

Care of the Patient with Myasthenia Gravis

AANN Clinical Practice Guideline Series



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Preface

In 1997, the American Association of Neuroscience Nurses (AANN) created a series of patient care guidelines, the AANN Reference Series for Clinical Practice, to meet its members' needs for educational tools. To better reflect the nature of the guidelines and the organization's commitment to developing each guideline based on current literature and evidence-based practice, the name of the series was changed in 2007 to the AANN Clinical Practice Guideline Series. This first edition guideline, *Care of the Patient with Myasthenia Gravis*, represents another milestone in the series. *Care of the Patient with Myasthenia Gravis* promotes evidence-based practice for the patient with myasthenia gravis (MG) across the life continuum. Nursing care of the patient with MG has evolved from a focus on a singular pathology with a limited number of pharmacologic agents to more a diverse disease process amenable to various management strategies, including pharmacologic, immunomodulation, and thymectomy along with consideration for self-care activities and prevention of complications.

The goal of this guideline is to offer evidence-based recommendations on nursing activities that have the potential to maximize outcomes for patients of all ages and all types of MG. Not all recommendations concern activities independently performed by registered nurses (RNs), but nurses are responsible for implementing and monitoring the outcomes of these activities. The evidence presented here may help nurses make appropriate choices when caring for patients with MG. Dependent on scope of practice regulations, advanced practice nurses may have independent or collaborative responsibilities for activity performance. Thus, this guideline may assist them in the management of patients with MG as well. Resources and recommendations must describe the best practices that can enable RNs to provide optimal care for persons with MG. Accordingly, adherence to these guidelines is voluntary, and the ultimate determination regarding their application must be made by practitioners in light of each patient's individual circumstances. This reference is an essential resource for nurses providing care to the patient with MG. It is not intended to replace formal learning but rather to augment the clinician's knowledge base and provide a readily accessible reference tool. The nursing profession and AANN are indebted to the volunteers who have devoted their time and expertise to this valuable resource, which was created for those who are committed to excellence in the care of the patient with MG.

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I. Introduction

A. Purpose

1. The purpose of this guide is to review and evaluate literature about myasthenia gravis (MG), with a concentrated focus on the adult with acquired MG, and to create a reference for neuroscience nurses who care for the patient with MG across the continuum of care throughout the lifespan.

B. Guideline goal

1. The goal of this guideline is to help nurses provide consistent, current, and evidence-based care to the patient with MG. Topics include epidemiology; types and classifications of MG; pathophysiology; clinical and diagnostic presentation; symptom management, including surgical interventions; nursing assessment and intervention; and patient and family education.

C. Assessment of scientific evidence

1. A review of literature published between January 2000 and September 2012 was conducted using PubMed/MEDLINE and CINAHL databases with the following search terms: myasthenia gravis, neuromuscular junction (NMJ), neuromuscular transmission, thymectomy, evidence-based practice nursing, research, and myasthenia gravis clinical trials. The search was extended to earlier years because of the lack of more recent references on select topics. Several publications dated earlier than 2000 are included because of their historical clinical significance.
2. The Myasthenia Gravis Foundation of America guidelines (Howard, 2008) were assessed and incorporated in this document as appropriate and needed.
3. For the AANN Clinical Reference Series, data quality is classified as follows:
 - a. Class I: Randomized controlled trial without significant limitations or meta-analysis
 - b. Class II: Randomized controlled trial with important limitations (e.g., methodologic flaws or inconsistent results) and observational studies (e.g., cohort or case-control)
 - c. Class III: Qualitative study, case study, or series
 - d. Class IV: Evidence from expert committee reports and/or expert opinion of the guideline panel; standards of care and clinical protocols that have been identified.

4. The *Clinical Practice Guidelines* and recommendations for practice are established based upon the evaluation of the available evidence (American Association of Neuroscience Nurses [AANN], 2005; Guyatt & Rennie, 2002; Melnyk, 2004):
 - a. Level 1 recommendations are supported by class I evidence.
 - b. Level 2 recommendations are supported by class II evidence.
 - c. Level 3 recommendations are supported by class III and IV evidence.

II. MG Overview

A. Definition of MG

1. MG is an autoimmune neuromuscular disease leading to fluctuating muscle weakness and fatigability.
2. MG is the most common primary disorder of neuromuscular transmission (Sanders, 2011).
3. The muscle weakness is caused by a disruption in normal neuromuscular transmission by binding of autoantibodies to proteins involved in signaling the NMJ. Circulating antibodies block, interfere, or alter Acetylcholine receptors (AChR) at the postsynaptic NMJ, inhibiting the stimulative effect of the neurotransmitter Acetylcholine (ACh) (Merrigioli, 2009).
4. MG is most commonly associated with dysfunction of the nicotinic AChR (Silvestri & Wolfe, 2012). Less commonly, MG is associated with autoantibodies causing dysfunction of the muscle-specific kinase (MuSK) protein (Silvestri & Wolfe, 2012).
5. MG may be classified in a variety of ways, including
 - a. immune versus nonimmune (congenital) or acquired versus nonacquired (congenital) MG
 - b. ocular versus generalized MG
 - c. early-onset versus late-onset MG
 - d. thymoma-associated MG
 - e. MG with no detectable AChR antibodies or MuSK antibodies (antibody-negative MG). In antibody-positive MG, antibodies on the receptors impair normal neuromuscular transmission (Howard, 2008; Keesey, 2004; Trouth, Dabi, Solieman, Kurukumbi, & Kalyanam, 2012).
6. Muscles become progressively weaker during periods of activity or repetitive use (fatigue) and improve after periods of rest.

