

Welcome

Myasthenia Gravis is a disease that requires skill and experience to safely treat, is often misunderstood by clinicians and is lacking in appropriate information for those affected by it. The goal of this packet is to be a bridge between poor communication in clinic, lack of access to Myasthenia Gravis board certified physicians and incorrect information proliferated online.

This patient packet is meant solely as a supplementary guide to assist Myasthenics, their caregivers and clinicians in executing optimal care through appropriate education.

This is not meant to diagnose, treat or replace a physician's care but rather offer up tertiary information as an extra layer of support and safety.

The information provided has been selected from the Myasthenia Gravis Hope Foundation, the Muscular Dystrophy Association, Myasthenia Gravis Foundation of America, the National Institute of Neurological Disease and Stroke and other special partners.

It is our hope and our goal that this resource will imbue a better sense of what you or your loved one may be fighting and encourage safer, more positive and symbiotic relationships with your clinical providers.



What is Myasthenia Gravis?

Myasthenia Gravis (MG) is a neuromuscular, autoimmune disease that affects neuromuscular transmission of the skeletal (voluntary) muscles, which leads to generalized weakness of the upper and lower extremities, bulbar, ocular and respiratory muscles or localized weakness identified by increasing fatigability, commonly found in repetitive movement.

It is classified as the most prevalent disorder of the neuromuscular junction, with an annual incidence of 14-20 patients per 100,000 with an estimated 30,000 to 65,000 cases in the United States alone. As awareness and education continues to grow, the population of diagnosed patients increases.

It is the widely held belief that Myasthenia Gravis is under diagnosed and may have a slightly higher rate of occurrence than currently known. The usual cause is an acquired immunological abnormality, but some cases result from genetic abnormalities at the neuromuscular junction.

Myasthenia Gravis is most commonly correlated with AChR antibodies that come against acetylcholine receptors (AChR) in the post-synaptic motor end plate. The majority of Myasthenics will be AChR positive with an occurrence rate between 80-90%. A secondary form of Myasthenia Gravis is the MuSK positive antibody with a patterned correlation seen in young women, involving antibodies against muscle-specific tyrosine kinase (MuSK). A tertiary collection of individuals have no antibodies for either AChR nor MuSK, and are clinically assigned as seronegative. Seronegative does not mean that the patient does not have Myasthenia Gravis. Care providers who suspect Myasthenia Gravis in an individual who does not present in labs should move on to secondary and tertiary testing. Clinically, seronegative patients share a similarity in presentation to patients with AChR antibodies. Myasthenia Gravis is commonly misdiagnosed as a stroke, Bells-palsy, psycho-somatic disorder(s), anxiety, Parkinson's and Multiple Sclerosis.

The presentation of Myasthenia Gravis generally begins with ocular weakness that results in ptosis (drooping of the eyelid) and diplopia (double vision). Not all who present with ocular weakness will move on to generalized weakness. The incidence rate of progression to generalized MG is greater than 85%. Generalized weakness can be a slow progression or have rapid onset and is seen with difficulty with walking, talking, speaking, breathing, swallowing, exercising, maintaining neck flexion, falling, slurred speech, a nasal or raspy voice etc.

Myasthenia Gravis should worsen with repetitive activity and improve with rest.

While treatments and critical care have advanced greatly in recent years, the qualification that most patients can achieve a normal or nearly normal life is greatly misleading. Medications and emergency intervention has made it possible to enjoy a high rate of a normal life span but often comes with difficult side effects and aggressive therapies. It is difficult to qualify what normal or nearly normal means for each individual Myasthenic and is often a source of contention amongst the majority of the population.

Please be aware that while Myasthenia Gravis has fundamental proponents that allow for a baseline of care, it also offers a unique presentation in it's nuances. Known lovingly as the snow flake disease, MG is as variable in symptoms and response in each individual as a snowflake, which makes it essential to connect with a specialist in the treatments and care of MG.

Common Medical Terms for Myasthenia Gravis

Acetylcholine: is the neurotransmitter used at the neuromuscular junction—in other words, it is the chemical that motor neurons of the nervous system release in order to activate muscles and is responsible for contraction. Acetylcholine is the substance the nervous system uses to activate skeletal muscles, a kind of striated muscle. These are the muscles used for all types of voluntary movement, in contrast to smooth muscle tissue, which is involved in a range of involuntary activities such as movement of food through the gastrointestinal tract and constriction of blood vessels.

Acetylcholine Receptor: is an integral membrane protein that responds to the binding of acetylcholine, a neurotransmitter necessary for contraction and activation. The receptor allows for the completion of acetylcholine to finalize contraction of the muscles.

Acetylcholinesterase inhibitor: is a chemical or a drug that inhibits the acetylcholinesterase enzyme from breaking down acetylcholine, thereby increasing both the level and duration of action of the neurotransmitter acetylcholine. Pyridostigmine (Mestinon) is classified as an acetylcholinesterase inhibitor. Mestinon is typically the first line drug of choice because it is the only drug that chemically increases the amount of acetylcholine available to stimulate the receptors, which consequently provides more contraction of the muscles, helping to reverse flaccidity or weakness.

Anticholinergic: is a chemical substance that blocks the neurotransmitter acetylcholine in the central and the peripheral nervous system (preventing contraction and increasing weakness, often to a notable or moderate to severe degree in Myasthenics). Common anticholinergic drugs are Atropine, Robinul, Dramamine, Benadryl, Sominex, Advil PM, Unisom, etc..

Atropine and Robinul can be used under strictly supervised circumstances to reverse a cholinergic crisis.

AChR (antibodies): AChR antibodies hinder the action of acetylcholine, a chemical (neurotransmitter) that transmits messages between nerve cells. The antibodies do this in three major ways:

"Binding" antibodies attach to the acetylcholine receptors on nerve cells and may initiate an inflammatory reaction that destroys them.

"Blocking" antibodies may sit on the receptors, preventing acetylcholine from binding.

"Modulating" antibodies may cross-link the receptors, causing them to be taken up into the muscle cell and removed from the neuromuscular junction.

Approximately 85% of MG patients have this antibody and, when detected with an elevated concentration the AChR antibody test is strongly indicative of MG.

MuSK (antibodies): antibodies to muscle-specific kinase (MuSK), a receptor tyrosine kinase that is essential for neuromuscular junction development, found in 15% of individuals negative for AChR antibodies and up to 40% in the remaining seronegative individuals. One of the more striking differences is the female predominance of patients with MuSK, ranging between series from 78% to 100% women. Individuals with MuSK antibodies are less likely to respond positively to acetylcholinesterase inhibitors and have greater pronounced neck, shoulder and respiratory involvement without ocular weakness.

Seronegative: a negative result in biochemistry or in blood work. A seronegative test for MG does not necessarily mean the individual does not have MG, but rather that further testing needs to be completed outside of lab work.

Common Medical Terms for Myasthenia Gravis (continued)

Neuromuscular Junction: is the junction where neurons (cells that processes and transmits information through electrical and chemical signals) communicate to neurotransmitters (acetylcholine) and to non-neuronal cells such as those in muscles. At the neuromuscular junction, the nerve fiber is able to transmit a signal to the muscle fiber by releasing acetylcholine (and other substances), causing muscle contraction. (It is at this junction that antibodies from our immune system attack and intercept the communication between the neurons, acetylcholine and muscles, causing weakness.)

Autoantibodies: Autoantibodies are antibodies (immune proteins) that mistakenly target and react with a person's own tissues or organs. One or more autoantibodies may be produced by a person's immune system when it fails to distinguish between "self" and "non-self."

