Management of Acute Exacerbations and Crisis in Myasthenia Gravis

For Healthcare Providers

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Disclosures

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- Argenx
  - Patient Education Speaker
- Johnson & Johnson/Janssen
  - Contributor

Outline

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- Introduction
- Definitions, Symptoms, & Risk Factors
- Outpatient Management
- Navigating the Emergency Room
- Inpatient Management
- Prevention

INTRODUCTION

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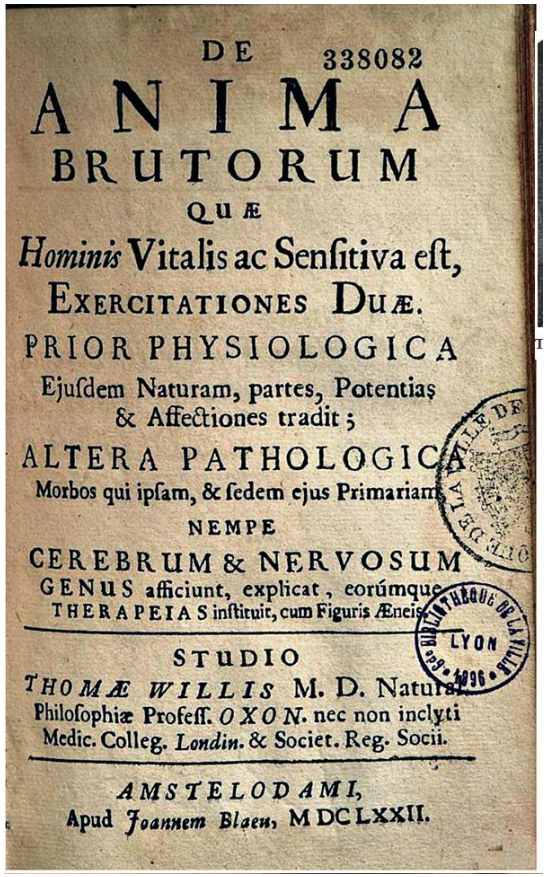
HISTORY



DE 338082

ANIMA BRUTORUM

QUÆ

Hominis Vitalis ac Senſitiva eſt,

EXERCITATIONES DUÆ.

PRIOR PHYSIOLOGICA

Ejuſdem Naturam, partes, Potentias & Affectiones tradit;

ALTERA PATHOLOGICA

Morbos qui ipſam, & ſedem ejus Primariam,

NEMPE

CEREBRUM & NERVOSUM GENUS afficiunt, explicat, eorúmque THERAPEIAS inſtituit, cum Figuris Æneis.

STUDIO

THOMÆ WILLIS M. D. Naturæ Philoſophiæ Profeſſ. *OXON.* nec non inclyti Medic. Colleg. *Londin.* & Societ. Reg. Socii.

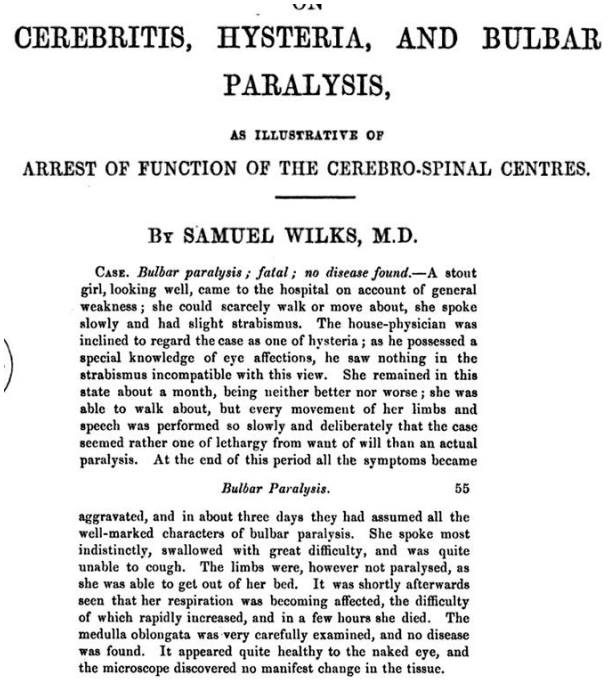
AMSTELODAMI,

Apud *Joannem Blaeu*, MDCLXXII.

Thomas Willis 1621-1675

'At this time I had under my charge a prudent and honest Woman, who for many years hath been obnoxious to this sort of spurious Palsie, not only in the members, but also in her tongue: she for some time can speak freely and readily enough, but after she has spoken long, or hastily, or eagerly, she is not able to speak a word but becomes mute as a Fish, nor can she recover the use of her voice under an hour or two'.

Two Discourses Concerning the Soul of Brutes (1685)



CEREBRITIS, HYSTERIA, AND BULBAR PARALYSIS,

AS ILLUSTRATIVE OF

ARREST OF FUNCTION OF THE CEREBRO-SPINAL CENTRES.

By SAMUEL WILKS, M.D.

Case. *Bulbar paralysis; fatal; no disease found.*—A stout girl, looking well, came to the hospital on account of general weakness; she could scarcely walk or move about, she spoke slowly and had slight strabismus. The house-physician was inclined to regard the case as one of hysteria; as he possessed a special knowledge of eye affections, he saw nothing in the strabismus incompatible with this view. She remained in this state about a month, being neither better nor worse; she was able to walk about, but every movement of her limbs and speech was performed so slowly and deliberately that the case seemed rather one of lethargy from want of will than an actual paralysis. At the end of this period all the symptoms became

Bulbar Paralysis. 55

aggravated, and in about three days they had assumed all the well-marked characters of bulbar paralysis. She spoke most indistinctly, swallowed with great difficulty, and was quite unable to cough. The limbs were, however not paralysed, as she was able to get out of her bed. It was shortly afterwards seen that her respiration was becoming affected, the difficulty of which rapidly increased, and in a few hours she died. The medulla oblongata was very carefully examined, and no disease was found. It appeared quite healthy to the naked eye, and the microscope discovered no manifest change in the tissue.

- Officially Named in 1895
  - Myasthenia: muscle and weakness
    - Gravis: heavy or grievous

Photos courtesy of: https://neuromuscular.wustl.edu/mtime/mgddx.htm
Keesey, John. Myasthenia Gravis. Archives of Neurology, Volume 55, 1998

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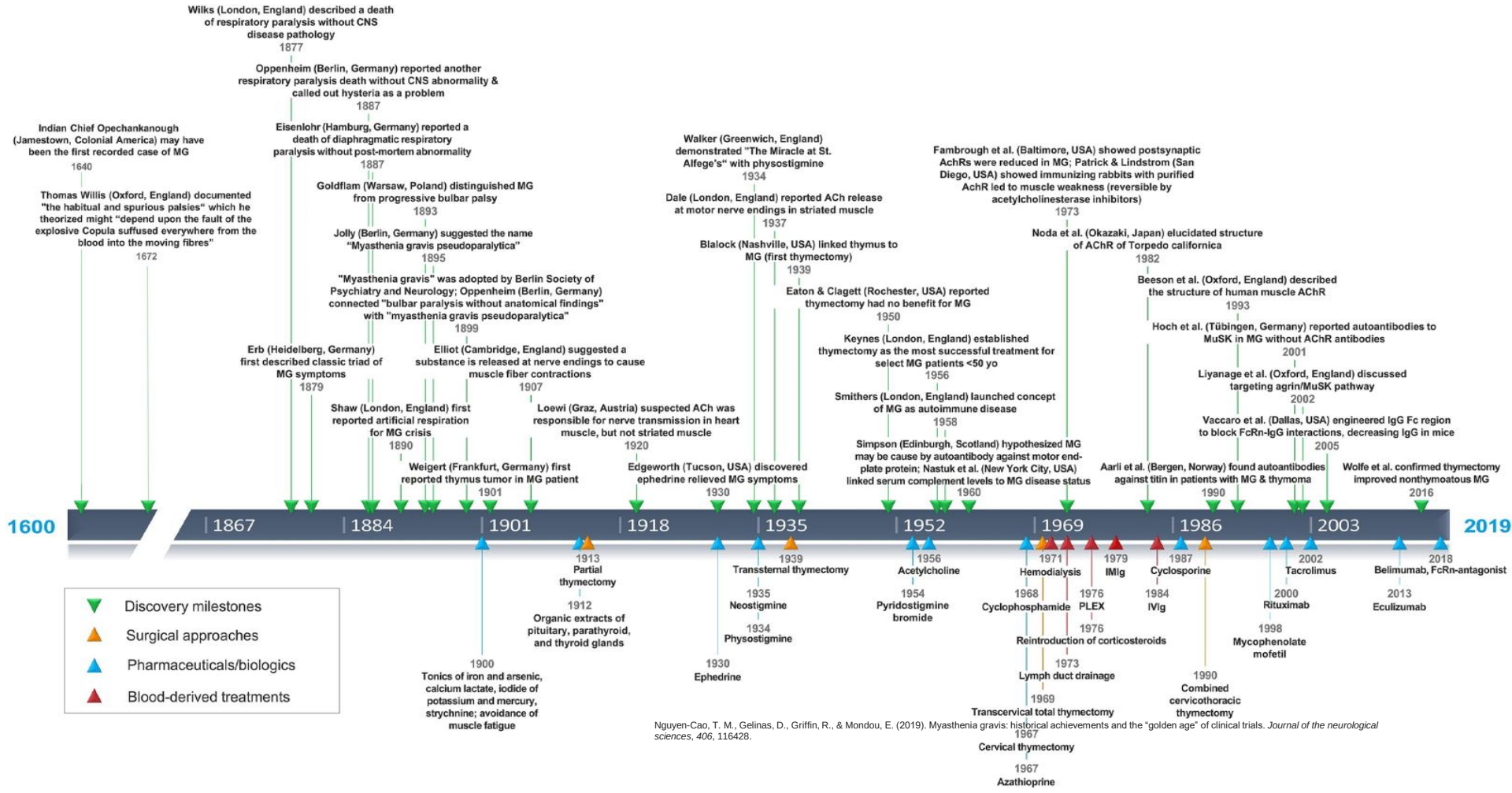