- a. MG weakness is fluctuating and increases after use of the affected muscle groups. It typically worsens during the course of the day.
 - i. Mild MG is characterized by mild ocular, facial, bulbar, respiratory, or limb muscle weakness with occasional, intermittent, or rare (not daily) symptoms of weakness. Early in the disease, the symptoms may be absent to minimal upon awakening or after a period of rest (Grob, Brunner, Namba, & Pagala, 2008).
 - ii. Severe MG is characterized by some, but not necessarily all, of the following symptoms: moderate to severe facial weakness, spontaneous diplopia and ptosis, reduced forced eye closure, dysphagia that interferes with safe swallowing, dysarthria, dyspnea with a vital capacity of less than 50% of normal, head drop, and proximal or distal muscle weakness severe enough to interfere with independent performance of activities of daily living (ADLs) (Grob et al., 2008). Enteral feeding and/or ventilator assistance may be required.
 7. Muscles that control eyes and eyelids, facial expressions, chewing, talking, and swallowing are most commonly affected (Juel & Massey, 2007).
 8. The first noticeable symptom may be weak eye muscles, diplopia or ptosis (two-thirds of patients) (Conti-Fine, Milani, & Kaminski, 2006), difficulty swallowing, or slurred speech (Drachman, 1994).
- B. Scope of the problem
1. Disease prevalence in the United States is estimated at 20 cases per 100,000 (Phillips, 2003).
 2. MG is diagnosed in two to seven of every 10,000 people in Western countries (Muscular Dystrophy Association [MDA], 2009).
 3. Better awareness has resulted in increasing prevalence, especially in people older than age 50 (Aarli, 1999; Pallaver, et al., 2011; Somnier, 2005).
 4. MG occurs in all ethnic groups (Myasthenia Gravis Foundation of America, Inc. [MGFA], 2012a).
- C. Age- and gender-related risks for developing MG
1. Women who are younger than age 40 are at increased risk (Alsheklee, Miles, Katirji, Peston, & Kaminski, 2009; Howard, 2008).
 2. People who are 50–70 years of age of either sex are at increased risk (Alsheklee et al., 2009; Howard, 2008).
 3. Women are affected more than men at a ratio of about 3:2 (Alsheklee et al., 2009).
 4. Women are more affected during their second and third decades (Howard, 2008).
 5. Among men, diagnosis commonly occurs during the sixth decade (Howard, 2008; Phillips, 2004).
- D. Age of onset
1. Average age of onset in women is 28 years; in men, the average age of onset is 42 years (MDA, 2009).
 2. Late-onset MG
 - a. Defined as the onset of disease after age 50 in the patient with no clinical or paraclinical evidence of a thymoma, a tumor of the thymus gland (Aarli, 1999, 2008).
 - b. Ocular symptoms are easily missed in elderly people because of normal aging of the eyelids (Aarli, 2008).
 - c. The main immunological difference in late-onset MG is the presence of antibodies to muscle titin, also known as connectin, a protein vital for muscle contraction (detected in approximately 50% of patients), and lower mean concentration of antibodies to AChR (Aarli, 1999, 2008).
 - i. Titin is a protein that plays an important role in muscles used in movement and heart contraction. It is an essential component of sarcomeres, the basic unit of muscle contractions (U.S. National Library of Medicine National Institutes of Health Department of Health & Human Services, 2012).
- E. Racial differences
1. African Americans
 - a. In seronegative generalized MG (negative for AChR antibodies), African Americans have a higher rate of positive muscle-specific kinase antibodies (MuSK-Ab) than Caucasians with seronegative generalized MG (Oh, 2009). MuSK-Ab are antibodies against MuSK protein. MuSK is a polypeptide required for formation of the NMJ.

B. Congenital myasthenic syndromes (CMS)

1. Present at birth but may not manifest until childhood or adult life; symptoms usually begin within the first 2 years of life and range from mild to severe; and weakness does not usually progress.
2. CMS is not caused by autoimmune processes but rather synaptic malfunction, which in turn is caused by genetic mutations (Engel, Ohno, & Sine, 2003).
3. The defect may be presynaptic, synaptic, or postsynaptic at the NMJ (Keesey, 2004).
4. The inheritance pattern is typically autosomal recessive (National Institute of Neurological Disorders and Stroke, 2012).
5. The three main categories of CMS are named for the part of the affected NMJ (Engel et al., 2003; Keesey, 2004; MDA, 2009).
 - a. Presynaptic (nerve cell)
 - i. Insufficient release of ACh
 - b. Postsynaptic (muscle cell)
 - i. ACh receptors are missing or don't stay open long enough.
 - ii. AChR deficiency or mutations in membrane or ACh binding sites
 - c. Synaptic (space between nerve and muscle cells)
 - i. ACh receptors stay open too long.
 - ii. Acetylcholinesterase (AChE) deficiency (Keesey, 2004)

C. Transient neonatal MG

1. Occurs as a result of transplacental passage of maternal autoantibodies interfering with the function of the NMJ (Batoocchi et al., 1999).
2. Occurs in about 9%–30% of infants born to mothers with autoimmune MG and is transient, lasting a few weeks to 4 months. Symptoms resolve as maternal autoantibodies leave the neonate's circulation (Tellez-Zenteno, Hernández-Ronquillo, Salinas, Estanol, & da Silva, 2004).
3. Careful observation of infants is required in a special infant care unit with nurses familiar with MG for the first several postpartum days (Burke, 1993).
4. Symptoms may occur within hours after birth and may include generalized weakness, hypotonia, weak cry, poor suck and swallow, facial paresis, and respiratory distress (Papazian, 1992).

VII. Immune versus nonimmune MG

- A. This MG classification may overlap with previously described subtypes.

B. Immune MG (Agius et al., 2003)

1. Type 1: high AChR antibodies without titin or MuSK antibodies
2. Type 2: titin antibodies present with AChR antibodies
3. Type 3: MuSK antibodies present without AChR antibodies.

C. Nonimmune MG

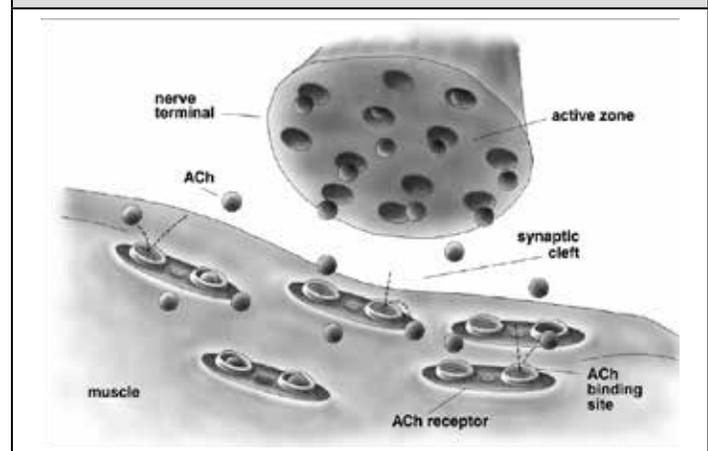
1. Congenital, which, as described previously has a genetic etiology (Engel et al., 2003; Keesey, 2004)

VIII. Neurophysiology of the neuromuscular junction

A. Structure of the NMJ (Howard, 2008; Ruff, 2003)

1. The NMJ, also known as the motor end-plate, is composed of the nerve terminal, the synaptic cleft, and the postsynaptic membrane (**Figure 1**).
2. The nerve terminal is a highly specialized region that forms a small bulb (the synaptic bouton or presynaptic terminal) that contains synaptic vesicles. Synthesis and packaging of the neurotransmitter, ACh, occurs within the presynaptic nerve terminal. Packaged transmitter (vesicles) collects in regions called active release sites or zones. Typically, there is one end-plate region for one muscle fiber in most skeletal muscles (Howard, 2008).
3. The synaptic cleft separates the nerve terminal from the postjunctional region of the muscle end-plate.
4. The muscle membrane enfolds to increase surface area, and at the crests of these folds are the sites of the AChR.