Usually the immune system is able to discriminate between foreign substances ("non-self") and the body's own cells ("self"). It produces antibodies only when it perceives that it has been exposed to a threat ("non-self"), such as bacteria or viruses. However, when the immune system ceases to recognize one or more of the body's normal constituents as "self," it may produce autoantibodies that react with its own cells, tissues, and/or organs. This may cause inflammation, damage, and/or dysfunction of organs or systems, leading to signs and symptoms of autoimmune disorders.

Flaccidity: lack of muscular contraction or strength.

Ocular: Ocular myasthenia gravis is a form of myasthenia gravis (MG) in which the muscles that move the eyes and control the eyelids are easily fatigued and weakened. People with ocular MG have trouble with sight due to double vision and/or drooping eyelids. Their eyes do not move together in balanced alignment, causing them to see "double" images. One or both eyelids may droop to cover all or part of the pupil of the eye, thus obstructing vision. These symptoms may be mild to severe. Eye weakness often changes from day to day and over the course of a day. Problems with the eyes are often worse at the end of the day or after the eyes have been used for a prolonged period of time. Many people with ocular MG find that their eye problems are temporarily improved if the eyes are rested by closing them for several minutes when symptoms are troubling.

Ptosis: The eyes do not appear to be opened fully. If the eyelid covers the pupil of the eye, then the vision of that eye will be obstructed. The medical term for drooping eyelids is ptosis (pronounced "toe-sis").

Diplopia: The medical term for double vision (seeing two images rather than one) is diplopia. This results from weakness of the muscles that move the eyes together in alignment. Some people experience blurred vision rather than double vision when the eyes are not properly aligned.

Bulbar: Weakness and fatigue in the neck and jaw that can make it difficult to talk, chew, swallow and hold up the head. Bulbar weakness tends to give speech a slurred, nasal quality. It also can lead to frequent choking spells, and make eating unpleasant and tiresome.

Hypophonia: "soft speech" that can be found in MG patients who have weakness of the diaphragm or bulbar weakness. Results from lack of appropriate contraction of the vocal cords. The quality of speech sounds nasal when there is weakness of the palatal muscles, or it may be of low intensity.

Dysphonia: weakness of the larynx which causes difficulty speaking and the voice to sound hoarse.

Common Medical Terms for Myasthenia Gravis (continued)

Dysarthria : changes in speech due to weakness of the lips, tongue, vocal folds, and/or diaphragm. Signs of dysarthria may be "slurred," "choppy," or "mumbled" speech that may be difficult to understand. Slow rate of speech, rapid rate of speech with a "mumbling" quality, limited tongue, lip, and jaw movement, abnormal pitch and rhythm when speaking and changes in voice quality, such as hoarse or breathy voice or speech that sounds "nasal" or "stuffy".

Dysphagia: difficulty in swallowing medications or consuming adequate food or liquids. Nasal regurgitation, particularly of liquids, may occur due to palatal weakness.

Dyspnea: shortness of breath (typically associated with lung disease and not necessarily should be associated with Myasthenia Gravis as our lungs are not the cause of shortness of breath, but rather, our respiratory muscles are). It is important to communicate with a care provider that your diaphragm is flaccid which should help them understand to look at your respiratory muscles rather than your lungs.

Tachypnea: rapid shallow breathing that is seen with MG patients who are compensating for weak respiratory muscles.

Respiratory muscles: involvement of the muscles of respiration (diaphragm and rib muscles – also known as inspiratory muscles). Respiratory weakness produces the most serious symptoms in myasthenia gravis. Respiratory muscle weakness that leads to respiratory insufficiency and pending respiratory failure is a life-threatening situation called "myasthenic crisis." It may occur spontaneously during an active phase of the disease or may be precipitated by a variety of factors including surgery, infections, certain medications, or tapering of immunosuppression.

Myasthenic Crisis: a complication of myasthenia gravis characterized by worsening of muscle weakness, resulting in respiratory failure that requires intubation and mechanical ventilation. Not all cases of myasthenic crisis will present as respiratory failure. Some patients will present with a sudden or gradual worsening of symptoms that rest and home medication regimens do not relieve. The gradual worsening may involve more than the respiratory muscles and may present without respiratory weakness at first. Some signs of a pending myasthenic crisis are: failure to lie flat on your back, inability to speak more than a few words, a raspy, hoarse or nasal voice, elevated heart rate and respirations, continual clearing of secretions, a weak cough and weak neck flexion. (Oxygen usage is helpful but does not alleviate respiratory distress in MG patients. Monitor CO₂ levels.)
Bottom line: if you feel something is wrong or you are struggling, even if you feel it is not severe, seek immediate medical help. It is always better to be safe than sorry.

Cholinergic Crisis: a pronounced muscular weakness (or hyper activation of muscles) and respiratory paralysis caused by excessive acetylcholine, as a result of over medication with anticholinesterase drugs (Mestinon/pyridostigmine). Cholinergic crisis is defined as an over stimulation of the neuromuscular junction. Some signs of cholinergic crisis: excessive salivation/lacrimation, sweating/flushing, nausea/vomiting, diarrhea/cramping, muscle twitching, urinary incontinence, increased respiratory difficulty, choking, increased respirations, double/blurred vision, slurred speech, hypophonic/nasal speech, increased muscle weakness.

Common Medical Terms for Myasthenia Gravis (continued)

Hypercapnia: excessive carbon dioxide in the bloodstream, typically caused by inadequate respiration. This is seen in crisis when the respiratory muscles are flaccid and CO₂ elevates. This can often present as “sleepiness” in a patient even though they are still struggling to breathe.

Thymus: a lymphoid organ that produces T cells for the immune system. It is not fully understood what relationship exists between the thymus gland and MG, but it is believed that it overproduces the antibodies that create our muscle weakness. It is fairly well accepted that in the average Myasthenic, the removal of the thymus gland (thymectomy) can aid in stability and in some, provide remission.

Thymectomy: the complete surgical removal of the thymus gland.

Thymoma: a rare, usually benign tumor arising from thymus tissue that requires removal once the patient has been stabilized. Very rarely is a thymoma cancerous (malignant).

Negative Inspiratory Force (NIF): this is the greatest negative pressure the patient can generate. It is measured asking patients to inhale as hard as they can with measurement of the negative pressure that they generate using a non-invasive pressure gauge. This is a measurement of the strength of the inspiratory muscles, primarily the diaphragm that is done at the patient's bedside. If a myasthenic is struggling with their respiratory, it is recommended that an ER orders the NIF and FVC (discussed below) in order to determine the nature of the respiratory muscles.

Forced Vital Capacity (FVC): this is the largest volume of gas that a patient can exhale. Patients are asked to take a full breath in and then exhale maximally (as much as possible), with measurement of the exhaled volume. FVC reflects a global measurement of the patient's ventilatory ability, which takes into account inspiratory and expiratory muscle strength as well as pulmonary compliance. In other words, it helps a doctor and respiratory therapist determine what your key respiratory muscles are doing and how strong they are by their ability to contract. It is important to measure your respiratory strength via these two articulated, non-invasive bedside tests.

While some therapists and doctors may focus more on the numbers that the myasthenic gives through these tests, it is just as important for the trend to be watched.

Remission: a reversal of some or all symptoms, occurs in about 20 percent of people with MG. Usually, the remissions are temporary, with an average duration of five years, but some people experience more than one remission during their lifetime. A few people have experienced apparently permanent remissions, lasting more than 20 years.

Overall Prognosis for MG: Weakness and fatigue in MG tend to fluctuate from day to day, and even during a single day. People with the disease are often strongest in the morning after a full night's sleep and weakest in the evening. Over a longer term, the symptoms of MG usually progress, reaching maximum or near-maximum severity within one to three years of onset in most people. In about 15 percent of people, the disease remains ocular, but in most it becomes generalized. If the disease remains ocular for three years, it usually doesn't become generalized.

Weakness serious enough to require full-time wheelchair use is not common in MG.

