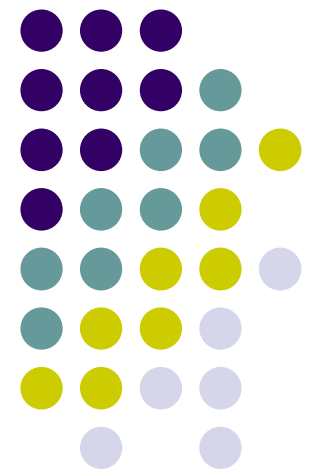
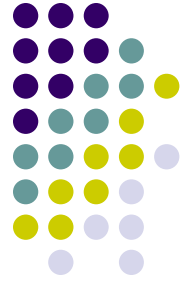


Myasthenia Gravis

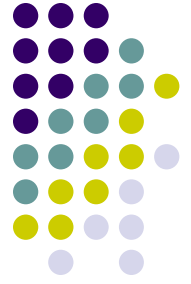
Susan Hotz, M.D.
Medical City Dallas Hospital
Dallas, Texas



Epidemiology



- 1/10,000
- 2 peaks of onset
 - 20-30's F>M
 - 60-80's mostly Males



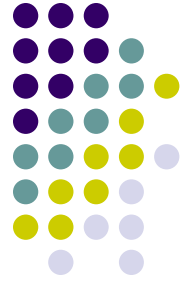
Classification

- Ocular
 - Bulbar
 - Generalized
-
- 10 to 15% limited to ocular involvement after 3 years



Autoimmune

- Neonatal: Transplacental passage of AChR antibodies or MuSk antibodies.
- Juvenile < 18 (Often ocular and seronegative)
- Early onset – 18 to 50
- Late onset > 50 (Increased incidence of a thymoma)



Non-autoimmune

- Congenital myasthenic syndrome – defects in proteins at the NMJ.
- Can be pre-synaptic or post-synaptic

Pathology

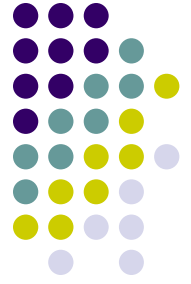
- Decreased number of AChR at the neuromuscular junction





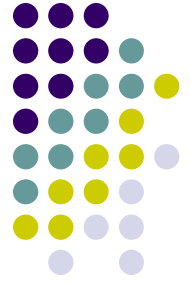
Clinical Presentation

- Most commonly presents with weakness of extraocular muscles (ptosis and/or diplopia)
- Bulbar involvement common eventually (dysphagia, dysarthria, dysphonia, jaw fatigue)
- Generally progresses over time so that 90% have bulbar and proximal limb weakness



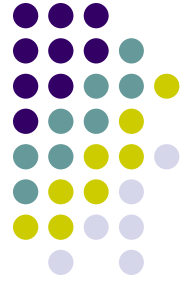
Muscle weakness

- Painless
- Fluctuates and usually worsens over the course of the day
- Worsens with prolonged use of affected muscles
- Proximal weakness more common
- May involve respiratory muscles
- Bowel and bladder function preserved



Causes of exacerbations

- Reduction in medication in treated patients
- Systemic illness or infection
- Increased body temp or fever
- Thyroid dysfunction
- Pregnancy and menstrual cycle
- Emotional or physical stress
- Drugs that affect neuromuscular transmission



Physical Exam

- Pupils unaffected
- Ptosis often worsens after 60 seconds of sustained upgaze
- Proximal muscle fatigue
- Preserved tendon reflexes
- No sensory finding



Differential Diagnosis

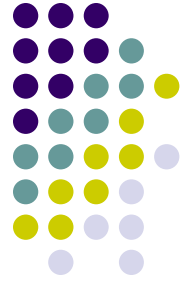
- Stroke
- Multiple Sclerosis
- ALS
- GBS
- Lambert Eaton Myasthenic Syndrome
- Botulism
- Oculopharyngeal muscular dystrophy



Disorders assoc. with MG

- Thymus hyperplasia or thymoma
- Other autoimmune conditions (Graves disease, RA, SLE, pernicious anemia)
- Often a family history of autoimmune disease

Thymus



- Abnormalities found in 80% of MG patients
- Probably the site of exposure of autoreactive B and T cells to AChR
- May be a site of considerable production of AChR antibodies
- 65% of early onset MG patient have thymic hyperplasia
- 30% of late onset patients have a thymoma