Figure 1. Normal Neuromuscular Junction



Artist's rendition of the myasthenic neuromuscular junction. The nerve terminal of a single synaptic bouton contains synaptic vesicles of acetylcholine (ACh).
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- B. The chemistry of neurotransmission (Howard, 2008; Ruff, 2003)
1. The neurotransmitter at peripheral NMJs is ACh. Synthesis occurs in the cytoplasm of the nerve terminal with processing of acetate + choline with the help of choline acetyltransferase. Most of the transmitter is stored in vesicles. ACh is released in discrete packages (quanta) when nerve activation occurs. ACh molecules released by the presynaptic neuron bind with the AChR on the postsynaptic muscle membrane folds.
 2. ACh binding to the AChR stimulates opening of sodium channels, and sodium flows into the cell while a lesser amount of potassium flows out. The sodium influx causes depolarization of the muscle fiber, which initiates a release of calcium from intracellular (sarcoplasmic reticulum) stores. The increase in intracellular calcium stimulates muscle contraction.
 3. AChE is located deep in clefts of these postsynaptic folds. Unbound ACh in the synaptic cleft is hydrolyzed by AChE into choline and acetate, which are taken back into the nerve terminal for resynthesis.
- C. Neuromuscular transmission (Howard, 2008; Ruff, 2003)
1. The presynaptic events of neuromuscular transmission include the nerve action potential (AP) depolarizing the axonal membrane of the nerve terminus, producing a voltage-dependent increase in calcium conductance.
 - a. Extracellular calcium enters the axon terminal to initiate ACh release. Exocytosis of the synaptic vesicle contents occurs at highly specialized release zones and discharges the ACh into the synaptic cleft. There is prompt diffusion across the synaptic cleft to the AChR complex.
 2. The postsynaptic events of neuromuscular transmission include the binding of ACh molecules with postsynaptic AChR receptors. These ACh receptors are located primarily at the crests of postsynaptic folds. Binding produces a change in the shape of the ACh-AChR complex; with an increased permeability of sodium and potassium, the opening of individual ionic channels results in the local depolarization of the end-plate zone, which produces an

action potential and muscle contraction. Postsynaptic depolarization is terminated by passive diffusion of ACh out of the primary and secondary synaptic clefts and enzymatic hydrolysis of ACh into choline and acetate by AChE.

IX. Pathophysiology of acquired MG

- A. Acquired MG is an autoimmune disorder that is attributable to a T-cell dependent, antibody-mediated deterioration of the neuromuscular junction, thereby altering the nerve impulse transmission processes (Trough et al., 2012).
- B. AChR antibody mechanism (Howard, 2008; Mays & Butts, 2011)
1. An antibody-mediated attack on the postsynaptic muscle results in the loss of the postsynaptic muscle's normal folded shape. AChRs are degraded by autoantibodies and complement activity, so the concentration of AChRs on the muscle end-plate membrane is reduced.
 2. Antibodies bind to and block the AChR binding sites.
 3. Immunoglobulin G and complement components attach to and damage the muscle membrane, reducing the efficiency of synaptic transmission.
 4. Although ACh is released normally, its effect on the postsynaptic membrane is diminished because of decreased AChR or decreased AChR binding sites. The postsynaptic membrane is less sensitive to ACh, and there is a reduced probability that nerve impulses will be followed by a muscle AP. (Howard, 2008; Mays & Butts, 2011).
- C. Role of the thymus
1. There is a relationship between the thymus gland and acquired MG, although whether it plays a primary or secondary role in the pathogenesis of MG is unclear. The thymus is the central organ for immunological self-tolerance, which is the capacity to recognize self versus nonself with the appropriate immunological responses. It is suspected that this loss of ability to recognize self versus nonself plays a role in the breakdown in tolerance that leads to the autoimmune attack on AChR in MG.
 2. The thymus contains myoid cells, which are striated muscle cells within thymal tissue that express the AChR antigen,

antigen-presenting cells, and immunocompetent T cells.

3. The normal thymus targets and deletes AChR-specific T cells in the thymus before they enter the periphery.
4. In the patient with MG who has an abnormal thymus, tolerance is lost and results in the development of antibodies against AChR and other proteins involved in NMJ activity.
5. The thymus is abnormal in most patients with acquired MG.
 - a. Thymic hyperplasia: 65% of patients with acquired MG have microscopic changes of hyperplasia that resemble the histology of active peripheral immune organs (Angelini, 2011; Howard, 2008; Phillips, Torner, Anderson, & Cox, 1992). These hyperplastic features include the presence of germinal centers, which are areas within lymphoid tissue at which B cells interact with helper T cells to produce antibodies. The precise role of the thymus is not entirely clear (**Figure 2**).
 - b. Thymoma
 - i. Among patients who have MG, 10%–15% have a tumor of the thymus. These patients tend to be between the ages of 30 and 60 years and have more severe disease and higher levels of AChR antibodies (Howard, 2008).