Nguyen-Cao, T. M., Gelinas, D., Griffin, R., & Mondou, E. (2019). Myasthenia gravis: historical achievements and the "golden age" of clinical trials. *Journal of the neurological sciences*, *406*, 116428.

Nguyen-Cao, T. M., Gelinas, D., Griffin, R., & Mondou, E. (2019). Myasthenia gravis: historical achievements and the "golden age" of clinical trials. *Journal of the neurological sciences*, *406*, 116428.

EPIDEMIOLOGY

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- A rare autoimmune neurological disorder
  - 10-20 cases per 100,000
- Age distribution
  - Peak around 30 years old, another peak at 50 years old
  - Younger patients more commonly female

Dresser, L., Wlodarski, R., Rezania, K., & Soliven, B. (2021). Myasthenia gravis: epidemiology, pathophysiology and clinical manifestations. *Journal of clinical medicine*, *10*(11), 2235.
Punga, A. R., Maddison, P., Heckmann, J. M., Guptill, J. T., & Evoli, A. (2022). Epidemiology, diagnostics, and biomarkers of autoimmune neuromuscular junction disorders. *The Lancet Neurology*, *21*(2), 176-188.

EPIDEMIOLOGY

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- Ocular vs Generalized
  - 66% of patients will have purely ocular symptoms at onset
  - 50-70% of patients with ocular symptoms at onset will generalize, typically in the first 2-3 years
- Antibody Positive vs Seronegative
  - AchR Abs: 80-85%
  - MuSK Ab: 5-7%
  - LRP4 Ab: 1-2%
- Early vs Late Onset
  - Early: <50yrs old at time of diagnosis
  - Late: >50yrs old at time of diagnosis
  - Early onset: may have more aggressive disease
  - Late onset: medical comorbidities may have more impact on disease course and treatment

Hehir, M. K., & Li, Y. (2022). Diagnosis and Management of Myasthenia Gravis. *CONTINUUM: Lifelong Learning in Neurology*, *28*(6), 1615-1642.

DEFINITIONS, SYMPTOMS, & RISK FACTORS

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EXACERBATION VS CRISIS

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- Myasthenia Gravis Exacerbation
  - A worsening of any MG symptom/symptoms
  - Range in severity

- Myasthenia Gravis Crisis
  - A severe exacerbation resulting in respiratory failure requiring ventilatory support

EPIDEMIOLOGY OF MG EXACERBATION & CRISIS

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- At least 70% of patients will experience an exacerbation
- A myasthenia gravis crisis occurs in about 15% of patients
  - Typically, in the first 2 years after symptom onset
  - May be the initial presentation for some patients
- Majority of patients who suffer a crisis will make a full recovery
  - Complications: Intubation, Infection, Cardiac

Neumann, B., Angstwurm, K., Mergenthaler, P., Kohler, S., Schönenberger, S., Bösel, J., ... & German Myasthenic Crisis Study Group. (2020). Myasthenic crisis demanding mechanical ventilation: a multicenter analysis of 250 cases. *Neurology*, *94*(3), e299-e313.
Wendell LC, Levine JM. Myasthenic crisis. The Neurohospitalist 2011;1:16-22.
Zochodne DW. Emergency Neurologic Consultation In The Intensive Care Unit: Neuromuscular Disorders. CONTINUUM: Lifelong Learning in Neurology 2003;9:62-79.

WHO IS AT RISK?

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- Patients were more likely to experience a crisis if:
  - Older age
  - Late onset MG
  - Higher MGFA class
  - Other medical comorbidities including other autoimmune conditions

Subgroups				
EOMG & AID−	50	3 (6)	1	
EOMG & AID+	12	2 (16)	3.13 (0.46–21.27)	0.242
LOMG & AID−	26	10 (39)	9.79 (2.39–40.08)	0.002
LOMG & AID+	8	6 (75)	47.00 (6.49–340.65)	<0.001

de Meel, R. H., Lipka, A. F., van Zwet, E. W., Niks, E. H., & Verschuuren, J. J. (2015). Prognostic factors for exacerbations and emergency treatments in myasthenia gravis. *Journal of neuroimmunology*, *282*, 123-125.

Table 1. Myasthenia Gravis Foundation of America Clinical Classification [18].

Class	Clinical symptoms
I	Any ocular weakness
II	Mild Weakness. May also have ocular muscle weakness of any severity
II A	Predominantly affecting limb, axial muscles, or both. May also have lesser involvement of oropharyngeal, respiratory muscles or both
II B	Predominantly affecting ororpharyngeal, respiratory muscles, or both. May also have lesser or equal involvement of limb, axial muscles or both
III	Moderate weakness affecting other than ocular muscles. May also have ocular muscle weakness of any severity
III A	Predominantly affecting limb, axial muscles, or both. May also have lesser involvement of oropharyngeal, respiratory muscles or both
III B	Predominantly affecting ororpharyngeal, respiratory muscles, or both. May also have lesser or equal involvement of limb, axial muscles or both
IV	Severe weakness affecting other than ocular muscles. May also have ocular muscle weakness of any severity
IV A	Predominantly affecting limb, axial muscles, or both. May also have lesser involvement of oropharyngeal, respiratory muscles or both
IV B	Predominantly affecting ororpharyngeal, respiratory muscles, or both. May also have lesser or equal involvement of limb, axial muscles or both
V	Defined by intubation, with or without mechanical ventilation, except when employed during routine postoperative management

Heldal, A. T., Eide, G. E., Romi, F., Owe, J. F., & Gilhus, N. E. (2014). Repeated acetylcholine receptor antibody-concentrations and association to clinical myasthenia gravis development. *PLoS One*, *9*(12), e114060.

Provoking Factors/Triggers

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TABLE 2 Comparison of patients with and without exacerbation

	Patients with exacerbation	Patients with no exacerbations
Patients	77	50
Seropositive	53 (69%)	27 (54%)
Thymectomy	16 (21%)	7 (14%)
MG treatment at time of exacerbation		
Steroids	98 (46%)	
Plasma exchange	20 (9%)	
IVIG	73 (34%)	
Mycophenolate mofetil	32 (15%)	
Azathioprine	95 (45%)	
Pyridostigmine (<120 mg/day)	32 (15%)	
Pyridostigmine (≥120 mg/day)	136 (61%)	

	Patients with exacerbation	Patients with no exacerbations
Total MAUC-MG prescribed	119	67
Zithromax	21 (18%)	10 (15%)
Fluoroquinolones	29 (24%)	20 (30%)
Gentamycin	1 (1%)	7 (10%)
Magnesium	15 (13%)	13 (19%)
Beta-blocker	45 (38%)	16 (24%)
Prednisone	8 (7%)	1 (1%)

Abbreviation: IVIG, intravenous Immunoglobulin.