Myasthenia Gravis Emergency Assessment and Treatment

Immediate attention must be directed towards evaluation of the airway, breathing and circulation in patients with Myasthenia Gravis who present with respiratory compromise, or are otherwise medically unstable. Respiratory muscle weakness is common in MG, and it is important to note that patients with respiratory weakness may be severely dyspneic, hypoxic, or hypercarbic without evidence of tachypnea, agonal respirations, or distress. Maintain a calm, compassionate, pain-free, stress-free environment to avoid further medical decline.

Do NOT rely on the O2 saturation level (pulse ox) or ABG to diagnose/predict a respiratory crash. These parameters may not change until it is too late and breathing ceases.

If there is even slight evidence of respiratory distress, move patient to the ICU. Myasthenia Gravis patients can “crash” quietly without much warning! Do the respiratory function tests listed below ASAP!

BREATHING CAPACITY TESTS MUST BE PERFORMED IMMEDIATELY (Explained further in additional section of the packet.)

Negative Inspiratory Force (NIF) should have a magnitude greater than 30 (less than 20 is an indication for mechanical ventilation)

Forced Vital Capacity (FVC) should have a magnitude greater than 1.5 Liters (Values less than 1.5mL/kg are an indication for mechanical ventilation).

CAUTION: Asking the MG patient to do multiple trials/attempts on the NIF or FVC can further weaken respiratory muscle weakness!!!

Bilateral positive airway pressure (Bi Pap) may delay or eliminate need for endotracheal intubation. Avoid intubation if at all possible. Keep a low threshold to begin Bi Pap or intubate if respirations are shallow or labored. Facial, neck and chest-wall weakness may mask signs of distress. Rapid sequence intubation may be performed without the use of neuromuscular blocking drugs that may cause further respiratory deterioration.

Emergency Assessment (continued)

NOTE:

Most respiratory diseases feature damage to the lungs and/or airways which result in rapid changes in the pulse ox (the tool that rests on your finger non-invasively to measure your oxygen output).

Myasthenia Gravis is an exception. This is because the lung tissue is fine while the respiratory muscles are weak. The diaphragm begins to flutter, the intercostal (rib) muscles no longer function properly and the pharyngeal muscles collapse. This causes rising carbon dioxide levels. Left untreated, the patient eventually no longer desires to breathe and remains calm because of the changes in carbon dioxide levels, creating a sleepiness that beguiles the true nature of what is happening.

There is no outward sign of struggle in spite of the patient's insistence to the contrary. At the same time, arterial oxygen levels (tested and monitored through ABG's) may remain high, giving incorrect feedback as to the true precarious state of the MG patient. Monitoring carbon dioxide levels is, therefore, crucial in the patient with shallow or difficult breathing and during a crisis. Many healthcare providers aren't familiar with the above and are quick to write off MG patients in crisis as being anxious or as a somatic case (a person who feels extreme anxiety about physical symptoms such as pain or fatigue. The person has intense thoughts, feelings, and behaviors related to the symptoms that interfere with daily life). Somatic disorders often categorically believe that patients do not have real health issues and claim these patients believe falsely that they cannot breathe (shortness of breath), their doctor is not doing a good enough job, spends a lot of time and energy (inappropriately) dealing with health concerns etc.

It is easy for clinicians and therapists who are unfamiliar with Myasthenia Gravis and how it impacts the respiratory system to inappropriately assign a Myasthenic's muscle weakness as a somatic disorder.

(Special thanks for Sally O'Meara, RN for her expertise.)

Emergency Care by First Responders

Patients with myasthenia gravis (MG) can experience respiratory muscle weakness leading to respiratory insufficiency. Pending respiratory failure necessitating intubation is a life-threatening situation and defined as myasthenic crisis. Prompt recognition of impending respiratory paralysis is the key to the successful management of a myasthenic crisis.

Respiratory assessment:

Check for retraction of extracurricular fossa and intercostal spaces as indicators of respiratory accessory muscle usage. Use of accessory respiratory muscle in MG patients is an important sign that respiratory effort may not be sustained. However, generalized muscle weakness in MG patients can at times mask accessory muscle usage.

Paradoxical breathing, failure to lie supine and inability to speak more than a few words are indicators of diaphragm weakness. Weak neck flexion also correlates with diaphragm dysfunction.

Tachypnea- rapid shallow breathing is seen with MG patients to compensate for weak respiratory muscles.

Pulse oximetry is NOT a good indicator of respiratory strength in MG patients as abnormalities often develop only after life-threatening respiratory failure has already occurred. This is distinct from other causes of respiratory failure. Careful observation of respiration and bedside measurements (forced vital capacity, single breath count) are more reliable indicators of respiratory status than pulse oximetry in MG patients.

Single breath count test: Ask patient to count out loud after maximal inspiration. Ability to reach 50 indicates a normal respiratory function. Single breath count of less than 15 indicates a dangerous low forced vital capacity (FVC).

Immediate treatment:

Oxygen usage is helpful but does not alleviate respiratory distress in MG patients.

Titrate to keep oxygen saturation at 94-98% on pulse oximetry.

If breathing is inadequate, provide assistance with ventilation immediately. Non-invasive ventilation may be given via bag-valve mask (BVM) or CPAP.

Invasive ventilation is needed when airway patency cannot be maintained or when non-invasive ventilation is unsuccessful.

Transport the patient immediately to nearest emergency facility. Bring medical history paperwork if patient has them readily available.

Emergency Care by Physicians

Pulmonary function testing should be performed immediately. FVC and NIF are primary parameters to measure respiratory muscle strength, especially in patients without obvious respiratory distress.

Measure forced vital capacity (FVC) and every two to six hours thereafter.

Consider FVC and NIF values together along with clinical signs and symptoms of distress.

Pulse oximetry and arterial blood gas (ABG) measurements are NOT good indicators of respiratory strength in MG patients as abnormalities often develop only after life-threatening respiratory failure has already occurred. Careful observation (dyspnea and use of accessory muscles) and bedside measurements (forced vital capacity, single breath count) are much more informative than pulse oximetry or ABG results.

Single breath count test- Ask patient to count out loud after maximal inspiration. Ability to reach 50 indicates a normal respiratory function. Single breath count of less than 15 indicates a dangerous low forced vital capacity (FVC).

Decision to initiate assisted ventilation:

Do not wait for ABG to show hypoxemia or hypercapnia. These are late developing signs that appear only immediately prior to respiratory arrest in MG patients.

Weak respiratory muscles may suddenly fatigue, producing precipitous respiratory collapse. Elective intubation is preferable to emergency intubation or respiratory arrest.

The standard 20/30 rule (FVC less than 20 ml/kg or NIF less than 30 cmH₂O) are the best indicators of the need for ventilator support.

Bi Pap is an alternative to intubation in MG patients without hypercapnia who are able to clear secretions

The use of neuromuscular blockers for intubation may impair neuromuscular function and delay extubation.

The initial ventilator mode is typically “assist control/volume control.”

Indicators of need for ICU admission: MG patients with deterioration or impending crisis should be admitted to an intensive care unit; orthopnea, dyspnea at rest, weak cough, prominent neck flexion weakness, difficulty in clearing secretions, rapid shallow breathing, use of accessory muscles, paradoxical abdominal breathing,

baseline FVC less than 30 mL/kg of ideal body weight even if the patient does not show signs of respiratory distress, broken speech in need of pause and breathe after every a few words.

Emergency Care by Physicians (continued)

MG is characterized by repetitive muscle weakness- the muscles become weaker as they are used. Trend of numbers over time is more important than general parameters.

A declining NIF or NIF worse than 20 cm H₂O and FVC less than 10 to 15 mL/kg should prompt intubation.

