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PBL-IV

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Classifications of MG

Classifications

- Modified Osserman and Genkin classification.
- Oosterhuis classification.
- Result classification.

Table 168-1. Osserman and Genkins Classification

I. Pediatric myasthenia gravis
  A. Neonatal group (1%)
    1. Infants born of myasthenic mothers
    2. Self-limited, lasting no more than 6 weeks after birth
    3. Probably caused by transplacental transfer of circulating acetylcholine receptor antibodies
  B. Juvenile group (9%)
    1. Nonmyasthenic mother
    2. Onset any time from birth to puberty
    3. Tends to be permanent
    4. Familial involvement
    5. Myasthenia gravis disability classified as in adult myasthenia gravis

II. Adult myasthenia gravis
  A. Group 1: Ocular (15–20%)
    1. Limited to ocular muscles
    2. Forty percent ultimately develop clinically generalized disease
    3. Electromyographic results may be positive in peripheral muscles
  B. Group 2A: Mild generalized disease (30%)
    1. Involves cranial, limb, and truncal muscles
    2. Respiratory musculature spared
    3. Good response to anticholinesterase drugs
    4. Low mortality
  C. Group 2B: Moderately severe generalized disease (20%)
    1. Significant diplopia and ptosis
    2. Bulbar muscle involvement: dysarthria, dysphagia, feeding difficulty
    3. Limb weakness
    4. Exercise intolerance
  D. Group 3: Acute fulminating disease (11%)
    1. Abrupt onset
    2. Most severe symptoms appear by 6 months
    3. Early respiratory muscle involvement
    4. Severe bulbar, limb, and truncal weakness
    5. Poor response to anticholinesterases
    6. Frequent crises
    7. High mortality
    8. Thymoma relatively frequent
  E. Group 4: Late severe disease (9%)
    1. Progression from milder disease after 2 years
    2. High incidence of thymoma
    3. Relatively poor prognosis

Table 168-2. Oosterhuis Classification: Global Clinical Classification of Myasthenic Severity

Class 0

No complaints, no signs after exertion or at special testing.

Class 1

No disability. Minor complaints, minor signs. The patient knows that he or she still has myasthenia gravis, but family members or outsiders do not perceive it. The experienced doctor may find minor signs at appropriate testing (e.g., diminished eye closure, some weakness of the foot extensors or triceps muscles, the arms cannot be held extended for 3 minutes). The patient may have complaints such as heavy eyelids or diplopia only when fatigued and inability to perform heavy work.

Class 2

Slight disability, clear signs after exertion. The patient has some restrictions in daily life (e.g., cannot lift heavy loads, cannot walk for more than half an hour, has intermittent diplopia). Bulbar signs are not pronounced. Family members are aware of the signs, but outsiders, inexperienced doctors included, are not. Weakness is obvious at appropriate testing.

Class 3

Moderate disability, clear signs at rest. The patient is restricted in domestic activities, needs some help in clothing; meals have to be adapted. Bulbar signs are more pronounced. Signs of myasthenia gravis can be observed by an outsider.

Class 4

Severe disability. The patient needs constant support in daily activities. Bulbar signs are pronounced. Respiratory function is decreased.

Class 5

Respiratory support is needed.

Comments

Table 168-3. Results of Treatment Classification

I. Complete remission
   A. Without any medication
   B. With medication
      1. Immunosuppressive drugs
      2. Corticosteroids
      3. Anticholinesterases
      4. Combinations of 1, 2, and 3
II. Improvement
   A. Marked
   B. Moderate
III. Unchanged
IV. Worse
V. Dead