Investigations

- AChR or MuSK antibodies (highly specific)
- Tensilon test (Edrophonium) an injectable short acting acetylcholinesterase inhibitor. Injection transiently increase Ach and improves weakness
- Repetitive Nerve stimulation – repetitive stimulation at 2 or 3Hz produces a decrement of greater than 10%. Not specific
- Single Fiber EMG – look for jitter. Highly sensitive and not specific



Ancillary tests

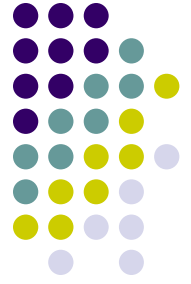
- CT chest to rule out thymoma
- Pulmonary function tests
- Speech therapy eval
- TSH/free T4
- Vitamin B12 level (pernicious anemia)



Treatment - Cholinesterase inhibitors

- Mestion (pyridostigmine) inhibits acetylcholinesterase and increases the amount of acetylcholine available to bind to the AChR
- Neostigmine – IV useful in the ICU setting but not as an outpatient
- Does not affect disease course
- Side effects –increased sweating, salivation, lacrimation, abdominal cramps, and diarrhea

Treatment - Corticosteroids



- Immunosuppressive therapy
- Initially high doses may worsen symptoms
- Every other day dose may reduce adverse effects
- Side effects – osteoporosis, elevated blood sugars, weight gain, hypertension, peptic ulcer, avascular necrosis of the hip, etc



Treatment - Mycophenolate

- Mycophenolate (Cellcept) – suppresses B-cells, less toxic than other immunosuppressive medications
- Expensive
- Side effects –fatigue, increased risk of infection, pancytopenia, increased risk of lymphoma



Treatment - Azathioprine

- Azathioprine (Imuran) – suppresses both B & T cells
- Side effects – flu like symptoms, infections, hepatotoxicity, pancreatitis, myelosuppression, increased risk of lymphoma
- Follow CBC and LFT's weekly for 8 weeks, and then monthly



Treatment - Cyclosporine

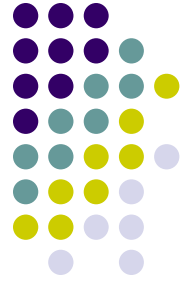
- Cyclosporine (Neoral) – used only when above treatments fail since it is expensive and has more side effects
- Metabolized by the P450 pathway
- Side effects include hepatotoxicity, nephrotoxicity, hypertension, gingival hyperplasia, neuropathy, tremor, increased infections, etc.



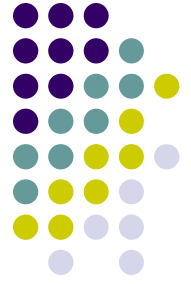
Treatment – IV Ig

- IV Ig (many brands) – useful for a MG crisis or acute decline. Onset of improvement in 7 to 10 days
- Half life is 21 days
- Side effects – acute renal failure, aseptic meningitis, headache, anaphylaxis, pancytopenia
- Very expensive

Treatment – Plasma Exchange



- Useful for an acute decline or MG crisis
- Reduces antibodies by 50 to 70%
- Onset 7 to 10 days
- Duration of benefit 2 to 8 weeks
- Side effects – fatigue, bleeding, pancytopenia,
- Expensive



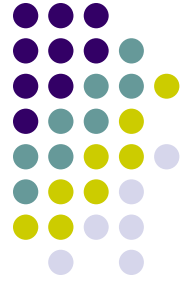
Thymectomy

- Early onset, young (< 60), seropositive patients
- Controversial – may take months to a year to see improvement
- 2X increase in the likelihood of remission



Drugs that worsen MG

- Antibiotics – aminoglycosides, macrolides, fluroquinolones
- Antiarrythmics- beta blockers, calcium channel blockers, quinidine, procainamide
- Antirheumatic – chloroquine, penicillamine
- Anesthetics – vecuroniums, succinylcholine, etc
- Ace inhibitors,
- Magnesium
- Dilantin
- Lithium
- Lidocaine
- Many others



Pregnancy and MG

- 1/3 stable, 1/3 worsen, 1/3 improve
- Higher risk of relapse in post-partum period
- 1/8 of pregnancies – neonatal MG will occur due to transplacental passage of antibodies
- May use steroids, cholinesterase inhibitors and IV Ig
- Plasmapheresis may cause volume shifts and remove progesterone so is generally avoided
- Magnesium sulfate for pre-eclampsia may worsen disease
- C-section in severe disease

Zoey!