A 10% decrease in FVC from upright to supine position indicates diaphragmatic weakness. This is a more sensitive indicator of respiratory muscle weakness than upright FVC alone.

FVC and NIF may be falsely low if the patient is unable to close mouth adequately around the mouthpiece due to bulbar weakness. A face mask may be used instead for these patients.

Discontinue cholinesterase inhibitors (mestinon) for intubated patients as they increase secretion production and risk of aspiration pneumonia. Glycopyrrolate should only be used with extreme caution as it can lead to mucous plugging.

Discontinue all medications that exacerbate MG muscle weakness (antibiotics, beta blockers). For a detailed list of medications potentially exacerbating MG symptoms, please [click here](#).

Consult neurology for specific treatment options (plasma exchange, IVIG, corticosteroids)

Identify and address triggers that may underline myasthenic crisis (infection, tapering of immunosuppression etc.).

Contraindicated Medication List

Note:

This list is meant to be a cautionary guide to facilitate safer care and better outcomes. Many different drugs have been associated with worsening myasthenia gravis (MG). However, these drug associations do not necessarily mean that a patient with MG should not be prescribed these medications because in many instances the reports are very rare and in some instances they might only be a “chance” association (i.e. not causal). Also some of these drugs may be necessary for a patient’s treatment. Therefore, some of these drugs should not necessarily be considered “off limits” for MG patients. Careful thought needs to go into decisions about prescription. It is advisable that patients and physicians recognize and discuss the possibility that a particular drug might worsen the patient’s MG. They should also consider, when appropriate, the pros and cons of an alternate treatment, if available. It is important that the patient notify his or her physicians if the symptoms of MG worsen after starting any new medication. We are only listing the more common prescription drugs with the strongest evidence suggesting an association with worsening MG.

It is always important to discuss medications with an expert before making any changes to your care regimen.

Alpha-Interferon

Analgesics: (Can potentially worsen respiratory drive in myasthenics. Use with caution)

Antibiotics: (Aminoglycosides, Amoxicillin, Clarithromycin, Chloroquine, Cipro Erthromycin, Hydroxychloroquine, Penicillin, Clindamycin, Polymyxin, Gentamicin, neomycin, streptomycin, tobramycin, kanamycin, Netilmicin, Ketek, Tetracycline, Augmenti, Blaxin, Zithromax, Quinilones, Cephalosporins are considered the safest class to try)

Anti Convulsants: (Dilantin, Gabapentin, Phenytoin and Barbiturates)

Antihistamines and Decongestants: (Benadryl, Sudafed, Claritin D. -inhibits achetylcholine post synaptically)

Antihelmintics

Antimuscarinic Drugs: (Medicines for Parkinsons; procyclidine, orphenadrine, trihexiphenidyl)

Antimuscarinic Drugs: (for urinary incontinence; oxybutynin, trospium, tolterodine)

Atropine (Anti-cholinergic; sometimes used to reverse a cholinergic crisis. Robinul is a safer cholinergic reversal by comparison only but may not be available in emergencies.)

Botox

Cardiovascular Drugs: (Beta Blockers, Bretylium, Calcium Channel Blockers, Propafenone, Quinidine, Quinine)

Corticosteroids (moderate to high doses have been shown to temporarily worsen MG. It is important that steroids are started low and worked up slowly to help avoid this scenario.)

CT Dye/Contrast/Iodinated Radiographic Contrast: (Iothalamic acid, diatrizoate meglumine, diatrizoate methylsulfate)

D-L-carnitine

General Anesthetics***: (atracurium, cisatracurium, doxacurium, gallamine, mivacurium, pancuronium, pipecuronium, rocuronium, tubocurarine, and vecuronium. Inhibits/Interferes with neuromuscular transmission. To be used in extreme caution)

Hyoscine (used to treat bladder spasms)

Hormones: (Estrogen, Progesterone, Birth Control Pill)

H-2 Receptor Antagonists

Contraindicated Medication List (continued)

Local Anesthetics (Lidocaine, Procaine, etc... Carbocaine is considered the safest in this family as it is shorter acting.)

Magnesium and Magnesium Products (natural or synthetic unless deficient in biochemistry.)

Muscle Relaxants

Neuromuscular Blocking Agents

Ophthalmic Drugs: (Acetazolamide, Proparacaine/tropicamide, Beta Blocker eye drops, Timolol, betaxolol hydrochloride, Echothiophate. ALL dilators are anticholinergic!)

Psychotropic Drugs: (Lithium, Phenothiazine, Tricyclic Antidepressants like Elavil)

Rheumatologic Drugs: (Cholorquine, D-Penicillamine)

Statins

ANY OTHER MEDICINE that has anticholinergic properties OR interferes with transmission at the junction/synapse. IF IN DOUBT: Always double check!

** Agents such as Sevoflurane, Isoflurane, Desflurane, Halothane, Enflurane, and Nitrous oxide are used for intubation as well as maintenance of anesthesia. Myasthenic patients require smaller amounts of these agents than normal, but the effects on neuromuscular transmission do not extend beyond the discontinuation of the agent, thus permitting rapid post-operative extubation of patients with myasthenia gravis.

***Drugs such as Propafol and Opioids in therapeutic concentrations are considered to be safe for patients with defects of neuromuscular transmission.

Reference:

(List is exhaustively compiled from MG board certified physician Allan Weiss of St. Anthony's Neurology and the MGFA.)

Myasthenic vs Cholinergic Crisis

One of the most critical pieces of information you, a caregiver or a medical professional will ever need in caring for Myasthenia Gravis, is the need to appropriately determine if your symptoms are due to myasthenic or cholinergic crisis. Cholinergic crisis looks and acts very similarly to a myasthenic crisis. This can make it difficult for medical professionals to understand what is happening and to treat it appropriately.

Myasthenic crisis is disease induced. It is a by-product of the disease itself and can be exacerbated by underlying infection, surgery, stress, temperature extremes, uncontrolled/undiagnosed co-morbidities that are flying under the radar or lack of appropriate medication regimen that allows the disease process to flare, lack of hydration and nutritional support, and contraindicated medications/therapies both synthetic and natural. Myasthenic crisis *may* require additional mestinon or an adjustment of your current dose as well as additional tertiary therapies until you return to baseline neurological function again, *upon sole discretion of your treating physician*.

Some signs and symptoms of myasthenic crisis includes the following:

- Cannot lay flat in bed without feeling short of breath or gasping for air
- Rapid shallow breathing (especially more than 25 breaths/minute, also known as respirations in the clinical setting)
- Having to pause in the middle of a sentence to take a breath
- Weak cough, especially when mucus/saliva cannot be cleared from the throat
- The muscles between the ribs and around the neck pull in during breathing
- Cannot count out loud past 20 after a full breath of air (referred to as the single breath test)
- Waking up frequently during the night gasping for air
- Feeling restless, agitated, drowsy or confused (this can present as either low oxygen levels or elevated carbon dioxide levels)
- The chest wall moves inward instead of expanding when air is inhaled (paradoxical breathing)
- Feeling too tired to keep breathing - Also included is difficulty chewing or swallowing/choking on saliva, difficulty holding your neck up or opening your hand fully (palm up), raspy or nasal speech, liquids being swallowed and being pushed back up into your nasal cavity and/or difficulty sitting/standing in brief spurts.

Cholinergic crisis is a pronounced muscular weakness and respiratory paralysis caused by excessive acetylcholine, often apparent in patients suffering from myasthenia gravis as a result of over medication with anticholinesterase drugs.

The key difference here is that a cholinergic crisis is induced **only** by too much mestinon. This is a very critical piece here. If a doctor mistakes a cholinergic crisis for a myasthenic, he or she will likely attempt to resolve or stabilize the mistaken myasthenic crisis with additional mestinon (as is the usual protocol) or other tertiary therapies. This can quickly place the patient in a path for respiratory failure via an acute overdose.