X. Ocular only versus generalized MG

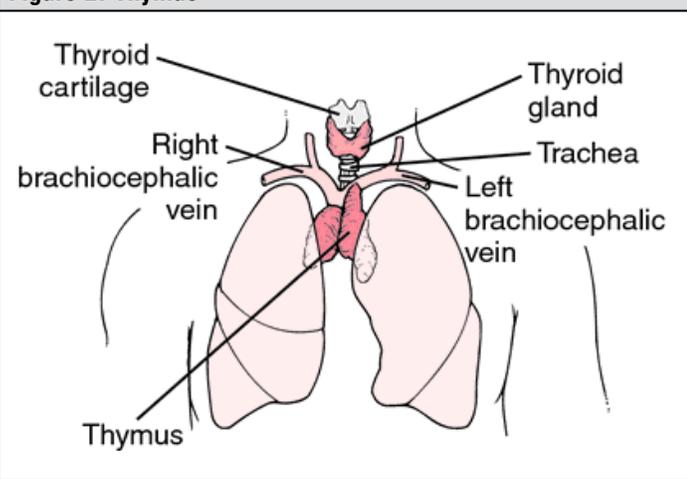
A. Ocular MG

1. Affects 50% of the MG population (Benatar & Kaminski, 2006).
2. Eyes
 - a. Ptosis and diplopia
 - b. Eyelid levator muscle and lateral rectus muscle (Conti-Fine et al., 2006; Hsu, Tsai, Wang, & Su, 2002)
3. Test: positive neostigmine (Prostigmin) or edrophonium (Tensilon) test
 - a. Edrophonium inhibits AChE
 - b. Given intravenously (IV)
 - c. A positive result with improvement or resolution of ptosis or muscle weakness is indicative of MG (Benatar, 2010).
4. AChR antibody test (blood analysis)
 - a. Positive AChR antibodies (present in 30%–50%) (Conti-Fine et al., 2006)
5. The “ice pack test” for diagnosis of ocular myasthenia involves placing an ice pack on the eyelids for 2 minutes. A positive result is at least a 2-mm improvement of ptosis. There is questionable specificity and sensitivity of this test because of the lack of research on this method (Benatar, 2006, 2010; Czaplinski, Steck, & Fuhr, 2003; Ellis, Hoyt, Ellis, Jeffery, & Sondhi, 2000; Ertas, Arac, Kumral, & Tuncbay, 1994; Golnik, Pena, Lee, & Eggenberger, 1999; Kubis, Danesh-Meyer, Savino, & Sergott, 2000).
Nursing recommendation: Nurses should monitor the results of the ice pack test with consideration for its limited value in the diagnosis of MG (Level 2).

B. Generalized MG

1. Affects 70% of the MG population (Conti-Fine et al., 2006)
2. May involve eyes
 - a. Ptosis and diplopia
 - b. Eyelid levator muscle and lateral rectus muscles
3. Progresses to bulbar, facial, and limb muscles
4. Tests: positive neostigmine (edrophonium) test
5. Positive AChR antibodies (present in 80%–90%) (Conti-Fine et al., 2006)
6. Positive MuSK antibodies (present in 20% if negative for AChR antibodies) (Vincente & Leite, 2005)
7. Positive electrodiagnostic testing
8. Associated with thymoma or thymic hyperplasia

Figure 2. Thymus



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XI. Clinical MG classification

- A. The Task Force of the Medical Scientific Advisory Board of the Myasthenia Gravis Foundation of America (Jaretski et al., 2000) designed a classification to identify subgroups of patients with MG who share distinct clinical features or severity of disease that may indicate different prognoses or responses to therapy (Table 1) (Howard, 2008; Jaretski et al., 2000).

XII. Description/clinical features of MG (Juel & Massey, 2007; Keeseey, 2004)

- A. Characterized by fatigable muscle weakness affecting ocular, facial, bulbar, respiratory, neck, and limb muscles
- B. Weakness increases with repetitive use (fatigue) and improves after periods of rest or sleep.
- C. The clinical course is variable and individuals may experience periods of exacerbation and remission of symptoms.
- D. MG is a chronic disease that most often is active during the first few years and is characterized

by exacerbations, remissions, and lability (Keeseey, 2004).

- E. Disease remissions are rarely complete or permanent.

XIII. Manifestations/symptoms

- A. Characteristic patterns of presenting weakness
- Ocular symptoms of ptosis and diplopia occur in more than 50% of patients, and half will develop generalized disease within 2 years (Benatar & Kaminski, 2006).
 - Bulbar symptoms (dysarthria, dysphagia, and fatigable chewing) may be seen initially in up to 15% of patients (Angelini, 2011).
 - Proximal limb weakness alone occurs in fewer than 5% of patients (Grob et al., 2008).
- B. Clinical features include fatigable muscle weakness in specific muscle groups.
- Ocular muscles: Variable eyelid weakness (ptosis) occurs in either eye and can alternate from one eye to the other over time. It may be severe enough to occlude vision. Extraocular muscle (EOM) weakness produces blurring of vision or double vision. An abnormal pattern can occur, such as an isolated oculomotor neuropathy, an internuclear ophthalmoplegia presenting as impaired adduction, or a vertical gaze paresis mimicking other disorders. The pupils are always spared (Mahadeva, Phillips, & Juel, 2008).
 - Bulbar muscles: Fatigable jaw weakness is often noted halfway through a meal or when chewing meat and other concentrated solid foods. The weakness may be noted by the need for patients to use their fingers under the jaw to keep their mouth closed. Hypophonic or nasal speech occurs with palatal weakness and may worsen with prolonged speaking. Dysphagia may also be present, with symptoms of nasal regurgitation when swallowing fluids; choking while eating foods with certain textures, such as peanuts, carrots, or steak; the need for liquids and gravies to swallow food boluses; taking a longer time to eat (fatiguing); weight loss; or aspiration pneumonia.
 - Facial muscles: Facial weakness often produces a transverse smile and an expressionless face. A transverse smile, also called a myasthenic snarl, is a contraction of the middle portion of the upper lip

Table 1. Myasthenia Gravis Foundation Clinical Classification and Defining Characteristics

Class	Defining characteristics
I	Any ocular weakness May have weakness of eye closure All other muscle strength is normal
II	Mild weakness affecting other than ocular muscles May also have ocular muscle weakness of any severity
IIa	Predominantly affecting limb, axial muscles, or both May also have lesser involvement of oropharyngeal weakness
IIb	Predominantly affecting oropharyngeal, 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
IIIa	Predominantly affecting limb, axial muscles, or both May also have lesser involvement of oropharyngeal muscles
IIIb	Predominantly affecting oropharyngeal, 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
IVa	Predominantly affecting limb and/or axial muscles May also have lesser involvement of oropharyngeal muscles
IVb	Predominantly affecting oropharyngeal, 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 The use of a feeding tube without intubation places the patient in class IVb.

Adapted from Howard J.F.: *Physician Issues*. In *Myasthenia Gravis: A Manual for the Health Care Provider*, [James F. Howard, Jr. (ed)]. Myasthenia Gravis Foundation of America, Chapter 1, Table 2.1, pg. 13, 2008. Used with permission.

while the upper mouth fails to contract (Juel & Massey, 2007).

4. Neck and limb weakness: A dropped head occurs, particularly later in the day because of weakness of neck extensors. Neck pain can occur due to the added effort of trying to keep the head up. The proximal arms (deltoid and triceps) are usually more involved than proximal legs (hip flexors), although distal presentations (wrist and finger extensors or ankle dorsiflexors) can occur.
5. Respiratory muscles: Breathing difficulty in generalized MG is characterized by increasing difficulty while supine or bending over; often, respiratory insufficiency is coupled with other bulbar symptoms (Grob et al., 2008). Respiratory muscle weakness may be sufficient to result in respiratory failure, and the patient is said to be in crisis. However, less severe respiratory muscle weakness may also interfere with sleep, resulting in daytime sleepiness and fatigue (Keeseey, 2004).