Pathophysiology

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

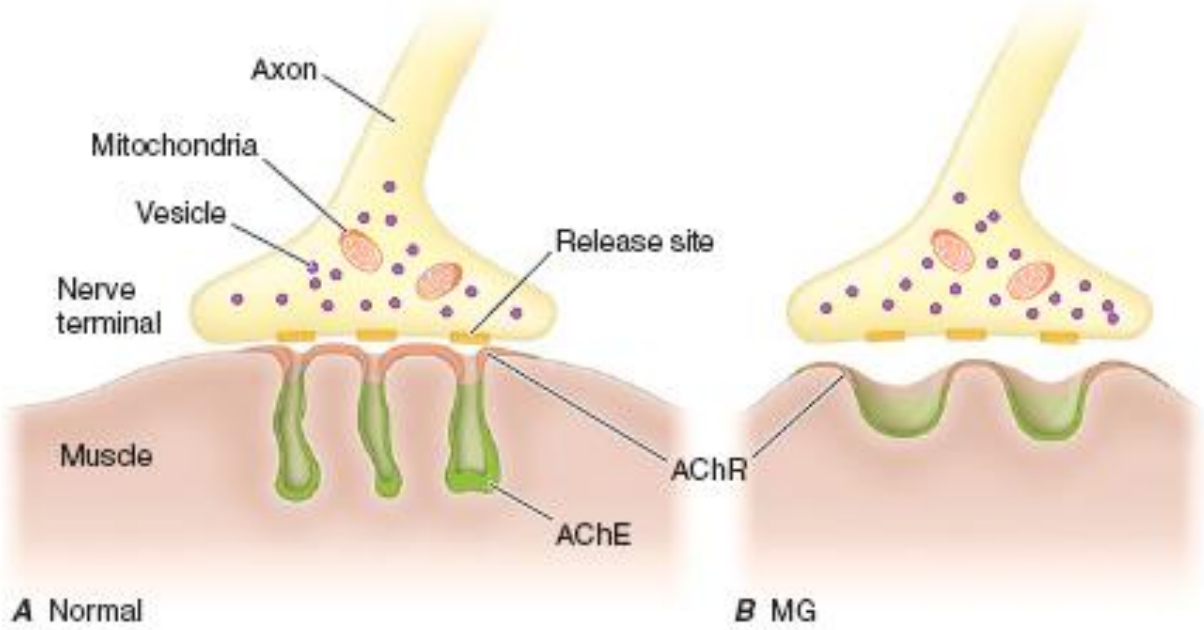


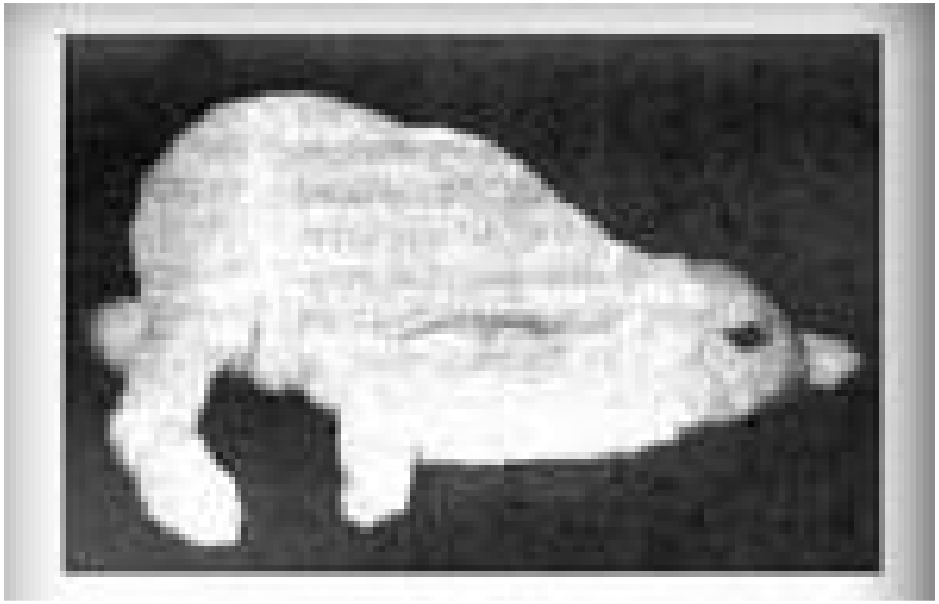
FIGURE 42-1

Diagrams of (*A*) normal and (*B*) myasthenic neuromuscular junctions. AChE, acetylcholinesterase. See text for description of normal neuromuscular transmission. The MG junction demonstrates a normal nerve terminal; a reduced number of AChRs (stippling); flattened, simplified postsynaptic folds; and a widened synaptic space. *(Modified from DB Drachman: N Engl J Med 330:1797, 1994; with permission.)*