Myasthenic vs Cholinergic Crisis (continued)

The best way to determine if you are having a cholinergic crisis is to monitor your medication regimen. It is recommended that each patient keeps a journal of their medication regimen and their coordinating responses. Depending on the patient's weight, metabolism, fluid retention and other factors, the peak release of mestinon in the body begins 30-60 minutes after ingestion of the oral tablet and 15-30 minutes after the ingestion of the syrup, with a peak potentially lasting as long as 120 minutes after ingestion.

After your mestinon dose (within the above stipulated time frames), do you notice that you are experiencing:- excessive salivation, mucous, bronchial secretions or tear production - profuse sweating that can sometimes come with waves of chills - vomiting/diarrhea - pronounced muscular weakness that mimics not having enough mestinon - slurring of speech/difficulty talking or chewing - dizziness and problems focusing your vision (miosis) - feeling/acting inebriated - losing urinary control - muscle spasms/twitching? These are some of the signs of a cholinergic crisis.

A cholinergic crisis can quickly escalate into respiratory failure or compromise in it's severe state. ***Often, cholinergic reactions begin with more mild symptoms and may only include one or two symptoms***, but if they go unnoticed, they ***can*** continue to build to more moderate and severe reactions. **If you are experiencing any of these symptoms, it is important to get prompt medical attention.**

***** PLEASE KNOW*****

Regardless of which crisis that might be happening, it is vital that you seek medical attention immediately. It is always better to be safe than sorry.

It is very important that respiratory therapy measure and assess the flaccidity or paralysis of the diaphragm/intercostal (rib) muscles (also known as your inspiratory muscles) and keep a close watch on your CO2 levels, regardless of the crisis or suspected crisis being experienced.

A NIF (negative inspiratory force) and VFC (vital force capacity) are two bed side tests that can measure non-invasively. It is also important to note that the NIF should be measured when the patient is not in the supine (flat on the back) position and sitting up in order to determine the true nature of the diaphragm. These tests (depending on how critical the patient is) should be repeated every 4 hours, at the discretion of the treating physician. ***Numerical parameters are singularly not as important as establishing a patient's trend. If they continue to decline, in spite of being in the "safe zone" numerically, it is recommended that they receive immediate and appropriate intervention.***

Am I Having a Myasthenic Crisis?

A myasthenic crisis is a severe form of myasthenia gravis. It is a life-threatening condition that happens if the muscles you use for breathing become very weak. ***Potential crisis situations should not wait to be triaged and treated until the patient is in severe state. If your Myasthenia Gravis is continually declining and not improving with your current at home regimen and rest, you need immediate evaluation by a skilled practitioner.***

A patient may be admitted to the hospital with a diagnosis of myasthenic crisis even though a ventilator is not needed yet. Appropriate and rapid treatment is needed in order to prevent a full myasthenic crisis and keep the patient breathing without a machine (ventilator). Sometimes it is hard to tell if shortness of breath is due to anxiety, COPD or asthma, MG muscle weakness or another underlying disorder and is often confused by medical providers. ***Not all struggles with respiratory will lead to crisis, but it is always appropriate to assume that it will and treat it accordingly as a care provider.***

Signs that breathing function is worsening include:

- Cannot lay flat in bed without feeling short of breath or gasping for air
- Rapid shallow breathing (especially more than 25 breaths/minute)
- Having to pause in the middle of a sentence to take a breath
- Weak cough, especially when mucus/saliva cannot be cleared from the throat
- The muscles between the ribs and around the neck pull in during breathing
- Cannot count out loud past 20 after a full breath of air
- Waking up frequently during the night gasping for air
- Feeling restless, agitated, drowsy or confused
- The chest wall moves inward instead of expanding when air is inhaled
- Feeling too tired to keep breathing * You continue to decline in spite of rest and appropriate medication regimen.

DO NOT ignore these signs or the general feeling of impending doom or that something is wrong. Get to an ER quickly and make sure they evaluate your diaphragm and intercostal muscles and carbon dioxide levels. Your lungs are secondary and not the primary issue in a myasthenic crisis. Breathing treatments are often prescribed in the emergency room for suspected breathing difficulty in MG but are contraindicated unless the patient has a co-morbidity of asthma, COPD or similar and can often worsen the MG. It is important to note that nebulizers will not address the underlying issue with diaphragmatic weakness in MG respiratory crisis. This is an inappropriate treatment and should indicate that the care provider is not understanding how to triage your symptoms or disease.

Bedside Pulmonary Function Tests

"MIP = Maximal Inspiratory Pressure. This is the greatest negative pressure the patient can generate, often also referred to as the NIF (Negative Inspiratory Force). It is measured asking patients to inhale as hard as they can with measurement of the negative pressure that they generate using a pressure gauge. This is a measurement of the strength of the inspiratory muscles, primarily the diaphragm."

This is considered one of several bedside PFT's or pulmonary function tests that is done when a Myasthenic is struggling with respiratory function and is considered essential in determining the true strength or flaccidity (paralysis/weakness) of the diaphragm.

Another gold standard for Myasthenics in respiratory distress is the FVC. "FVC = Forced vital capacity. This is the largest volume of gas that a patient can exhale. Patients are asked to take a full breath in and then exhale maximally, with measurement of the exhaled volume. FVC reflects a global measurement of the patient's ventilatory ability, which takes into account inspiratory and expiratory muscle strength as well as pulmonary compliance."

"As with any critically ill patient, the decision to intubate should be based primarily on clinical assessment at the bedside. Important elements include work of breathing, respiratory rate, oxygenation variables, and trends in these values. Other indications for intubation would include bulbar dysfunction with an inability to handle secretions and protect the airway. Significant hypoxemia would suggest either ongoing aspiration or atelectasis, either of which would be very concerning. The overall tempo of the illness and clinical context, including trends in pulmonary function, provides some additional information."

Since Myasthenia Gravis requires an appropriate evaluation of respiratory muscle strength to help determine appropriate (and sometimes rapid) courses of action, it is highly recommended that patients establish their respiratory trend under three different scenarios.

1. When you feel strong or on a good day.
2. When you are experiencing a flare or are symptomatic.
3. When you are struggling with respiratory symptoms, ideally evaluated under a therapist or doctor.

This will help establish a baseline or trend to give your care provider and respiratory therapist a better idea of where you as an individual truly is, instead of looking to categorical patient averages.

While some therapists and doctors may focus more of the numbers that the patient gives through these tests, it is just as important for the trend or patterned to be watched. I always encourage a patient to request these tests ASAP upon entering the ER to establish a baseline to work off of, even if you feel your breathing is not critical. These tests are non-invasive and are typically repeated in the hospital every four hours barring more critical situations.

(Special thanks to Josh Farkas, RT, for lending his expertise.)

At Home Respiratory Tests

These tests do not replace the appropriate evaluation of the true state of your respiratory strength from a trained clinical professional. This is offered as a means to help you understand how to better evaluate your symptoms and varying scenarios as they wax and wane, while hopefully reducing stress and anxiety during symptoms that can be quite frightening.

Feeling short of breath or winded and not sure how to evaluate it?

A simple (and strange) way of checking diaphragm strength is to sniff. That's right. Sniff. Can you quickly and sharply inhale or sniff? Doing so requires diaphragm strength and contraction. Not being able to do so can be an indicator that your diaphragm may be struggling with contraction. Sounds silly, but it's a good and quick way to check parameters.

Another way to check your respiratory strength at home is the single breath test.

Inhale as much air as you can in a single breath. As you exhale, quickly count out loud until you need to breathe again. What number did you get to?

< 20 : It is strongly recommended that you seek immediate medical attention.

