
    - Swallowing may be difficult and aspiration may occur with fluids—coughing and choking while drinking
  - Neck muscles
    - Neck flexors affected more than extensors

Clinical presentation

- Limb muscle weakness
  - Upper limbs more common than lower limbs

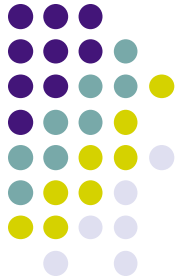
Upper Extremities

Deltoids
Wrist extensors
Finger extensors
Triceps > Biceps

Lower Extremities

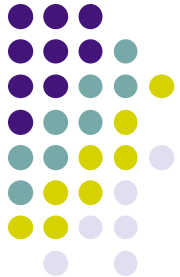
Hip flexors (most common)
Quadriceps
Hamstrings
Foot dorsiflexors
Plantar flexors

Clinical presentation



- Respiratory muscle weakness
  - Weakness of the *intercostal muscles* and the *diaghram* may result in CO2 retention due to hypoventilation
    - May cause a neuromuscular emergency(myasthenic crisis)
  - Weakness of *pharyngeal muscles* may collapse the upper airway
    - Monitor negative inspiratory force, vital capacity and tidal volume
    - Do NOT rely on pulse oximetry
      - Arterial blood oxygenation may be normal while CO2 is retained

Clinical presentation



- Occular muscle weakness
  - Asymmetric
    - Usually affects more than one extraocular muscle and is not limited to muscles innervated by one cranial nerve
    - Weakness of lateral and medial recti may produce a pseudointernuclear opthalmoplegia
      - Limited adduction of one eye with nystagmus of the abducting eye on attempted lateral gaze
  - Ptosis caused by eyelid weakness
  - Diplopia is very common

Clinical presentation

- Co-existing autoimmune diseases
  - Hyperthyroidism
    - Occurs in 10-15% MG patients
      - Exopthalamos and tachycardia point to hyperthyroidism
      - Weakness may not improve with treatment of MG alone in patients with co-existing hyperthyroidism
  - Rheumatoid arthritis
  - Scleroderma
  - Lupus

Clinical presentation

- Causes
  - Idiopathic
  - Penicillamine
    - AChR antibodies are found in 90% of patients developing MG secondary to penicillamine exposure
  - Drugs

Clinical presentation

- Causes
  - Drugs
    - Antibiotics (Aminoglycosides, ciprofloxacin, ampicillin, erythromycin)
    - B-blocker (propranolol)
    - Lithium
    - Magnesium
    - Procainamide
    - Verapamil
    - Quinidine
    - Chloroquine
    - Prednisone
    - Timolol
    - Anticholinergics

Differentials

- Amyotropic Lateral Sclerosis
- Basilar Artery Thrombosis
- Brainstem gliomas
- Cavernous sinus syndromes
- Dermatomyositis
- Lambert-Eaton Myasthenic Syndrome
- Multiple Sclerosis
- Sarcoidosis and Neuropathy
- Thyroid disease
- Botulism
- Oculopharyngeal muscular dystrophy
- Brainstem syndromes

Work-up

- Lab studies
  - Anti-acetylcholine receptor antibody
    - Positive in 74%
    - 80% in generalized myasthenia
    - 50% of patients with pure ocular myasthenia
  - Anti-striated muscle
    - Present in 84% of patients with thymoma who are younger than 40 years

Work-up

- Lab studies
  - Interleukin-2 receptors
    - Increased in generalized and bulbar forms of MG
    - Increase seems to correlate to progression of disease

Work-up

- Imaging studies
  - Chest x-ray
    - Plain anteroposterior and lateral views may identify a thymoma as an anterior mediastinal mass
  - Chest CT scan is mandatory to identify thymoma
  - MRI of the brain and orbits may help to rule out other causes of cranial nerve deficits but should not be used routinely

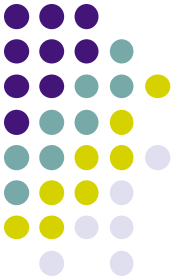
Work-up

- Electrodiagnostic studies
  - Repetitive nerve stimulation
  - Single fiber electromyography (SFEMG)

  - SFEMG is more sensitive than RNS in MG

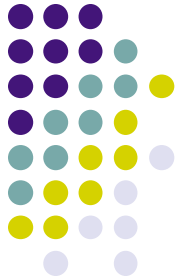
Electrodiagnostic studies:

Single-fiber electromyography



- Generalized MG
  - Abnormal extensor digiti minimi found in 87%
  - Examination of a second abnormal muscle will increase sensitivity to 99%
- Occular MG
  - Frontalis muscle is abnormal in almost 100%
  - More sensitive than EDC (60%)