Gummi, R. R., Kukulka, N. A., Deroche, C. B., & Govindarajan, R. (2019). Factors associated with acute exacerbations of myasthenia gravis. *Muscle & nerve*, *60*(6), 693-699.

PROVOKING FACTORS

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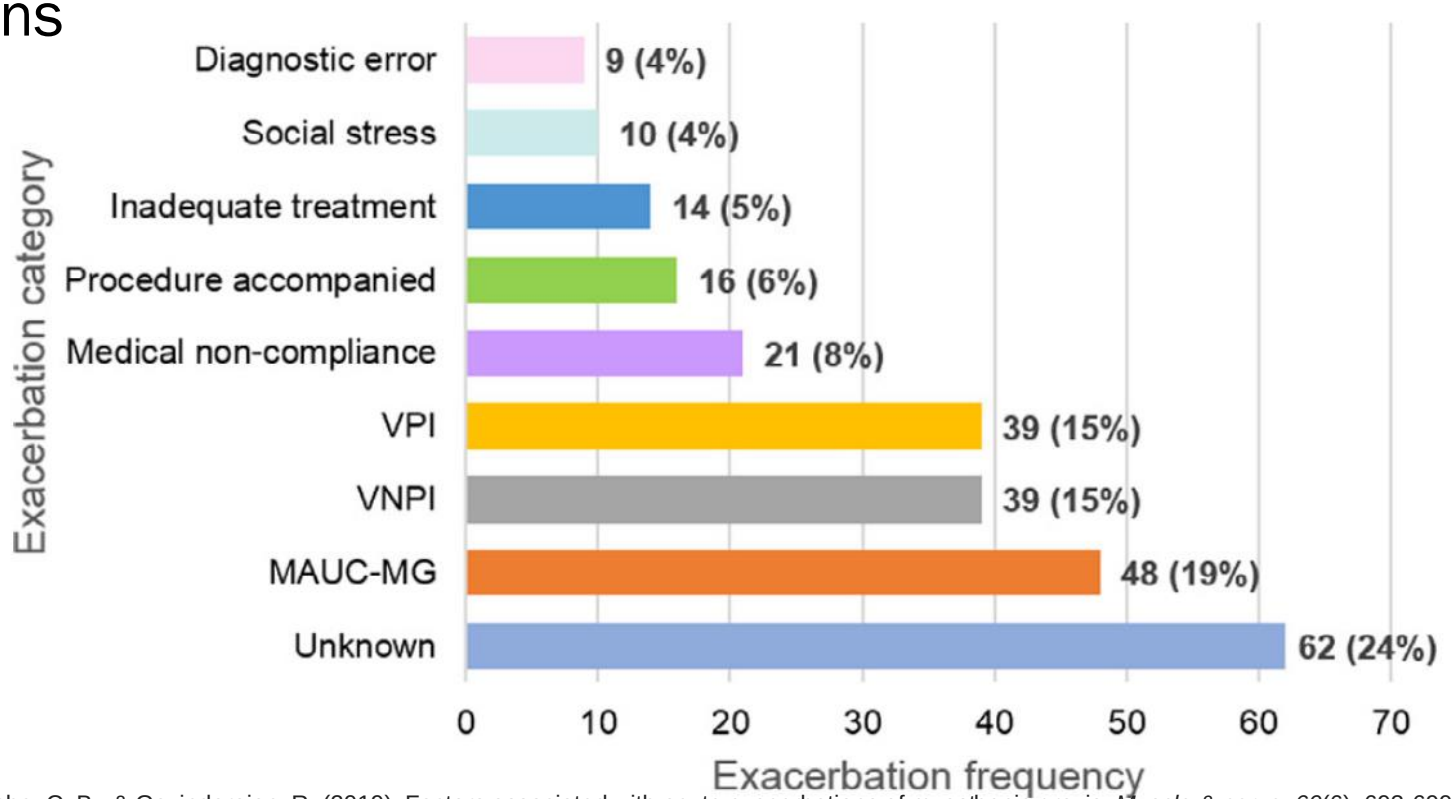
- 70% of cases are provoked by an identifiable cause
  - Infection
  - Surgery
  - Medications



Gummi, R. R., Kukulka, N. A., Deroche, C. B., & Govindarajan, R. (2019). Factors associated with acute exacerbations of myasthenia gravis. *Muscle & nerve*, *60*(6), 693-699.

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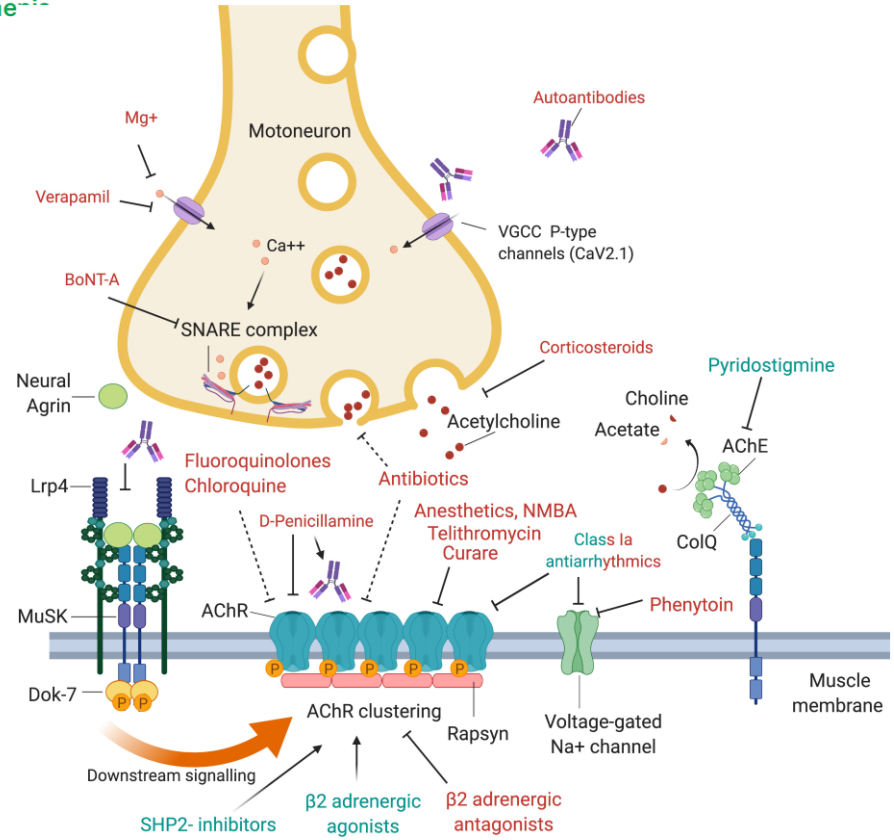
Cautionary Drugs in Myasthenia Gravis[a]

Drugs with US Food and Drug Administration (FDA) boxed warnings for use in myasthenia gravis

- Telithromycin (no longer available in the United States)
- Fluoroquinolones (ciprofloxacin, moxifloxacin, levofloxacin)

Drugs to use with caution, if at all, in myasthenia gravis

- Botulinum toxin
- D-penicillamine
- Chloroquine
- Hydroxychloroquine
- Quinine
- Magnesium
- Macrolide antibiotics (erythromycin, azithromycin, clarithromycin)
- Aminoglycoside antibiotics (gentamicin, neomycin, tobramycin)
- Corticosteroids[b]
- Procainamide
- Desferrioxamine
- Beta-blockers
- Statins
- Immune checkpoint inhibitors (pembrolizumab, nivolumab, atezolizumab, avelumab, durvalumab, ipilimumab)



[a] Data from Myasthenia Gravis Foundation of America.[37]

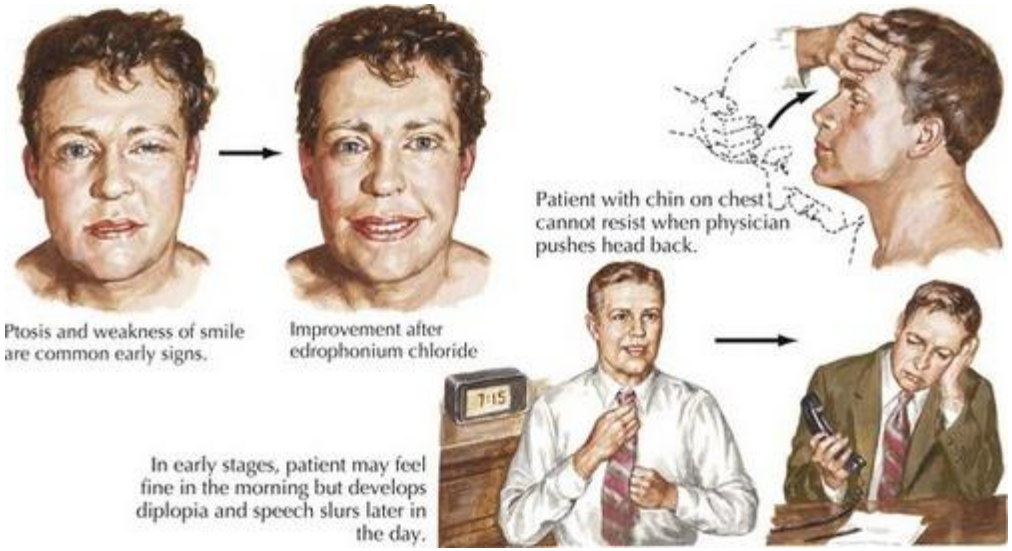
[b] Corticosteroids may cause transient worsening of symptoms in the first 2 weeks but are part of the standard treatment for myasthenia gravis. Close monitoring should be in place when initiating steroids.