< 30 : It is strongly recommended that you call your neurologist for assistance and evaluation.

<40 : It is recommended that you maintain a watch but this is overall considered a safe numeric parameter.

> 40 : This is considered a very stable parameter.

These tests are not the only indicator for respiratory strength but they can be a good baseline to learn and develop if breathing difficulty does become an issue for the Myasthenic. ***Concerning symptoms, even if mild, should be triaged with your overall presentation and healthy history.***

If you still aren't sure, please know it's ALWAYS better to be safe rather than sorry. Go get evaluated and don't feel guilty about it. Taking care of you is always worth the trip.

Common Exacerbators of MG

Stress, lack of sleep, poor hydration, inadequate nutrition, infection, changes in temperature (especially with extreme conditions), underlying co-morbidities or autoimmune disorders, hyperthyroidism or hypothyroidism, menstruation, contraindicated drugs or a poorly controlled medication regimen can all play crucial roles in an acute exacerbation of Myasthenia Gravis. Eliminating or treating the underlying cause should allow for a return of the baseline neurological function.

Each myasthenic is different in what may or may not become an exacerbator or trigger for flare ups of their symptoms. It is essential to optimal care that you pay attention to what worsens your MG and find ways to avoid exacerbators when possible. When not possible, be prepared for extra rest and self care to help your body through the flare. Healthy coping mechanisms to reduce stress or the negative impact of triggers are important to develop but should not be used on their own as treatment if an exacerbation leads to a further weakening or distress of your MG.

A myasthenic may need assistance in returning to baseline function in the acute setting with a temporary change in medications or additional therapies, *at the sole discretion of your care provider.*

Not all exacerbations will lead to a crisis, but they have the potential to increase the chances of crisis when not appropriately amended.

As always consult your care provider before making any changes to your medications.

Commonly Used Medications in MG

Mestinon is the first line drug in treating Myasthenia Gravis. It works by preventing the breakdown of the neurotransmitter acetylcholine in your body. Acetylcholine is required for full and complete muscular function, specifically the contraction of muscles. The majority of patients will experience positive results from using Mestinon, with a noticeable reduction of muscle weakness during use. Not all however will benefit from this drug. Since there is no standard dose for mestinon, it is important that you work closely with a knowledgeable care provider who will customize the dose that is most beneficial to you. It is common to need adjustments to this drug during flares, changes in temperature or stressful events and as the disease may wax or wane. Common side effects are GI cramping, nausea, vomiting and diarrhea and minor muscle twitching.

Corticosteroids are widely accepted and used in the treatment of autoimmune disease. Notable improvement or stabilization of symptoms transpires in the vast majority of patients treated with positive results occurring between 70 and 75%. It is recommended that steroids are started at lower doses and gradually titrated up for better tolerance and reduction of an acute myasthenic exacerbation. Most patients will see a positive improvement in weakness within the first four to eight weeks of therapy with some enjoying drug induced remission from an appropriate dosing regimen. Some studies suggest an aggressive and early approach to more mild cases increase the opportunity to halt progression. Thymoma and early onset myasthenics typically enjoy exceptional positive responses from steroid therapy both pre and post operatively. Side effects to steroid therapy can be difficult to tolerate and can range in severity and presentation. A patient's overall health history should be especially determined before beginning steroids.

Immunosuppressants are the tertiary option for Myasthenics who are not at optimum in their response to mestinon or mestinon and steroids alone. As with any immunosuppressant therapy, the risk for contracting multiple or recurrent infections is elevated than patients who are not on immune suppression therapy.

Azathioprine (Imuran) is chosen according to health history and is shown in multiple studies to reverse symptoms in most patients but the patients often must wait for any effects to be felt between 4 to 8 months. This drug requires frequent monitoring of blood panels. Upon symptom improvement, the benefit is continued for as long as the medication is maintained, with recurrence of symptoms within several months after being reduced below therapeutic levels. Patients who fail corticosteroids may respond to azathioprine and the reverse is also true. Because azathioprine has a delayed therapeutic response, it is frequently started in concurrence with steroid therapy with the hope that the steroids may be tapered once the azathioprine begins efficacy in the body. Roughly one-third of treated patients experience mild dose-dependent side effects that does not necessitate stopping treatment but may require a reduction of the dosage.

Commonly Used Medications in MG (continued)

Mycophenolate mofetil (Cellcept) has a similar mechanism of action to azathioprine and has been used effectively in a wide swath of myasthenics. Like azathioprine, there is an inhibition of B and T cell lymphocytes and helps control mediated weakness similarly to azathioprine. Those who do not tolerate azathioprine may be switched to mycophenolate mofetil as their health history and symptomology allows. Mycophenolate mofetil carries with it an increased risk for certain types of cancer, nausea, vomiting, headaches, bone marrow suppression, sepsis, hypertension, tremor, neoplasia, depression, teratogenicity and an increased risk of infection. Mycophenolate mofetil is generally well tolerated with side effects mainly contained to gastrointestinal intolerance such as cramping and diarrhea.

Cyclosporine, like azathioprine was originally created as an organ rejection drug. Cyclosporine works by inhibiting predominantly T-lymphocyte-dependent immune responses and can sometimes prove effective in treating myasthenia gravis. While the majority of patients with myasthenia gravis show improvement on this medication within 1 to 2 months after starting therapy, it is poorly accepted outside of low therapeutic doses and comes with significant side effects. Like azathioprine, its efficacy and viability is maintained as long as appropriate, therapeutic doses are administered. Optimum improvement and stability is seen six months or longer after initiating the medication. After achieving the maximal response, the dose is titrated down to the minimum required to maintain improvement. It is very important to note that more adverse side effects are noted with this medication including renal toxicity and hypertension. Additionally, many drugs are contraindicated with cyclosporine and should be avoided or used with caution.

Eculizumab is a medication that is still in clinical trials and its immediate and long term benefits to treating MG is still not fully know. It is humanized monoclonal antibody to the fifth component of complement (C5), it has thus far exhibited some success in improving strength and thus quality of life in refractory Myasthenics, a group of myasthenics that struggle to obtain control over the disease with current, traditional therapies.

Thymectomy

Myasthenia Gravis is classified as an autoimmune, anti-body mediated, T-cell dependent, immunological attack on the post synaptic membrane of the neuromuscular junction.

The thymus gland is considered the main engine or driver of T-cell production and regulation in the body. Experts do not all agree that it is viable potential treatment in stabilizing or inducing a greater chance for remission, however, poor documentation in preceding decades may be a contributing factor. The thymus gland's function is to receive "immature" T cells that are created within the red bone marrow and teach the immature cells how to become functional, mature T cells who are used solely to attack foreign cells. The thymus gland plays its greatest role in childhood, enlarging until puberty where it subsequently begins to shrink at the onset of puberty and into full adulthood. As the thymus shrinks, its tissues are replaced by adipose tissue. Anatomy and Physiology Instructor Tim Taylor describes the diminished role of the thymus this way: "the shrinking is due to the reduced role of the thyroid in adulthood – the immune system produces most of its T cells during childhood and requires very few new T cells after puberty". In a healthy adult, the thymus should be residual and continue to shrink throughout maturity.

Now, a thymectomy is not for everyone. There are several grains of salt to consider before saying no or yes to this surgical treatment.

1) Age, Onset, Severity and Type of MG (AChR, MuSK or Seronegative etc) all play a large role in the viability and efficacy of the thymectomy. Those studied and recorded who stand the best chance of achieving possible remission and stabilization are those who have it removed within the first year of diagnosis, are AChR positive and are generally under the age of sixty. Hyperplasia of the thymus gland is considered by some to be a main aggressor in more moderate and severe cases. Removal of a hyperplastic gland has been documented to show an increase in the stability of symptoms and offers the greatest increase for remission. MuSK and thymoma myasthenics have the small potential to worsen with the thymectomy. It is encouraged that your specialist helps you navigate if you are eligible for this procedure.