XIV. Clinical course

- A. The clinical course is variable.
- B. Patients may experience periods of exacerbations and remissions (Keeseey, 2004).
 1. Exacerbations (worsening of symptoms) may be caused by systemic illness (e.g., viral or respiratory infections), fever, hypo- or hyperthyroidism, surgery, emotional upset, pregnancy, menstrual cycle, and drugs that affect neuromuscular transmission.
 - a. Myasthenic crisis: respiratory failure attributable to myasthenic weakness. Other less life-threatening signs and symptoms of myasthenia crisis include increased generalized muscle weakness; tachycardia; and pale, cool skin.
 - b. Cholinergic crisis: respiratory failure resulting from a high dose of cholinesterase inhibitors. Other less life-threatening signs and symptoms of cholinergic crisis include increased generalized increased muscle weakness; small pupils; bradycardia; increased secretions; diarrhea and abdominal cramping; and red, warm skin.
 2. Remissions: inactive stage (Howard, 2008)
 - a. Remissions are rarely complete or permanent.

XV. Diagnostic tests

- A. Laboratory tests such as measuring the level of AChR in the serum and physical examination can diagnose autoimmune MG in most patients.
 1. MG can be diagnosed by serological testing for AChR antibodies; specificity is higher than 98%, but sensitivity is low and variable (around 85% for generalized MG, 44% for ocular MG) (Benatar, 2010).
 2. In the patient who is AChR seronegative, further testing can be completed to check for MuSK antibodies. MuSK antibody testing is reliable in generalized MG but not in ocular MG (Stickler, Massey, & Sanders, 2005).
 3. Confirmation of diagnosis and response to medication can be accomplished by administering an IV AChE inhibitor drug such as edrophonium chloride (Tensilon) and monitoring for a rapid but brief resolution of symptoms, such as improvement in ptosis, dysconjugate gaze, grip strength, or respiratory function. (Angelini, 2011; Keeseey, 2004).
 - a. IV edrophonium chloride is of rapid, short duration, with onset in 30 seconds and lasting about 5 minutes.
 - b. Atropine (0.6 mg) should be available in the event that side effects occur (Meriggioli & Sanders, 2004).
 - c. Rare risk of side effects includes bradycardia, asystole, and bronchoconstriction; emergency medications must be available (Angelini, 2011; Keeseey, 2004).
 - d. IV edrophonium chloride is contraindicated in the patient with bronchial asthma or cardiac dysrhythmias because edrophonium may result in cholinergic side effects (Meriggioli & Sanders, 2004).
 - e. Edrophonium is used less often than previously but remains available in the United States (Angelini, 2011).
 - f. Sensitivity for the edrophonium test has been reported at 0.88 and 0.92 for ocular and generalized MG, respectively; the specificity has been found to be as high as 0.97 for both ocular and generalized MG (Benatar, 2006; Nicholson, McLeod, & Griffiths, 1983).
 - g. If the IV test cannot be administered, an oral anticholinesterase medication

such as pyridostigmine (Mestinon) can be given (Gold, Hohlfeld, & Toyka, 2008; Keeseey, 2004).

- i. Symptom resolution onset will be slower with oral administration, with response over 1–2 hours.
- ii. If taken orally, edrophonium must be taken with food or after a meal to lessen gastrointestinal stimulation (Keeseey, 2004).

Nursing recommendation: Nurses should know the adverse events associated with diagnostic testing in MG and how to manage those side effects as needed. Nurses should monitor for results and adverse events associated with the use of edrophonium for diagnostic testing in MG and manage adverse events appropriately (Level 2).

B. Electrodiagnostic testing

1. Repetitive nerve stimulation (RNS)
 - a. In RNS, a peripheral nerve is repetitively overstimulated and the muscle action potential is recorded.
 - b. A surface electrode is placed over the muscle, and a reference electrode is placed over a distal tendon or bony prominence, where minimal electrical activity is recorded.
 - c. RNS depletes the synaptic vesicles of ACh, resulting in a decremental response in the muscle action potential.
 - d. The cutoff for normal/abnormal response may vary between laboratories, but a decrease of more than 10% is usually considered abnormal. Reports of sensitivity and specificity are variable related to inconsistencies in administration and interpretation of the test (Benatar, 2006; Costa, Evangelista, Conceicao, & de Carvalho, 2004; Keeseey, 2004; Meriggioli & Sanders, 2004).
2. Single-fiber electromyography (SFEMG)
 - a. A concentric needle is used to identify and record action potentials from single muscle fibers.
 - b. Testing may be conducted using mild voluntary activation of the muscle or with microstimulation; neuromuscular jitter is produced.
 - c. SFEMG measures the instability preceding the neuromuscular block, while RNS measures the neuromuscular block.
 - d. SFEMG is highly sensitive for diagnosis but is not 100% sensitive (Benatar,

2006; Keeseey, 2004; Meriggioli & Sanders, 2004).

3. Electrodiagnostic study testing is uncomfortable for patients.

Nursing recommendation: Nurses should be familiar with electrodiagnostic testing in MG. Nurses should prepare patients for their experience, including the likelihood of some discomfort (Level 2).

C. Other

1. The “ice pack test” (see section X.A.5)
 2. Diagnostic imaging of the anterior mediastinum can help to determine if a thymoma is present. Chest X rays are inferior to computed tomography and/or magnetic resonance imaging for recognition of thymoma (Benatar, 2006; Keeseey, 2004, Meriggioli & Sanders, 2004).
- Nursing recommendation:** Nurses should understand and explain the “ice pack test” and diagnostic imaging to the patient and family to lessen fear and anxiety and elicit cooperation and participation (Level 2).