Pathophysiology

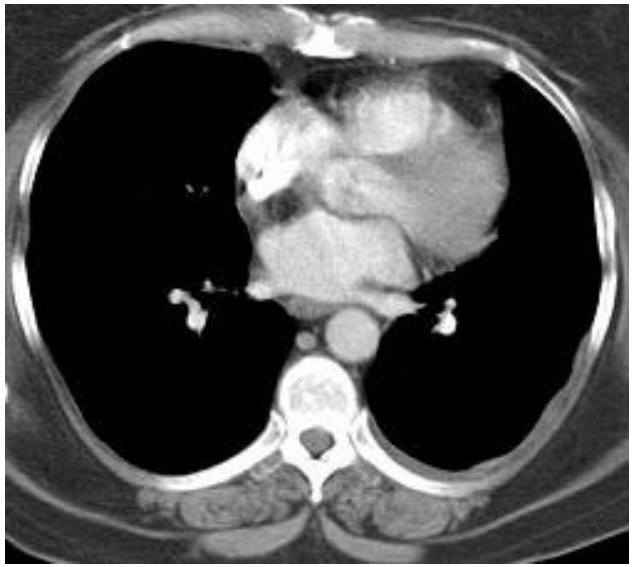
- Anti-AChR antibody is found in 80-90% of patients with MG
  - Proven with passive transfer experiments
  - Increase turnover of AChR
  - Blockade at AchR
  - Damage postsynaptic ms. membrane

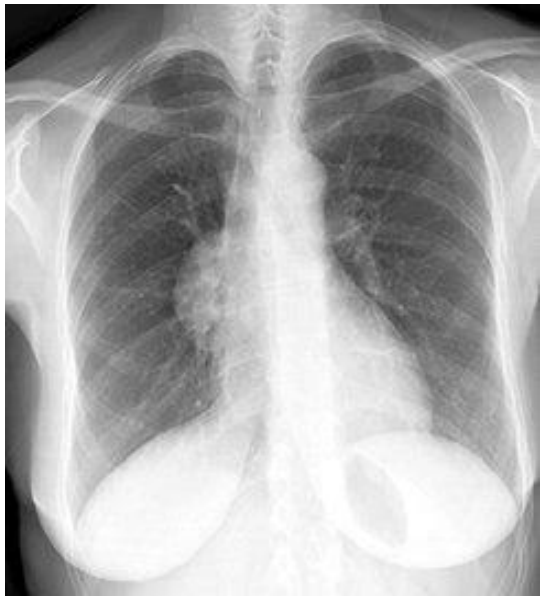
- MG may be considered a B cell-mediated disease
  - Antibodies



Pathophysiology

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





Etiology

- Causes
  - Idiopathic
  - Penicillamine
  - Drugs

Iatrogenic MG

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

- D-penicillamine
- Alpha interferons
- Bone marrow transplantation
- Botox

Investigations

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 (MuSK)
    - Found in 40% of patients who are Anti-AchR NEGATIVE