2) Thymoma is a usually benign tumor that is created from the surrounding epithelial cells of the thymus gland. A thymoma is found in roughly 10-15% of myasthenic patients and requires removal upon stabilization of the patient. In the rare event that the thymoma is malignant, surgical methods may not be enough and a doctor may want to involve an oncologist to employ chemotherapy or radiation to help ensure the thymoma is no longer a threat. It is estimated that up to one half of myasthenics with a thymoma will experience no symptoms of the tumor. Symptoms can include chest pain or pressure, difficulty swallowing and generalized myasthenic weakness. Thymoma is often discovered on chest x-rays, CT scans or MRI's.

3) Scans such as x-rays, CT's and MRI's are used to help determine if a thymoma is present but they are often used as the sole diagnostic criteria for eligibility for thymectomy. However, because the thymus gland is anterior and superior to the heart and posterior to the sternum, it is very difficult to clearly discern the true nature of the thymus gland, if it is hyperplastic or not and if removal is necessary. The thymus can also grow into the neck and throughout the chest cavity with finger like extensions and can be difficult to see all potential thymic tissue that has strayed from the gland in these scans. *These scans should be a starting point and not a sole determinant.*

Thymectomy (continued)

4) It has not been well documented by physicians pre, peri or post operatively the patient's condition and then response before and after thymectomy so the efficacy of this surgery is well contested and poorly documented in many clinical circles. Any research done on the thymectomy should be ideally filtered through this knowledge.

5) The different types of surgical approaches matter.

The transternal thymectomy can be full or partial (determined by the length of the cut of the sternum and desire for cosmetic recovery) and offers the maximal view of the thymus gland, especially helpful in hyperplastic or thymoma positive patients but it also incurs the most pain and holds the greatest risk for complications. Due to the ability for thymic tissue to regrow, this is notably an ideal approach in the long term consideration.

Transcervical offers less recovery time and less post-operative inhibition and is the least invasive approach. A scope placed under the sternum and is used to visualize the thymus gland and surrounding tissue. It is classified as contraindicated for those with a thymoma and requires a highly specialized surgeon familiar with the approach. This thymectomy also relies on accurate visualization of the thymus and any hyperplastic tissue from the scope rather than the surgeon's full and open view of the neck and surrounding chest cavity.

VATS is a video-assisted thoracoscopic thymectomy that is used more commonly in place of the transternal thymectomy. This approach may require the transversement of the heart and can run a slightly greater risk of phrenic nerve damage but offers a better post-operative outcome. According to the Cardiothoracic Surgeons Network, MG has solidified and positive long term outcomes from the VATS approach. "From 1998 to 2011, 155 VATS thymectomies were performed: 80 for non thymomatous myasthenia gravis, 40 for thymomas associated with myasthenia gravis, and 38 for thymomas. 93% were approached from the right side. Mean age was 44 years (range 12-83 years), mean duration of surgery was 143 minutes, and mean duration of hospital stay was 5 days. There was no hospital mortality and operative morbidity was 13%. Mean follow up was 5.5 years (range 2-11 yrs). Among myasthenic patients 93.4% had improvement in symptoms with 80% being asymptomatic and 21.3% in complete stable remission without medications. There was no statistical significance in remission rates between thymomatous and non- thymomatous myasthenia gravis."

Thymic tissue likes to hide away in adipose cells into the neck and throughout the chest cavity. While there are many approaches that surgeons have used and are comfortable with, there is more dynamic research backing the use of certain approaches than others in the full removal of residual tissue in the long term in regards to stability and potential remission. Keep in mind that your surgeon will recommend what he or she is comfortable with and that may or may not be in your best interest. Don't be afraid to shop around for a knowledgeable surgeon.

6) Always remember that each patient will respond differently. You must factor in all the above scenarios, plus consider the patient's overall health. Are there other things that are exacerbating the MG such as other aggressive chronic illness or recurrent infection that may impact the long term efficacy?

7) *Thymic tissue can and does grow back if not completely removed.* This can cause the MG to relapse or come back stronger and harder than before so it is essential that you and your surgical team look to the immediate as well as the future when considering all of your options.

Coping with Insurance Denials

Insurance denials are common and often stressful occurrences in treating Myasthenia Gravis. Mestinon (pyridostigmine), IVIG, Plasmapheresis, Rituxan, hospital stays etc., are often in the cross hairs between approval and denial. Many of the medications used to treat Myasthenia Gravis are off label and are therefore prone to frequent rejection. Fighting insurance denials can be a daunting task. Below are some suggestions to help support you in your efforts to fight back.

If treatment is denied, appeal the decision by phone and in writing immediately. Copy a lawyer on your letters. Sometimes a simple letter from a lawyer will encourage action.

- Contact your Insurance Commissioner. When you contact the Insurance Commissioner's Office, make sure to ask if your state offers the opportunity to have your claim be reviewed by an external organization, if all levels of appeal directly with the insurance company have been unsuccessful.
- Let the insurance company know that you will also contact the insurance commission, employer, and media to obtain assistance.
- Seek your doctor's help in filing an appeal. If your provider recommends a course of treatment, she/he is ethically bound to appeal on your behalf. Your insurance company may require that you complete written paperwork that clearly explains why the treatment is medically necessary. If possible include a description of the potential harm that will be done if the treatment is not approved.
- Obtain a written definition of medical necessity from the insurance company since this is a common basis for deciding whether to approve treatment.
- Keep a record of all communications with your insurance company and other organizations including dates, times, names of individuals you spoke with, and all correspondence you've received.
- Find out about your company's appeals process including how many times you can appeal, deadlines, types of documentation required, and if external appeals are available in your state. There are specific steps to make written appeals and legal timelines for the insurance company to notify you of its decision.
- Ask whether the insurance company has an Insurance Ombudsman who helps in situations where there is a disagreement between the company and patients/consumers. If you have a problem getting this information directly from your insurance company, contact the consumer hotline at your state Insurance Department or state Insurance Commissioner's office to request this information.

(A special thank you to MH America for their kind assistance and information.)

IVIG: Overview, Side Effects and Risks

IVIG is frequently seen as a common treatment for Myasthenia Gravis but it is not always well understood. While it is a beneficial therapy for many myasthenics, it is not indicated for everyone.

IVIG, also called gamma globulin or antibodies, is a highly purified blood product preparation that is derived from large pools of plasma donors. Plasma from approximately 1,000 to 10,000 persons is present in each unit or “lot” of IVIG. While this is a blood product, IVIG available in the United States, is purified and carefully screened to be free of all known transmissible diseases, including HIV, hepatitis, malaria, syphilis and many, many others. This medication is used to treat a variety of neurological and neuromuscular autoimmune disorders that affect the central nervous system, peripheral nerves, neuromuscular junction and muscles.

It is important to remember that IVIG is a blood product and should be treated as such. **The recommendation to improve safety and reduce the risk of complications is to titer from the lowest dose and slowly increase *as tolerated*. If the patient is showing signs of poor tolerance, it is recommended that the dose be lowered or temporarily stopped and restarted at the lowest infusion rate. Piggybacking fluids during infusions can also help decrease side effects. Signs of an allergic reaction require immediate attention.**

It is fairly common for patients to experience headache (which can be mild to severe), stiff neck, and fever during or shortly after an infusion. This is called aseptic meningitis syndrome. These symptoms are manageable and can be minimized or prevented by infusing IVIG very slowly. Patients may often feel fatigued or flu type symptoms for a day or two after their infusion.