XVI. Nursing assessment of the patient with MG (Vas-sar, Batenjany, Koopman, & Ricci, 2008)

- A. Symptom description to be obtained during the patient history
 1. Location of the weakness
 2. Quality or character of the weakness
 3. Quantity or severity of the weakness
 4. Timing (onset, duration, frequency) of the weakness and relation to medication administration
 5. Setting in which weakness occurs and/or worsens
 6. Aggravating or trigger factors (e.g., change in emotional state, heat, humidity, infection, surgery, menstruation)
 7. Alleviating factors (e.g., rest)
- B. Assessment techniques (Table 2 and Table 3) (Howard, 2008; MGFA, 2000)
 1. Ocular muscles
 - a. Eyelids for ptosis, diplopia (double vision), extraocular muscles
 2. Bulbar muscles
 - a. Chewing, swallowing, speech
 3. Facial muscles
 - a. Flattening of the nasolabial fold, smile symmetry, facial expression, resistance to eyelid and lip closure, inability to puff out cheeks
 4. Head and neck muscles
 - a. Head drop
 5. Limb muscles

- a. Test strength and fatigability of each of the proximal and distal muscle groups against gravity and resistance and observe and record (in seconds or minutes) how long it takes for the muscles to fatigue. The patient with MG has asymmetrical weakness, so it is important to compare each muscle group to the corresponding muscle group on the opposite side of the body. Muscle strength can be graded using the widely accepted scale in **Table 2** (Howard, 2008; Vassar et al., 2008). Muscle fatigue can be assessed by using the Quantitative Myasthenia Gravis Testing Method (**Table 3**) (Barohn 2000; Howard, 2008).

Nursing recommendations: Nurses should perform a comprehensive nursing assessment of the patient with MG that includes a detailed medical history and symptom description. Nurses should test all voluntary muscles for both muscle strength and fatigability to determine the severity of specific muscle weakness, the degree of functional impairment, and potential complications (**Table 4**) (Level 3).

C. Respiratory muscles

1. Observations to note include breathing activity and listening to the patient talk and count to 50, recording the number at which the patient stops to take a breath, any shortness of breath when the patient is lying down or bending over, increased respiratory effort, and frequent respiratory gasps. The rate, rhythm, and quality of respirations and the presence of anxiety or restlessness should be noted as well (Mehta, 2006).
Nursing recommendation: Nurses should perform a detailed physical assessment of respiratory status (Level 3).
2. Pulmonary function tests include negative inspiratory force (NIF) and forced vital

Grade	Interpretation
Grade 5	Normal muscle power
Grade 4	Movement against gravity and against resistance
Grade 3	Movement against gravity without resistance
Grade 2	Movement in the plane of action with gravity eliminated
Grade 1	Flicker of muscle movement in the gravity-eliminated position
Grade 0	No muscle movement, even with gravity eliminated

Sources: MGFA, 2000; Howard, 2008

Test item/Grade	None/0	Mild/1	Moderate/2	Severe/3	Score
Double vision on lateral gaze right or left (circle one), seconds	61	11–60	1–10	Spontaneous	
Ptosis (upward gaze), seconds	61	11–60	1–10	Spontaneous	
Facial muscles	Normal lid closure	Complete, weak, some resistance	Complete, without resistance	Incomplete	
Swallowing 4 oz. water (1/2 cup)	Normal	Minimal coughing or throat clearing	Severe coughing/choking or nasal regurgitation	Cannot swallow (test not attempted)	
Speech after counting aloud from 1 to 50 (onset of dysarthria)	None at 50	Dysarthria at 30–49	Dysarthria at 10–29	Dysarthria at 9	
Right arm outstretched (90 deg sitting), seconds	240	90–239	10–89	0–9	
Left arm outstretched (90 deg sitting), seconds	240	90–239	10–89	0–9	
Vital capacity, % predicted	80	65–79	50–64	<50	
Rt-hand grip, kgW					
Men	45	15–44	5–14	0–4	
Women	30	10–29	5–9	0–4	
Lt-hand grip, kgW					
Men	35	15–34	5–14	0–4	
Women	25	10–24	5–9	0–4	
Head lifted (45 deg supine), seconds	120	30–119	1–29	0	
Right leg outstretched (45 deg supine), seconds	100	31–99	1–30	0	
Left leg outstretched (45 deg supine), seconds	100	31–99	1–30	0	
Total QMG score (range, 0–39)					

From Howard J. F.: Physician Issues. In Myasthenia Gravis – A Manual for the Health Care Provider, (James F. Howard Jr [ed]). Myasthenia Gravis Foundation of America, Appendix 2.1, pg. 116, 2008. Used with Permission. Refer to source for more information regarding administration of the QMG Assessment Tool.

Body System	History/Observation	Measurement
Ocular	Alignment, diplopia Ptosis	Extra ocular movements (H pattern testing) Lid lag, fatigable ptosis (use pupil as a benchmark)
Bulbar Chewing Swallowing Speech	Restricted to soft foods, fatigues when chewing food such as steak Drooling, difficulty handling secretions, double swallows, nasal regurgitation	Count to 50, document the number at which speech changes; describe speech (e.g., slurred, nasal, soft)
Facial	Flattening of nasolabial fold	Resisted eyelid and lip closure, cheek puff, smile
Neck	Head drop	Resisted flexion and extension
Limbs Upper Lower		Strength testing: shoulders, triceps, wrist extension Strength testing: hip flexion, ankle dorsiflexion
Respiratory	Shortness of breath when lying down/bending over Increased respiratory effort Anxiety	Rate, rhythm, quality of respirations Pulmonary function tests

Sources: Abbott, 2010; Vassar et al., 2008; Weeks, 2012

capacity (FVC) in supine and sitting positions (Howard, 2008).

3. Oxygen saturation and blood gas analysis are not good indicators of chest muscle and diaphragm strength and the ability to support respiratory function (Howard, 2008).
Nursing recommendation: Nurses should assess the respiratory system appropriately and support respirations as needed until additional interventions are available (Level 3).

- iv. Neostigmine: One small randomized controlled trial using intranasal neostigmine versus placebo showed efficacy of an AChE inhibitor treatment (Mehndiratta, Pandey, & Kuntzer, 2011). All other AChE drug studies have been observational (Mehndiratta et al., 2011).
- v. AChE inhibitor drugs are titrated to the individual patient with consideration for side effects and muscle strength. Dose regimens vary between individuals (Angelini, 2011; Saperstein & Barohn, 2004).

Nursing recommendation: Nurses must administer and teach the patient with MG and their family to administer the correct dose of AChE inhibitors on time (Level 2). Nurses must also teach the patient and their family the signs and symptoms of overdose and adverse events (Level 2).

XVII. Treatment

- A. The goal is disease and symptom management (Angelini, 2011).
- B. Pharmacologic management (**Table 5**)
 1. Symptom management
 - a. AChE inhibitors slow the degradation of ACh to allow ACh to remain available at the NMJ; adverse effects include fasciculations, abdominal cramps, and diarrhea (Saperstein & Barohn, 2004; Skeie et al., 2010).
 - i. AChE inhibitors are also first-line treatment for children (Finnis & Jayawant, 2011).
 - ii. AChE inhibitors include pyridostigmine (Mestinon) and neostigmine.
 - iii. Pyridostigmine (Mestinon) is dosed up to 60 mg five times per day; this is usually the regimen at the beginning of the disease and for treatment of milder disease (Skeie et al., 2010).