Work-up

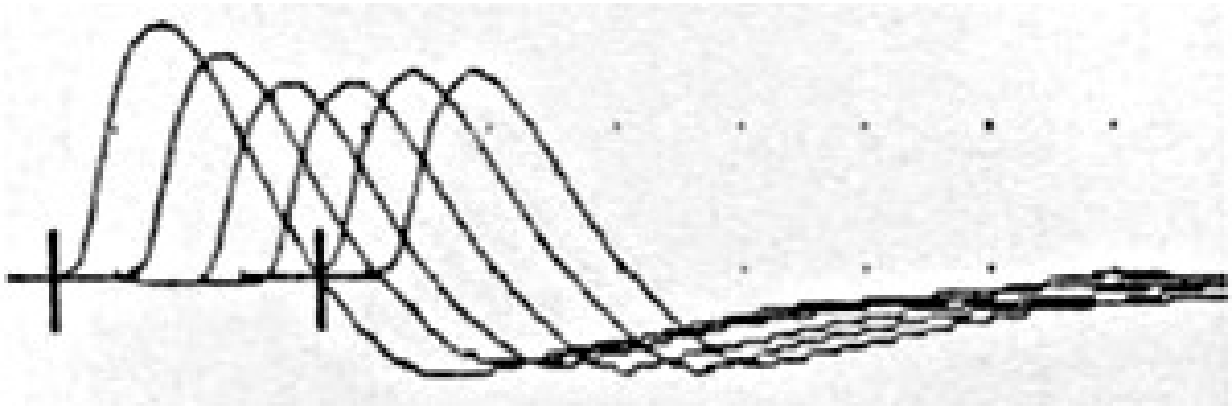
- Lab studies
  - Interleukin-2 receptors
    - Increased in generalized and bulbar forms of MG
    - Increase seems to correlate to progression of disease

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

Electrodiagnostic studies:
Repetitive Nerve Stimulation

- Low frequency RNS (1-5Hz)
  - Locally available Ach becomes depleted at all NMJs and less available for immediate release
    - Results in smaller EPSP's



Thymectomy

Present indications for thymectomy

- Patient with thymoma — the thymectomy is indicated all.
- If no thymoma — the patient age, symptoms, duration, severity, response to medication, sex are factors in decision-making.

Present indications for thymectomy

- Thymectomy is not recommended for the neonatal type of myasthenia gravis.
- In juvenile form — the reserve thymectomy for patient with more severe symptoms and lack of response to medical therapy.

Present indications for thymectomy

- In adult — Cooper, Jaretzki and Papatestas all believed patient with general symptoms should receive early thymectomy as soon as the diagnosis established.
- The ocular type — may try medical therapy for a year and if the symptoms interfere the daily life, the thymectomy should be considered.
- High incidence of unsuspected thymoma in patient older than 40y/o with ocular symptom only.