Birch, T. B. (2021). Neuromuscular Disorders in the Intensive Care Unit. *CONTINUUM: Lifelong Learning in Neurology*, *27*(5), 1344-1364.
Krenn, M., Grisold, A., Wohlfarth, P., Rath, J., Cetin, H., Koneczny, I., & Zimprich, F. (2020). Pathomechanisms and clinical implications of myasthenic syndromes exacerbated and induced by medical treatments. *Frontiers in Molecular Neuroscience*, *13*, 156.

SIGNS & SYMPTOMS

- Drooping Eyelids (Ptosis)
  - Can be unilateral or bilateral
- Neck Weakness
  - Head drop
- Facial Weakness
  - Decreased facial expressions
  - Jaw Fatigue
  - Impaired eye/lip closure
- Blurry Vision/Double Vision (diplopia)

- Limb Weakness/Fatigability
  - Difficulty with walking/rising from seated position/using stairs
  - Difficulty raising arms



Gilhus, N. E., Socrates, T., Amelia, E., Jacqueline, P., & Burns, T. M. (2019). Myasthenia gravis (Primer). *Nature Reviews: Disease Primers*, *5*(1).

SIGNS & SYMPTOMS

- Speech Changes (Dysarthria)
  - Slurred/Nasal Speech
- Difficulty Swallowing (Dysphagia)
  - Liquids and/or solids
  - Managing secretions
- Shortness of Breath (Dyspnea)
  - At rest or with activity
  - Worsening with laying flat (orthopnea)
  - Use of accessory muscles when breathing

Gilhus, N. E., Socrates, T., Amelia, E., Jacqueline, P., & Burns, T. M. (2019). Myasthenia gravis (Primer). *Nature Reviews: Disease Primers*, *5*(1).

OUTPATIENT MANAGEMENT

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Management

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- Minimal/Mild Exacerbations
  - Including ptosis, vision changes, mild extremity weakness
  - Obtain history
  - Schedule for virtual or in-office visit, if possible
  - Adjustments to treatment regimen
    - Pyridostigmine
    - Prednisone
    - IVIG or PLEX schedule
  - Low threshold for ED/hospital evaluation if symptom worsening

NAVIGATING THE EMERGENCY ROOM

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MODERATE & SEVERE EXACERBATIONS

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- Symptoms: Progressive difficulty swallow and/or progressive shortness of breath, moderate or severe muscle weakness
- Called EMS or immediately present to the nearest ER
- Evaluation by ER physician & staff
  - Triage
  - History & Physical
  - Labs & Imaging
  - Neurology & pulmonology consults, if available

BEDSIDE EXAMINATION

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- Neurological
  - Prolonged upgaze
  - Voice changes
  - Eye movements, facial strength, neck strength
  - Muscle strength – fatigability
  - Single Breath Count
    - Want greater than or equal to 20

BEDSIDE EXAMINATION

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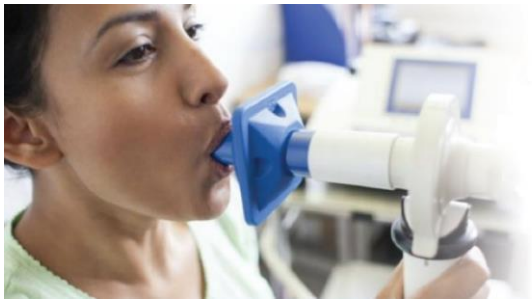
- Pulmonary Function Testing
  - Negative Inspiratory Force (NIF) or Maximum Inspiratory Pressure (MIP)
    - Normal NIF > -25cmH20
    - Normal MIP >-60cmH20
  - Functional Vital Capacity (FVC)
    - Normal is > 70-100%



- Important Note
  - Oxygen saturation is NOT a reliable measure of respiratory distress in patients with myasthenia gravis

ER MANAGEMENT

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- Antibiotics for potential infection
  - Important physician is familiar with antibiotics which should be used with caution
- Intravenous Fluids
- Correction of electrolyte abnormalities
  - Avoid high doses of magnesium
- Nothing by mouth until formal evaluation

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Checklist for a Myasthenia Gravis Emergency

- ❒ Take an updated list of all medications & treatments and treating physicians
- ❒ Keep a list of medications to be avoided or used with caution in patients with myasthenia gravis
- ❒ Inform the emergency room staff about your diagnosis of myasthenia gravis, your symptoms, and name of neurologist
- ❒ Share any recent changes (e.g. new medications) or symptoms (e.g. signs of infection, new cough)
- ❒ Make sure you have bedside pulmonary function testing performed including:
  - Negative Inspiratory Force (NIF) or Maximum Inspiratory Pressure (MIP)
    - Normal NIF > -25cmH20
    - Normal MIP >-60cmH20
  - Functional Vital Capacity (FVC)
    - Normal is > 70-100 %
- ❒ Make sure to have swallow function evaluated
  - Do not eat or drink until cleared by the physician
- ❒ If admitted to hospital, treatment may include intravenous immunoglobulin (IVIG) or plasma exchange (PLEX)
  - The treatment team should include a neurologist and pulmonologist
- ❒ Once stable, contact your primary neurologist to inform him or her of what has occurred and your status
- ❒ At the time of hospital discharge, call your neurologist to make a follow-up appointment in 1-2 weeks