- b. Immunosuppression
 - i. Immunosuppressive or immunomodulating agents can have either a general or targeted immunosuppressive effect.
 - ii. Corticosteroids such as prednisone have a generalized immunosuppressive effect. While these drugs decrease the immune attack on the proteins and receptors

Table 5. Medications Used in the Management of Myasthenia Gravis

Classification	Drug	Dose	Special Considerations (Recommendations)
Symptomatic Therapy: Acetylcholinesterase inhibitors	Pyridostigmine (Mestinon, Mestinon Time Span)	30, 60, 90, mg every 4-6 hours orally Mestinon SR 180 mg of a time-span (slow-release form) at bedtime	Doses increased and adjusted to efficacy and side effects Take 30-60 minutes before eating with bulbar symptoms Adverse gastrointestinal effects include nausea and vomiting, abdominal cramping, and diarrhea. Effectiveness may dissipate if taken with food May require an antidiarrheal agent Other side effects include increased salivation, drooling, and tearing; increased bronchial secretions; and perspiration. Late-evening time span preparations are indicated only with marked myasthenic weakness in the morning. A liquid form is available for children and adults with swallowing difficulties. Do not substitute regular Mestinon or generic pyridostigmine for Mestinon SR . The dose schedule for a particular patient may vary from time to time, even daily, particularly during periods of stress or infection (Mehndiratta, Pandey, & Kuntzer, 2011; MGFA, 2012b). Nursing recommendation: Nurses should administer and educate patients to take pyridostigmine as prescribed. (Level 2).
Glucocorticosteroids (GCS): General immunosuppressives for the short or long term	Prednisone Not FDA approved for MG	0.75–1.0 mg/kg daily or 60–100 mg on alternate days orally, option for long-term therapy; a lower dose (10–25mg) every other day may be used when combined with other treatments to decrease side effects	Option to slowly increase doses; after reaching near remission, gradual dose reduction Monitor for side effects. Increased risk for osteoporosis: exercise and supplement diet with increased calcium, vitamin D Increased risk for glaucoma; eye checks are needed Increased susceptibility for infection; take precautions such as immunization against the flu Increased risk for obesity, diabetes, hypertension, electrolyte imbalance (hypokalemia) (Schneider-Gold, Gaidos, Toyka, & Hohlfeld, 2005) Nursing recommendation: Nurses should monitor for side effects associated with glucocorticosteroids and adjust dosage as prescribed (Level 2).
Targeted immunosuppressive (long-term use)	Azathioprine (Imuran) Not FDA approved for MG	2–4 doses of 50 mg/day (2–3 mg per kg body weight/day) oral Often Initially combined with GCSs	Use an initial trial dose of 1-50 mg as a test dose for primary hypersensitivity. Divided daily doses are better tolerated than single doses. One dosing schedule is 50 mg/day and increase by 50 mg/day every 7 days until 150–200 mg/day is obtained. Dose decreases may result in worsening of symptoms. May administer with corticosteroids Gradual improvement in 6–12 months May cause flu-like illness in 10% of patients (Gold, Hohlfeld, & Toyka et al., 2008; Saperstein & Barohn, 2004) Discontinue if liver enzymes are elevated or white blood cells decrease below 3,000 cells/mm ³ (Saperstein & Barohn, 2004; Hart, Sathasivam, & Sharshar, 2007; Angelini, 2011). Nursing recommendation: Nurses should monitor for signs and symptoms of infection, hepatotoxicity, nephrotoxicity, bone marrow suppression, and skin cancer (Level 3).
Targeted immunosuppressive (long-term use)	Cyclosporine A (Sandimmune, Neoral) Not FDA approved for MG	Starting dose 5mg/kg body weight in 2 divided doses (q12h) Optimal dosing monitored by measuring trough drug levels	Steroid sparing if intolerant of Azathioprine Measure blood trough levels until ideal dosing is obtained and during drug dose change. Blood levels should be checked at 1 month and adjusted as needed. Monitor serum creatinine related to nephrotoxicity. Monitor for side effects Off-label status despite evidence (Tindall, Phillips, Rollins, Wells, & Hall, 1993; Ciafaloni, Nikhar, Massey, & Sanders, 2000) (Nursing recommendation: Nurses should monitor for nephrotoxicity (Level 3).
Targeted immunosuppressive (long-term use)	♦ Mycophenolate mofetil (CellCept) Not FDA approved for MG	1000–2000 mg/day orally Twice-per-day scheduling	Well-documented single case studies available; publication of a randomized clinical trial pending Gastrointestinal symptoms and infection possible side effects. Monitor complete blood count and differential every 2 weeks six times. and then monthly (Saperstein & Barohn, 2004). Nursing recommendation: Nurses should monitor for myelosuppression (Level 3).

Targeted immunosuppressive (long-term use)	♦ Methotrexate sodium (Methotrexate) Not FDA approved	7.5 mg to 15 mg/week orally	Well-documented single case studies available; publication of a randomized clinical trial pending Monitor for infection.
Targeted immunosuppressive (long-term use)	♦ Cyclophosphamide (Cytoxan)	500 mg/m ² every 4–12 weeks IV or 1–2 mg/kg body weight per day orally	Well-documented single case studies available; publication of a randomized clinical trial pending Adverse effects include myelosuppression, hemorrhagic cystitis, and increased risk for malignancy (Silvestri & Wolfe, 2012). Nursing recommendation: Nurses should monitor for myelosuppression, hemorrhagic cystitis, and increased risk for malignancy (Level 3).
Targeted immunosuppressive (long-term use)	♦ Tacrolimus (FK506) (Prograf)	0.1 mg/kg/day orally titrated to blood levels 0.2 (2 x 2–5mg/day) orally	Adverse effects include nephrotoxicity and hyperglycemia (Angelini, 2011) Nursing recommendation: Nurses should monitor for nephrotoxicity and hyperglycemia. (Level 3).
Other Immunosuppressive	♦ Rituximab (Rituxin)	375 mg/m ² IV weekly	For refractory MG, and MuSK MG Adverse effects include pancytopenia (Ibrahim, Dimachkie, & Shaibani, 2010; Silvestri & Wolfe, 2012). Nursing recommendation: Nurses should monitor pancytopenia associated with long-term immunosuppression (Level 3).