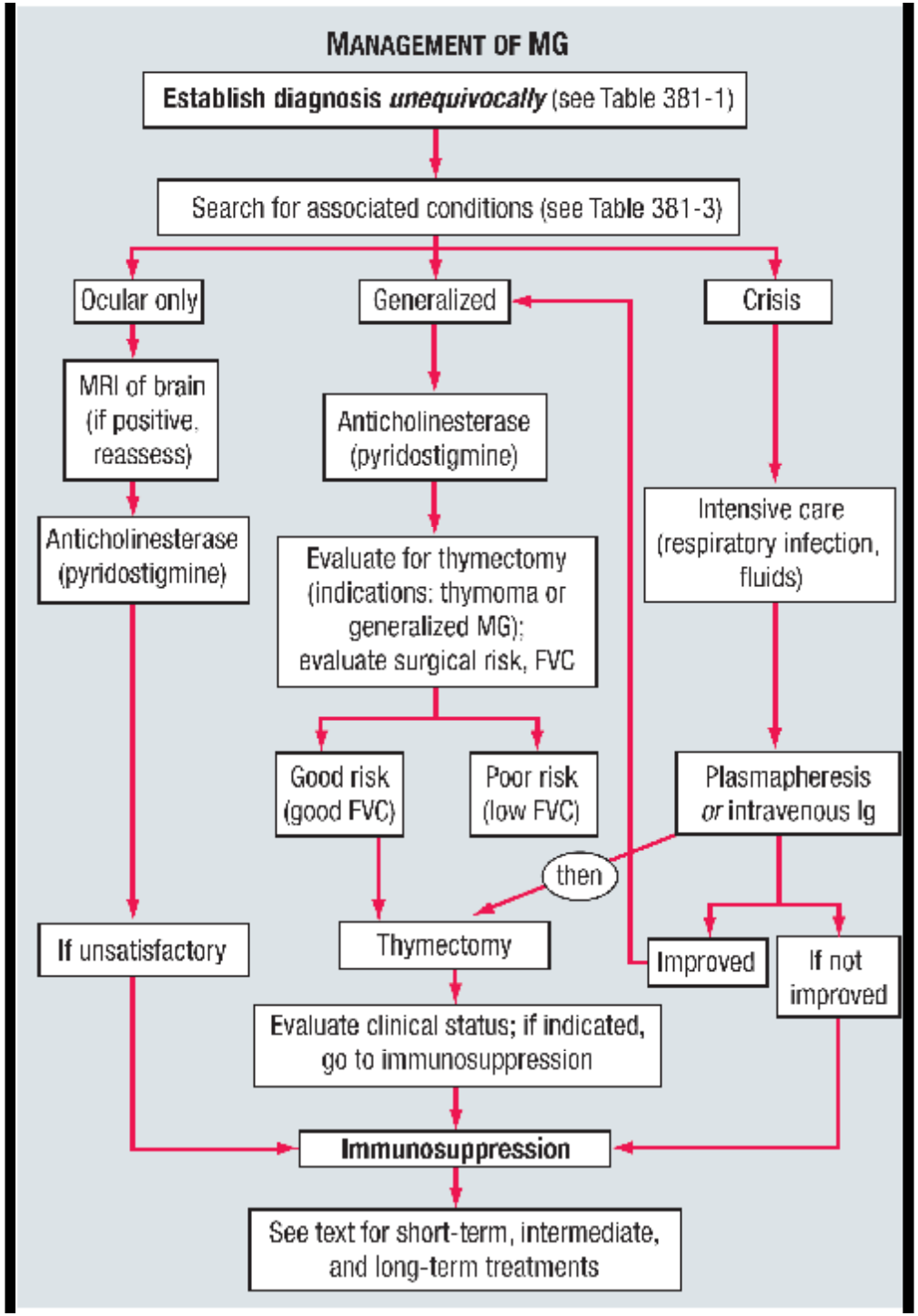
Result

- Adult patient without thymoma undergoing thymectomy has higher incidence of complete remission.
- Complete remove all thymic tissue fom mediastium and lower neck from standard transternal incision is required in surgical treatment of myasthenia gravis.

Table 168-5. Results of Thymectomy for Myasthenia Gravis

Postoperative Status	Percent of Patients[a]				
	Monden (1984)	Papatestas (1987)	Cooper (1988)	Jaretzki (1988)	Mulder (1989)
Remission	27[b]–21[c]	21	52	37	36
Improved	54[b]–70[c]	—	43	56	44
Operative benefit	81[b]–91[c]	—	95	94	80
Unchanged	—	—	5	4	18
Worse	—	—	0	0	1
Postoperative death	—	0	0	2	1

Management


MANAGEMENT OF MG
Establish diagnosis *unequivocally* (see Table 381-1)
Search for associated conditions (see Table 381-3)
Ocular only
Generalized
Crisis
MRI of brain (if positive, reassess)
Anticholinesterase (pyridostigmine)
Intensive care (respiratory infection, fluids)
Anticholinesterase (pyridostigmine)
Evaluate for thymectomy (indications: thymoma or generalized MG); evaluate surgical risk, FVC
Good risk (good FVC)
Poor risk (low FVC)
Plasmapheresis *or* intravenous Ig
then
If unsatisfactory
Thymectomy
Improved
If not improved
Evaluate clinical status; if indicated, go to immunosuppression
Immunosuppression
See text for short-term, intermediate, and long-term treatments

Differentials

Differentials

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

	Myasthenia Gravis	Lambert-Eaton	Botulism
Ocular/bulbar paresis	+	–	++ (early)
Limb weakness	+	+	+
Fatiguability	+	+	+
Post-exercise enhancement	–	+	+
Reflexes	N	↓	↓
ANS anticholinergic Sx	–	+	++
Sensory Sx	–	–	–
Associated conditions	Thymoma	Small cell carcinoma	GI SSx
Repetitive EMG stimulation	↓	↑ (rapid stimulation) ↓ (slow stimulation)	↑ (rapid stimulation) ↓ (slow stimulation)

Thank You