INPATIENT MANAGEMENT

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INPATIENT MANAGEMENT

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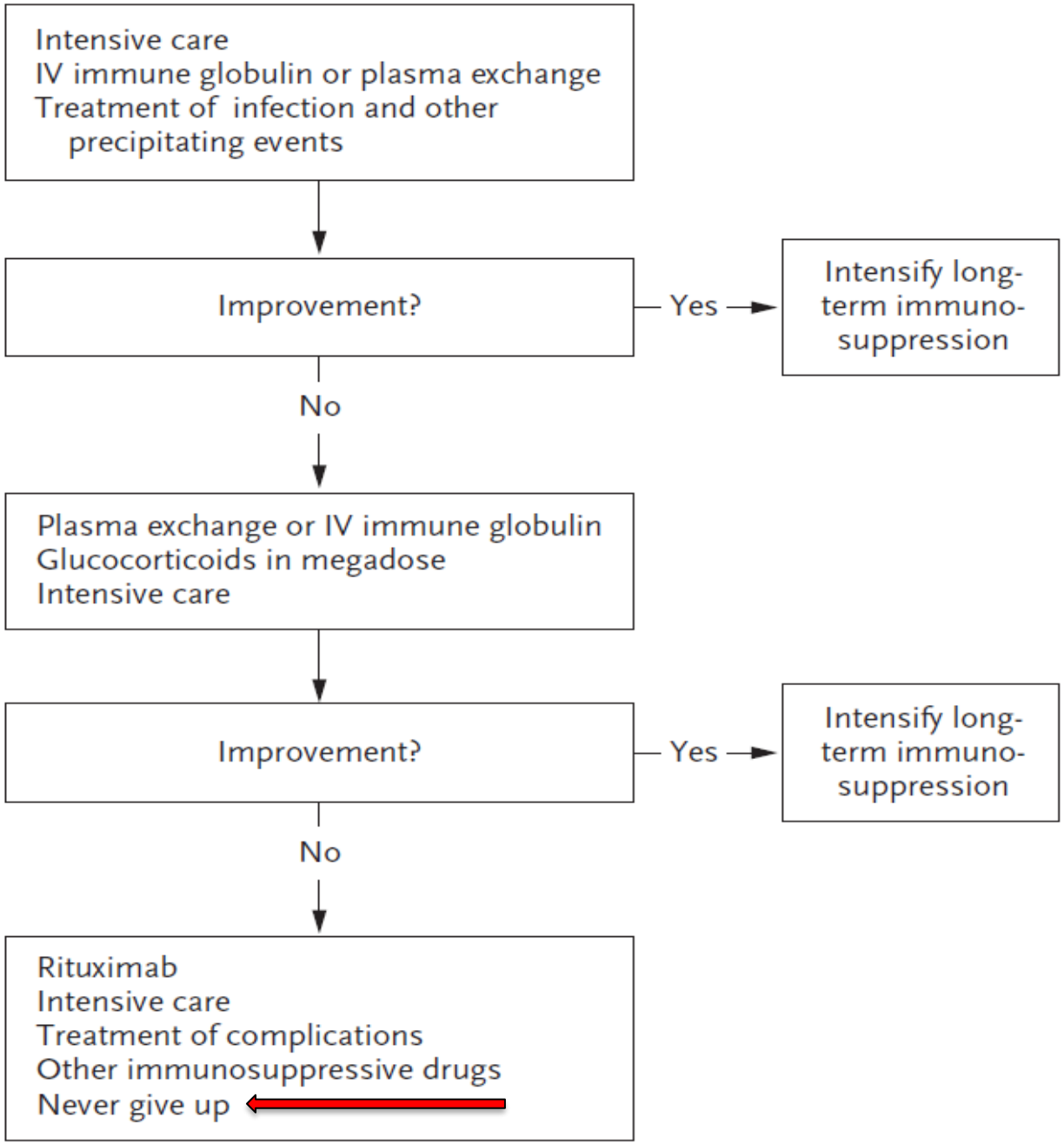
- Admit to an IMU or ICU
- Stop any contributing medications
  - Including pyridostigmine
- Regular monitoring of PFTs

- Start non-invasive ventilation, if possible
  - Can prevent/delay intubation in over 50% of patients with myasthenia
- Intubation
  - Consideration of elective intubation
- Cardiac monitoring
  - Severe arrhythmias ~20% of patients

B **Proposed Treatment for Severe Exacerbations of Generalized Myasthenia Gravis**



Longo, D. L. (2016). Nils E. Gilhus, MD. *N Engl J Med*, *375*, 2570-81.

INTRAVENOUS IMMUNOGLOBULIN (IVIG)

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- Infusion of purified pooled preparations of IgG antibody from plasma
- Immunomodulation through several mechanisms
- 2g/kg of patient weight divided over 4-5 days
- Use in caution in patients with cardiac/vascular history, including DVT, and in patients with kidney disease

▶ **IV Immunoglobulin**

Infusion-related events

- Headache
- Shivering
- Myalgia

Chest pain

Hyperviscosity (risk of thrombosis, including arterial events)

Aseptic meningitis

Acute kidney injury

Anaphylaxis (if IgA deficiency)

Transfusion reaction (including transfusion-related acute lung injury)

IgA = immunoglobulin A; IV = intravenous.

Farmakidis, C., Dimachkie, M. M., Pasnoor, M., & Barohn, R. J. (2020). Immunosuppressive and immunomodulatory therapies for neuromuscular diseases. Part I: Traditional agents. *Muscle & nerve*, *61*(1), 5-16.
Rabinstein AA. Acute neuromuscular respiratory failure. CONTINUUM: Lifelong Learning in Neurology 2015;21:1324-1345

PLASMA EXCHANGE (PLEX)

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- Directly removes immune factors such as autoantibodies, immune complexes, complement, and other non-specific inflammatory mediators
- 5 sessions scheduled every other day
- May require central venous catheter
- Use for caution in patients with infection, high bleeding risk

▶ **Plasma Exchange**

Venous catheter-related events

- Infection
- Pneumothorax
- Local hematoma

Hemodynamic instability (hypotension)

Hemoconcentration

Coagulopathy (mild)

Hypocalcemia

Removal of highly protein-bound drugs

Transfusion reaction (including transfusion related acute lung injury)

Farmakidis, C., Dimachkie, M. M., Pasnoor, M., & Barohn, R. J. (2020). Immunosuppressive and immunomodulatory therapies for neuromuscular diseases. Part I: Traditional agents. *Muscle & nerve*, *61*(1), 5-16.
Rabinstein AA. Acute neuromuscular respiratory failure. CONTINUUM: Lifelong Learning in Neurology 2015;21:1324-1345

IVIG vs PLEX

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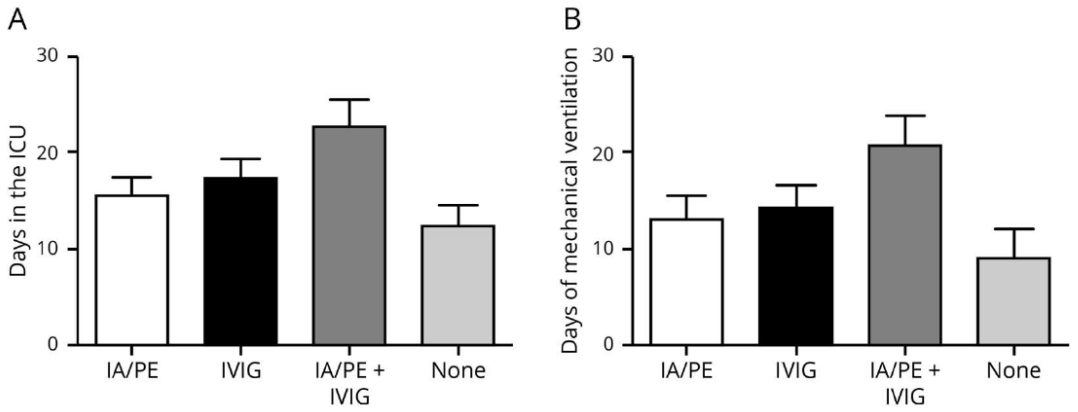
- Both IVIG and PLEX have similar effectiveness in treating myasthenia gravis exacerbation/crisis
- PLEX may result in a more rapid effect
- If incomplete effect from PLEX, IVIG may be given subsequently

- Decision depends on clinical patient characteristics, safety/tolerability, previous response, other patient specific factors

Figure 1 Treatment and outcome



Days in the intensive care unit (ICU) (A) and days of mechanical ventilation (B) of patients who were treated with immunoadsorption (IA) or plasma exchange (PE) (IA/PE; n = 56), IV immunoglobulins (IVIg; n = 66), IA or PE in combination with IVIg treatment (IA/PE + IVIg; n = 43), or without IA, PE, or IVIg (none; n = 34). Decedents (n = 30) and cases where the number of days of ventilation was not known exactly (n = 21, e.g., because of ventilation at discharge or transfers from other hospitals) were excluded. Bars show mean ± SD.

Neumann, B., Angstwurm, K., Mergenthaler, P., Kohler, S., Schönenberger, S., Bösel, J., ... & German Myasthenic Crisis Study Group. (2020). Myasthenic crisis demanding mechanical ventila multicenter analysis of 250 cases. *Neurology*, *94*(3), e299-e313.