Workup
Pharmacological testing

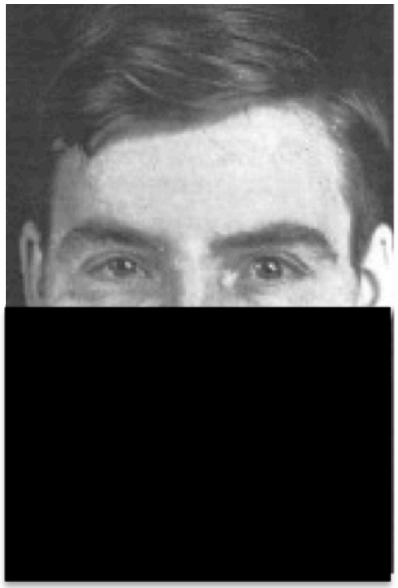


- Edrophonium (Tensilon test)
  - Patients with MG have low numbers of AChR at the NMJ
  - Ach released from the motor nerve terminal is metabolized by Acetylcholine esterase
  - Edrophonium is a short acting Acetylcholine Esterase **Inhibitor** that improves muscle weakness
  - Evaluate weakness (i.e. ptosis and opthalmoplegia) before and after administration

Workup
Pharmacological testing

Before

After



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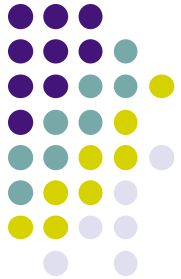
Workup
Pharmacological testing

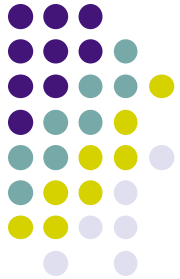


- Edrophonium (Tensilon test)
  - Steps
    - 0.1ml of a 10 mg/ml edrophonium solution is administered as a test
    - If no unwanted effects are noted (i.e. sinus bradychardia), the remainder of the drug is injected
    - Consider that Edrophonium can improve weakness in diseases other than MG such as ALS, poliomyelitis, and some peripheral neuropathies

Treatment

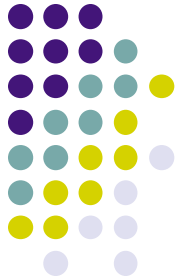
- AChE inhibitors
- Immunomodulating therapies
- Plasmapheresis
- Thymectomy
  - Important in treatment, especially if thymoma is present

Treatment



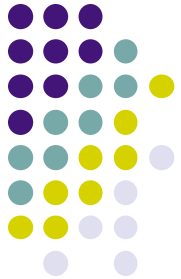
- AChE inhibitor
  - Pyridostigmine bromide (Mestinon)
    - Starts working in 30-60 minutes and lasts 3-6 hours
    - Individualize dose
    - Adult dose:
      - 60-960mg/d PO
      - 2mg IV/IM q2-3h
    - Caution
      - Check for cholinergic crisis
    - Others: Neostigmine Bromide

Treatment



- Immunomodulating therapies
  - Prednisone
    - Most commonly used corticosteroid in US
    - Significant improvement is often seen after a decreased antibody titer which is usually 1-4 months
    - No single dose regimen is accepted
      - Some start low and go high
      - Others start high dose to achieve a quicker response
    - Clearance may be decreased by estrogens or digoxin
    - Patients taking concurrent diuretics should be monitored for hypokalemia

Treatment
Behavioral modifications



- Diet
  - Patients may experience difficulty chewing and swallowing due to oropharyngeal weakness
    - If dysphagia develops, liquids should be thickened
      - Thickened liquids decrease risk for aspiration
- Activity
  - Patients should be advised to be as active as possible but should rest frequently and avoid sustained activity
  - Educate patients about fluctuating nature of weakness and exercise induced fatigability

Complications of MG

- Respiratory failure
- Dysphagia
- Complications secondary to drug treatment
  - Long term steroid use
    - Osteoporosis, cataracts, hyperglycemia, HTN
    - Gastritis, peptic ulcer disease
    - Pneumocystis carinii

Prognosis

- Untreated MG carries a mortality rate of 25-31%
- Treated MG has a 4% mortalitiy rate
- 40% have ONLY occular symptoms
  - Only 16% of those with occular symptoms at onset remain exclusively occular at the end of 2 years

Rehabilitation

- Strategies emphasize
  - Patient education
  - Timing activity
  - Providing adaptive equipment
  - Providing assistive devices
  - Exercise is **not** useful

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