Variation in blood pressure, shortness of breath, chills, fever, rashes and any allergic reactions must be closely monitored during the infusions. *Discuss your questions about side effects or possible allergic reactions with your physician and your infusion nurse PRIOR to starting treatment. It is always recommended that a care plan is developed prior to starting any infusions, including emergency responses and expectations. Vitals should be obtained before, during and after infusions, with the frequency of vitals occurring every hour during treatment.*

Administration of immunoglobulin subcutaneously (SCIG) is equally effective in treatment viability and has a lower incidence of serious adverse effects compared to IVIG, although it is not prescribed as often.

More serious side effects, such as allergic reactions, are rare, but have been reported. Should you develop an allergic reaction, your health care providers are sufficiently trained to handle this. Do not hesitate to contact your physician if your side effects are severe or persistent. It is possible to reduce the severity of the side effects associated with Ig infusions. Your physician may suggest premedication with acetaminophen or *antihistamines (use with caution in Myasthenia Gravis)*; corticosteroids are also an option your doctor might consider. It is also important to make sure that you are sufficiently hydrated before your infusions. Make sure that you are drinking plenty of water and getting proper nutritional support for several days before and after your infusion.

IVIG: Overview, Side Effects and Risks (continued)

The length of time it takes for an IVIG infusion will vary for each person. On average, it is between 4 to 6 hours. The specific dose ordered by your physician and your immediate health needs, in addition to your own tolerance to the medication, will determine your length of stay at the Infusion Center or hospital. The frequency of infusions will be dependent on individual response and need.

IVIG as a viable treatment is largely dependent on the patient's health history. IVIG is not meant for everyone and the risks may not necessarily outweigh the benefit for some.

IVIG therapy should be carefully monitored, and obtaining a history and performing a physical examination, *with an emphasis on obtaining information regarding cardiac, hepatic or kidney disease or a history of reactions to blood products or transfusion reactions, is prudent.*

Laboratory tests may include the following:

- Liver function tests
- Renal function tests
- CBC count with differential
- Hepatitis screen to assess for possible disease transmission by IVIG
- Immunoglobulin levels to exclude IgA deficiency: If no IgA antibodies are found, then anti-IgA antibody titers should be obtained.
- Rheumatoid and cryoglobulin levels, because IVIG can cause hematological complications

Undesirable effects from IVIG occur in less than 5% of patients. The most common adverse effects occur soon after infusions and can include headache, flushing, chills, myalgia, wheezing, tachycardia, lower back pain, nausea, and hypotension. ***If this happens during an infusion, the infusion should be slowed or stopped.*** IVIG is associated with rare cases of thrombosis. It has caused disseminated intravascular coagulation, transient serum sickness, and transient neutropenia. IVIG can precipitate acute myocardial infarction. ***Aseptic meningitis is a rare but well-recognized complication of IVIG therapy. It manifests as fever, neck stiffness, headache, confusion, nausea, and vomiting.*** IVIG should not be given to patients with sensitivity to thimerosal. IVIG has caused eczematous dermatitis and alopecia. Stroke has been reported in only two known cases.

(Special thanks for Noah S Scheinfeld, JD, MD, FAAD
and Phoenix Neurology Associates for their assistance and information.)

Plasmapheresis (PLEX)

Plasmapheresis is a term derived from Greek language used to describe different forms of extracorporeal plasma separation. Blood consists of four major components: red blood cells, white blood cells, platelets and plasma. Plasma represents the fluid portion of the blood, carrying proteins and other important substances throughout the body. The main purpose of plasmapheresis is to remove aberrant proteins or antibodies, thereby preventing their accumulation or ability to attack certain body systems. ***(Because of the rapid response to the removal of antibodies, PLEX is often the treatment of choice in responding to a myasthenic crisis although there is debate among experts as to its superiority in a head to head evaluation of IVIG treatment in crisis.)*** The procedure can be done either on an outpatient or inpatient basis. It is usually available in bigger medical centers and clinics. Plasmapheresis generally takes a few hours to perform, and the number of necessary treatments varies significantly based upon patient's specific diagnosis. Anticoagulant therapy is administered at the same time in order to prevent the formation of blood clots.

During the procedure a patient can lie down on a bed or recline in a chair, as long as the relaxation effect is accomplished. Two catheters are inserted – one into a large vein of the arm, and another one into the opposite arm (or sometimes even foot). Following their insertion the blood is taken from the patient and passed through a membrane; the separated blood cells are then combined with replacement fluids and returned to the patient.

Although approximately 40% of patients experience some type of complications, severe forms occur in less than one percent of all plasmapheresis procedures. Among the most common ones is hypotension (low blood pressure), which can manifest as dizziness, nausea and blurred vision. Insertion of the catheter can also cause problems such as bleeding or infection. Hypotension can occur as a result of rapid fluid shifts, and proper precautions should be taken to minimize complications such as unintended falls, can become thrombocytopenic and hypofibrinogenemic after plasmapheresis (especially if albumin is being used as a replacement product) and should be monitored for signs of bleeding.

Citrate toxicity can arise from anticoagulation therapy, prompting the urgent decrease of the anticoagulant flow rate to reduce the amount of citrates which bind to calcium in the blood. Calcium supplementation may also help in such instances. Although the transmission of hepatitis or HIV is a possibility, it is extremely rare in clinical practice. Patients can experience symptoms of hypocalcemia and or hypomagnesemia during and after the procedure and can be treated with replacement calcium and magnesium, respectively. ***(Caution with magnesium replacement in Myasthenics. Only offer when patient needs replacement. Do not use as a prophylactic measure.)***

PLEX frequently causes patients to become mildly hypothermic during the procedure, in which case they should be warmed appropriately.

Transfusion-related reactions, can be experienced in particular with FFP, and should be treated with diphenhydramine, solumedral, hydrocortisone, and/or epinephrine depending on the severity of the reaction. These reactions can occur during and after the transfusion.

On the whole, plasmapheresis is considered a safe procedure when conducted by experienced health care staff. Most of the potential complications are minor and not life-threatening. The improvement can be seen within days or weeks, and benefits usually last for several weeks, depending on the individual.

(Special thanks to Dr Tomislav Meštrović, MD, PhD and Elliot Stieglitz, MD)

Emotional Support

Grief, anger, denial, isolation, shame, anxiety and depression are all normal parts of the grieving process in learning to cope with Myasthenia Gravis. Often considered part of the beginning stages of learning to live with a chronic illness, the grief cycle can appear in varying manifestations over time and can repeat itself as the disease naturally waxes and wanes. Lingering struggles with any of these facets may require additional support from a trained counselor or physician.

Finding support is not always easy as those around you often grapple with understanding the disease and its impact on you. Some may even walk away from your life or quietly fade into the background as your disease naturally shifts your focus and priorities as well as their own.

Support groups comprised of other Myasthenia Gravis patients can go a long way in offering a sense of community, a re-alignment of identity and the freedom to be honest and open about individual struggles with the disease. Look for a local support group in your community or find one online.

Social media has exploded in the last several years in its offerings for online support groups. Easily accessed from the home, on the road or in the hospital, it provides an open channel for information, community and acceptance to flow and strengthen you emotionally.

Learning to cope will be molded by personal preference and your resources and immediate community support from family and friends. Coping mechanisms can offer safe and healthy means of relieving stress and anxiety due to symptoms and changes brought on by MG. Some benefit from talking with friends while others may enjoy listening to music, going for a ride in the car, watching TV or a movie, crafting, online shopping and so much more.

Talk to others and get inspired.

Finally, give grace to yourself and to others. You will be learning about MG and how it affects you along with everyone around you. It is a learning curve that is delicate and can be frustrating at times, so try to be patient, plug in to a healthy community online and remember that it is OK to not always feel OK.

Do not be afraid to get help if you are struggling to cope or find hope.

For online support groups, visit www.facebook.com or www.facebook.com/mgunmasked