OTHER MANAGEMENT OPTIONS

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- Corticosteroids
  - Often a part of the treatment plan for MG crisis
  - Must be used with caution as rapid administration or high dose steroids may cause worsening
    - Less likely in patients being treated with IVIG or PLEX
  - For non-intubated patients, doses should be started lower (10-20mg) and increased by 5mg every 2-3 days; goal typically 60-80mg/day
  - For intubated patients, higher initial doses may be tolerated

Farmakidis, C., Dimachkie, M. M., Pasnoor, M., & Barohn, R. J. (2020). Immunosuppressive and immunomodulatory therapies for neuromuscular diseases. Part I: Traditional agents. *Muscle & nerve*, *61*(1), 5-16.
Rabinstein AA. Acute neuromuscular respiratory failure. CONTINUUM: Lifelong Learning in Neurology 2015;21:1324-1345

PREVENTION

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LONGTERM MANAGEMENT

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A

B

TREATMENT OF MYASTHENIA GRAVIS WITH PHYSOSTIGMINE

To the Editor of THE LANCET

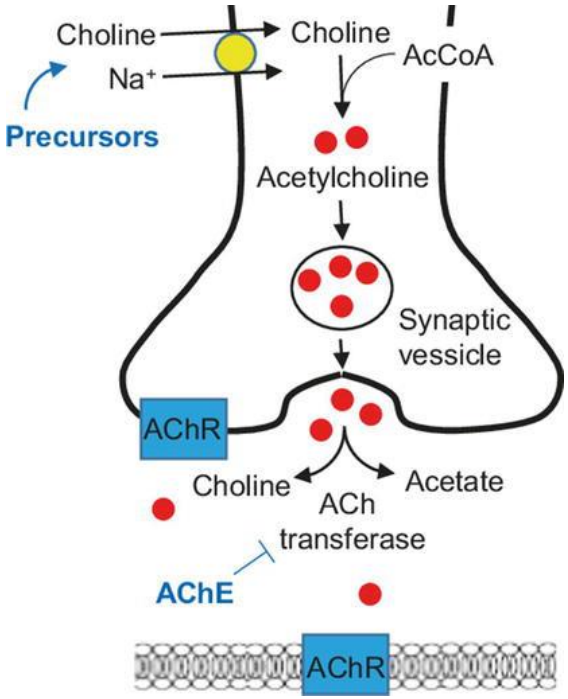
SIR,—The abnormal fatigability in myasthenia gravis has been thought to be due to curare-like poisoning of the motor nerve-endings or of the "myoneural junctions" in the affected muscles. It occurred to me recently that it would be worth while to try the effect of physostigmine, a partial antagonist to curare, on a case of myasthenia gravis at present in St. Alfege's Hospital, in the hope that it would counteract the effect of the unknown substance which might be exerting a curare-like effect on the myoneural junctions. I found that hypodermic injections of physostigmine salicylate did have a striking though temporary effect.

Mrs. M., aged 56, had had a previous attack of myasthenia gravis, lasting about six months, 14 years ago. Gastric ulcer four years ago. Non-specific infective arthritis seven months ago, now improved.

Towards the end of
was unable to hold he
used to fall forwards
She had to remain in
difficulty in sitting up
she had to hold it
eyelid began to droop
she was excited, swall
times regurgitated the
to the hospital on Marc
ness came on in the mi
The weakness is much
lessened by rest. It b
There is no wasting, an
The masseters respond
a myasthenic reaction
deltoid. Radiograms sh
The thymus is not enla

On April 11th treat
physostigmine salicylat
In from half an hour to an hour after the injection the left eyelid "goes up" (see Figure), arm movements are much stronger, the jaw drops rather less, swallowing is improved, and the patient feels "less heavy." The effect wears off gradually in from 2–4 hours. With injections

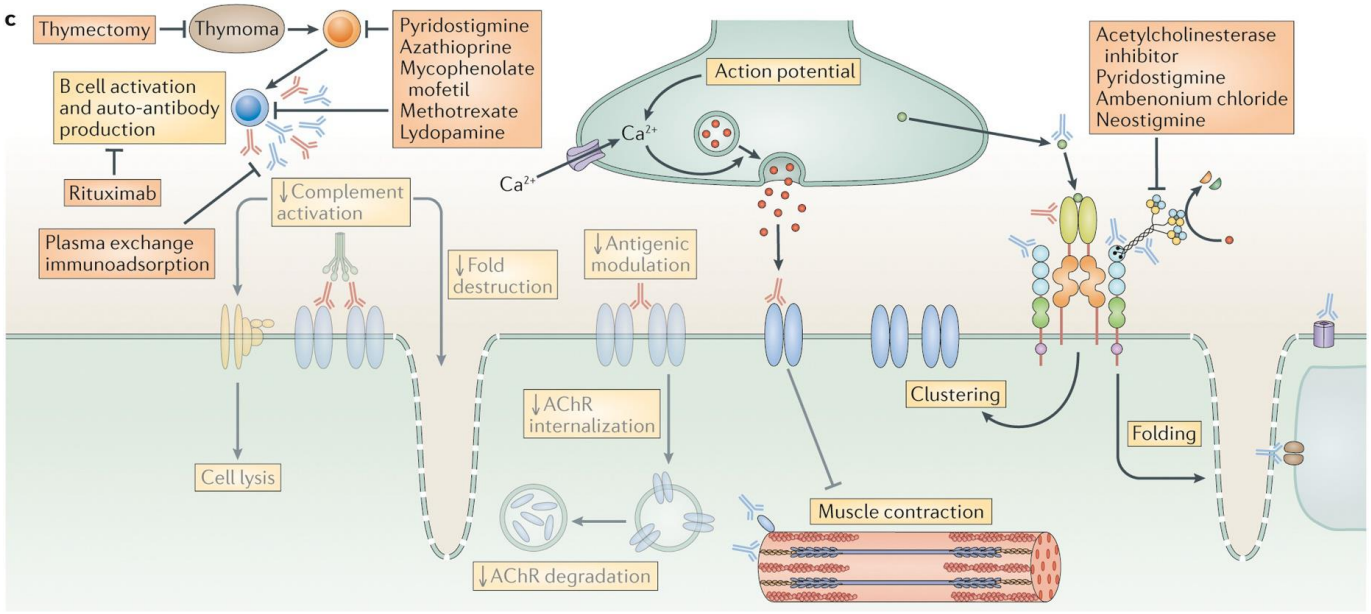
Before injection the patient cannot raise her left eyelid. Thirty minutes after it the eye is fully open. (The photographs are reproduced from a chronophotograph film and are reversed left for right.)

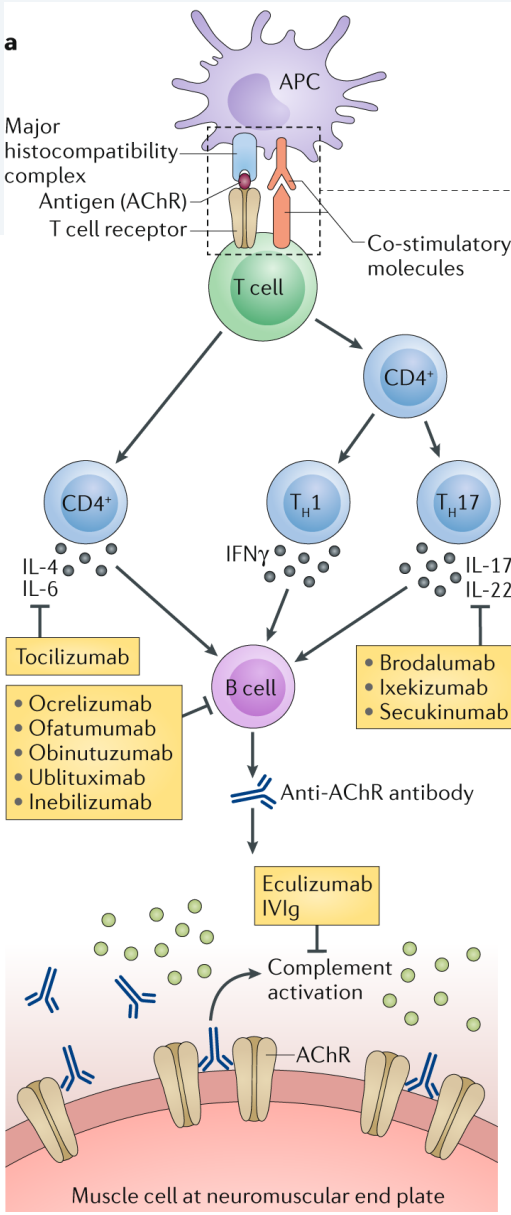


- Symptomatic Treatment
  - Pyridostigmine
    - Acetylcholine esterase inhibitor
    - Dosing variable
    - Side Effects: GI upset, increased saliva, increased tearing, runny nose, muscle cramping, muscle twitching

Vincent, A. (2002). Unravelling the pathogenesis of myasthenia gravis. *Nature Reviews Immunology*, *2*(10), 797-804.

IMMUNOMODULATORY TREATMENTS





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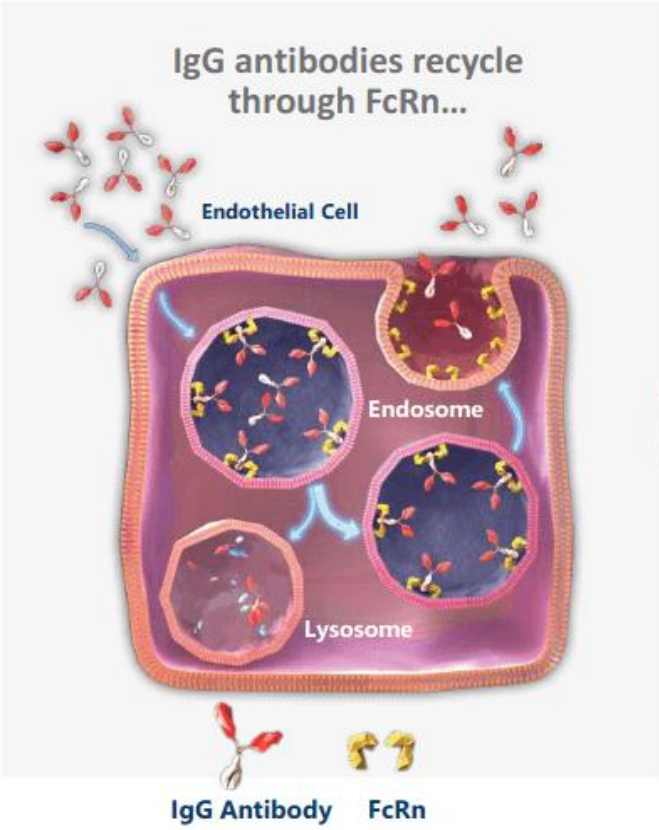

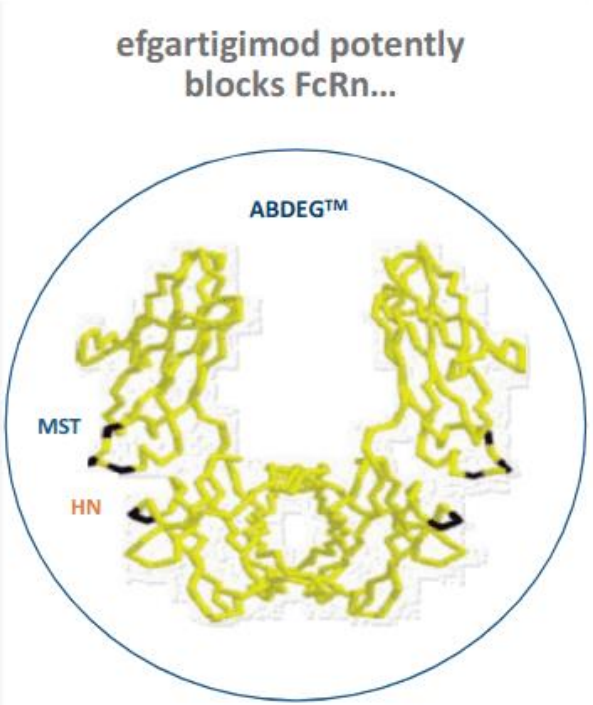

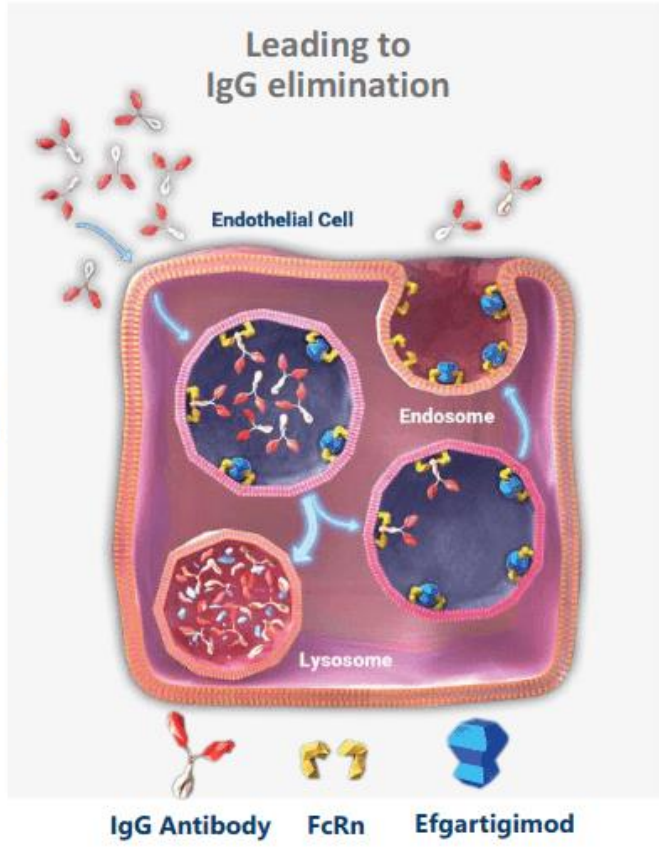

Image: https://seekingalpha.com/article/4378785-argenx-competitive-positioning-in-gmg-space

THYMECTOMY

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- Can be considered to improve long-term control of MG symptoms
  - Recommended for patients under 65yo and either AchR Ab+ or seronegative status
  - Usually earlier on in disease course and/or in patients with more severe and harder to control myasthenia gravis
  - Patient should be stable enough for surgery
  - Endoscopic surgery is preferred approach
  - May have preoperative use immunomodulatory therapy
- Surgery is recommended for thymoma regardless of age, disease severity, or antibody status

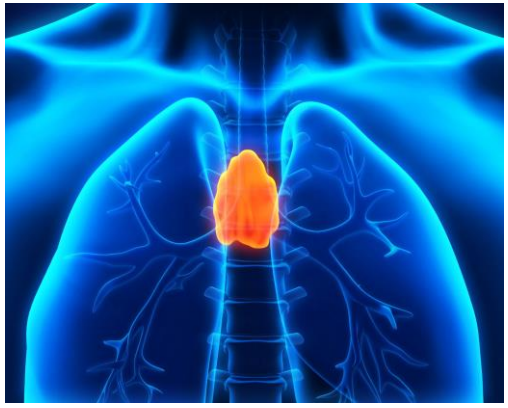
Article

November 1, 1941

THE TREATMENT OF MYASTHENIA GRAVIS BY REMOVAL OF THE THYMUS GLAND

PRELIMINARY REPORT

ALFRED BLALOCK, M.D.; A. McGEHEE HARVEY, M.D.; FRANK R. FORD, M.D.; et al



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https://www.verywellhealth.com/thymus-anatomy-4800309

THYMECTOMY

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Randomized Trial of Thymectomy in Myasthenia Gravis

Gil I. Wolfe, M.D., Henry J. Kaminski, M.D., Inmaculada B. Aban, Ph.D., Greg Minisman, M.A., Hui-Chien Kuo, M.S., Alexander Marx, M.D., Philipp Ströbel, M.D., Claudio Mazia, M.D., Joel Oger, M.D., J. Gabriel Cea, M.D., Jeannine M. Heckmann, M.B., Ch.B., Ph.D., Amelia Evoli, M.D., et al., for the MGTX Study Group*

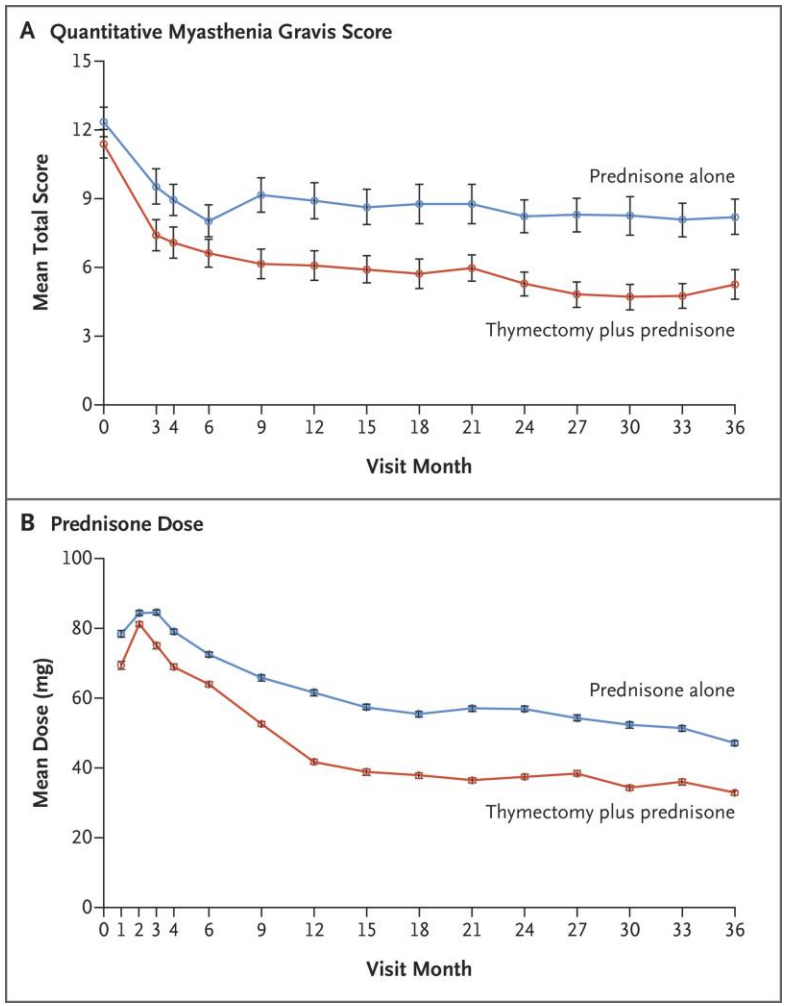

Table 2. Primary and Subgroup Analyses of the Primary Outcomes.*

Outcome	Prednisone Alone		Thymectomy plus Prednisone		Estimated Difference (95% CI)†	P Value‡
	value	*no. of patients*	*value*	*no. of patients*		
Primary analyses						
Time-weighted average QMG score over 3-yr period	8.99±4.93	56	6.15±4.09	62	2.85 (0.47 to 5.22)	<0.001
Time-weighted average alternate-day prednisone dose over 3-yr period (mg)	54±29	56	32±23	61	22 (12 to 32)	<0.001
Subgroup analyses						
Time-weighted average QMG score						
Prednisone use at enrollment						0.86
Yes	9.10±5.06	46	6.30±3.89	47	2.80 (0.11 to 5.49)	0.004
No	8.84±4.60	9	5.66±4.79	15	3.18 (−3.03 to 9.39)	0.12
Sex						0.57
Female	9.73±5.16	38	6.47±4.13	46	3.26 (0.34 to 6.18)	0.002
Male	7.45±4.11	18	5.23±3.95	16	2.22 (−1.96 to 6.40)	0.12
Age at disease onset						0.74
<40 yr	9.60±5.32	34	6.50±4.41	42	3.10 (−0.13 to 6.33)	0.007
≥40 yr	7.85±3.50	18	5.33±2.79	18	2.52 (−0.65 to 5.69)	0.02
Time-weighted average alternate-day prednisone dose (mg)						
Prednisone use at enrollment						0.91
Yes	56±31	46	35±25	46	22 (10 to 33)	<0.001
No	45±22	9	25±17	15	20 (4 to 37)	0.02
Sex						0.79
Female	54±27	37	33±25	45	21 (9 to 32)	<0.001
Male	55±34	19	31±18	16	24 (5 to 42)	0.01
Age at disease onset						0.81
<40 yr	55±30	33	35±25	41	20 (8 to 33)	0.002
≥40 yr	49±29	19	27±18	18	23 (7 to 39)	0.007

* CI denotes confidence interval.
† We used 95% confidence intervals in all analyses except for analyses involving the QMG score, for which we used 99.5% confidence intervals, per protocol.
‡ P values for between-group comparisons are based on two independent sample Student's t-tests. P values for interaction with treatment were based on fitting a general linear model separately for each variable.

Wolfe, G. I., Kaminski, H. J., Aban, I. B., Minisman, G., Kuo, H. C., Marx, A., ... & Cutter, G. R. (2016). Randomized trial of thymectomy in myasthenia gravis. *New England Journal of Medicine*, *375*(6), 511-522.

LIFESTYLE MODIFICATIONS

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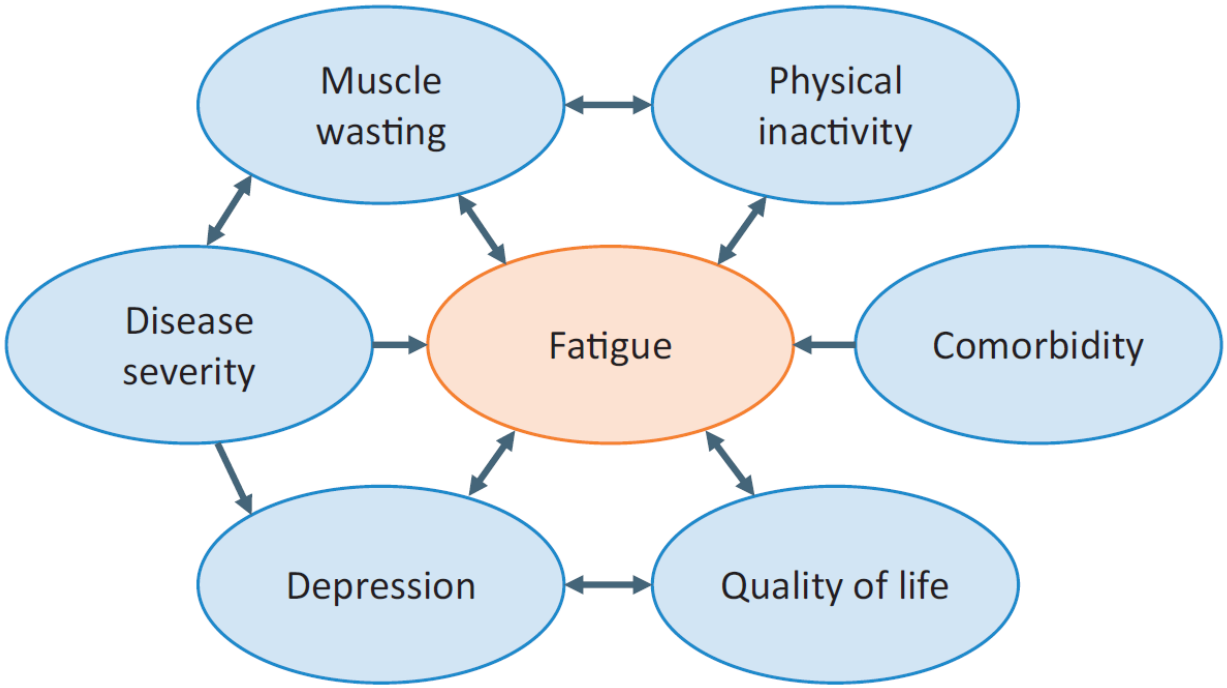
- Fatigue present in about 80% of patients with MG
- Management can include
  - Cognitive behavioral therapy
  - Weight Reduction
  - Pain control



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Ruiter, A. M., Verschuuren, J. J., & Tannemaat, M. R. (2020). Fatigue in patients with myasthenia gravis. A systematic review of the literature. *Neuromuscular Disorders*, *30*(8), 631-639.

LIFESTYLE MODIFICATIONS

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- Exercise
  - Able to be tolerated in most patients with MG
  - Aerobic exercise performed with more rest periods
  - Balance and stretching exercises
  - Avoidance of high temperatures
  - Type and length of exercise dependent on clinical/physical status
- Diet
  - Low gluten, avoid processed sugars, increased fruits and vegetables
  - Plant based
  - Evaluation of the gut microbiome

Hehir, M. K., & Li, Y. (2022). Diagnosis and Management of Myasthenia Gravis. *CONTINUUM: Lifelong Learning in Neurology*, *28*(6), 1615-1642.
Ruiter, A. M., Verschuuren, J. J., & Tannemaat, M. R. (2020). Fatigue in patients with myasthenia gravis. A systematic review of the literature. *Neuromuscular Disorders*, *30*(8), 631-639.

ADDITIONAL RECOMMENDATIONS

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- Early and accurate diagnosis
- Close outpatient monitoring
  - Especially early in disease course
- Patient and Provider Education
  - Early identification of exacerbation symptoms
- Management of Comorbidities
- Vaccinations
  - Including COVID-19 vaccination & booster

CONCLUSION

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CONCLUSION

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- Myasthenia gravis exacerbations are common though most are mild
- About 15% of patients with MG will experience a myasthenia gravis crisis requiring respiratory support
- Be prepared with medication list, medications to avoid, name of neurologist, and information on recent health changes
- Close monitoring of pulmonary function
  - Oxygen saturation is not a reliable measure of respiratory distress
  - May include elective intubation
- The majority of patients who experience an exacerbation or crisis will make a full recovery

CONCLUSION

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- Older patients and those with another autoimmune condition are more likely to experience an exacerbation
- Prevention includes
  - Establishing care with a neurologist/neuromuscular specialist early
  - Management of comorbidities, vaccination, and education
  - Achieving effective long-term treatment
- Recommend exercise and healthy diet

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