♦ Off-label option; available for nonresponders, in cases of very severe MG, or when intolerable side effects occur. Abbreviations: FDA, U.S. Food and Drug Administration; IV, intravenous; MG, myasthenia gravis. Source: Tindall et al., 1993; Cialaloni et al., 2000; Schneider-Gold et al., 2005; Gold et al., 2008; Hart et al., 2007; Vassar et al., 2008; Merigglioli, 2009; Mehdri-atta et al., 2011; Saperstein & Barohn, 2004; Angelini, 2011; Myasthenia Gravis Foundation of America, 2012b; Silvestri & Wolfe, 2012; Myasthenia Gravis Foundation of America, 2012b; Schneider-Gold, Gaidos, Toyka, & Hohlfeld, 2005; Vassar et al., 2008)

involved in MG, they also suppress general immune function significantly, increasing the risk for infection. Side effects to monitor include signs of infection, weight gain, hypertension, diabetes, osteoporosis, and psychosis (Gold et al., 2008; Saperstein & Barohn, 2004). Other signs of infection may be masked and can delay wound healing (Zaiontz & Lewis, 2011).

- iii. Immunosuppressive agents with a targeted immunosuppressive effect in MG include azathioprine (Im-muran), cyclosporine (Sandim-mune, Neoral), mycophenolate mofetil (CellCept), mycopheno-late sodium (Myfortic), cyclophos-phamide (Cytoxan), tacrolimus (Prograf), methotrexate sodium (Methotrexate), and rituximab (Rituxan). These agents block lym-phocyte production. Side effects to monitor include signs of infec-tion, bone marrow suppression, nephrotoxicity, and hepatotoxicity (Angelini, 2011; Gold et al., 2008; Saperstein & Barohn, 2004).
- iv. Drugs such as cyclosporine alter T-cell response (Conti-Fine

et al., 2006) and provide targeted immunosuppression. Side effects include infection, nephrotoxicity and hypertension (Saperstein & Barohn, 2004).

Nursing recommendation: Nurses should advise patients who are taking corticoste-roids to be aware of infection risk, practice good hand hygiene practices, and avoid ex-posure to people with infection (Level 2).

Nursing recommendation: Nurses should monitor for side effects associated with im-munosuppressants and minimize patient risk for infection by maintaining appropri-ate infection-control practices, including good hand hygiene and sterile technique for invasive procedures (Level 2). Nurses should administer antimicrobials as pre-scribed (Level 2).

Nursing recommendation: Nurses should monitor for signs and symptoms of adverse effects associated with all medications used in the management of MG as previously described, including those most common-ly associated with long-term immuno-suppressants/immunomodulating agents, specifically, infection, hepatotoxicity, neph-rotoxicity, bone marrow suppression, and skin cancer (Level 3).

C. Other therapies

1. Immunomodulation (Conti-Fine et al., 2006)

a. Plasmapheresis (therapeutic plasma exchange [TPE])

- i. Plasmapheresis, or TPE, has been used in acute myasthenic crisis and for treatment prior to thymectomy (surgical removal of the thymus gland). The American Academy of Neurology has published a guideline for the use of plasmapheresis for neurologic disorders including MG, but, because of the lack of large randomized controlled trials, cannot support or refute the use of plasmapheresis in MG (Gajdos, Chevret, & Toyka, 2002; Cortese et al., 2011).
- ii. The goal of plasmapheresis is the removal of receptor antibodies from the circulation (Gold et al., 2008; Keeseey, 2004). One retrospective study demonstrated improvement with plasmapheresis (Cortese et al., 2011).

Nursing recommendation: Nurses should monitor for improvement following plasmapheresis (Level 2).

- iii. Plasmapheresis separates the plasma from other components in blood, especially red blood cells. The patient's plasma is exchanged with donor plasma or albumin solution, and new plasma or albumin and red blood cells are returned to the patient (Cortese et al., 2011).
- iv. Plasmapheresis requires venous access, which involves either two large, durable peripheral veins or a central line using a catheter that has a dual lumen and is large and sturdy enough to withstand significant flow and pressures (Juel & Massey, 2007).
 - a) Complications of venous access (peripheral or central) include infection, pain, nerve damage, thrombosis, perforation, dissecting hematomas, or arteriovenous fistulas (Vassar et al., 2008).

Nursing recommendation: Nurses should monitor for complications associated with

venous access (Level 2).

- v. Adverse reactions associated with plasmapheresis relate to replacement fluids and are more common with fresh frozen plasma than with albumin (20% versus 1.4 %) (Sutton, Nair, & Rock, 1989).

- a) Side effects include hypotension resulting from fluid volume changes and hypocalcemia from citrate used during plasmapheresis, causing dizziness, paresthesias, and headache (Zaiontz & Lewis, 2011). Fluid overload, congestive heart failure, infections, and thrombotic and bleeding tendencies have been observed as well (Trough et al., 2012; Juel & Massey, 2007).

Nursing recommendation: Nurses should monitor for side effects associated with plasmapheresis including fatigue and hypotension (Level 2).

- b. Intravenous immunoglobulin G (IVIG) infusions
 - i. IVIG is a blood product composed of purified and concentrated immunoglobulins (antibodies) from the pooled plasma of many healthy donors. It binds circulating antibodies, thereby promoting ACh availability and muscle function.
 - ii. Randomized controlled trials (Gajdos, Chevret, Clair, Tranchant, & Chastang, 1997; Gajdos et al., 2005; Ronager, Ravnborg, Hermansen, & Vorstrup, 2001; Wolfe et al., 2002; Zinman, Ng, & Brill, 2007) have been published regarding the use of IVIG in the management of MG. One randomized controlled trial showed efficacy in management of exacerbations of MG compared with placebo (Patwa, Chaudry, Katzberg, Rae-Grant, & So, 2012). Other studies did not show any difference in regard to the efficacy of IVIG compared with plasma exchange (Patwa et al, 2012) nor any difference in dosages of 1 g/kg versus 2 g/kg nor IVIG versus methylprednisolone.

- iii. IVIG can be used as an acute intervention to decrease the severity of MG exacerbations or as a chronic maintenance therapy in MG or prethymectomy (Gold et al., 2008; Skeie et al., 2010).
 - iv. Response varies between 60% and 70% (Gold et al., 2008; Saperstein & Barohn, 2004).
 - a) Inconsistent improvement is seen among patients with MG who have acute exacerbations and in chronic maintenance therapy (Saperstein & Barohn, 2004).
 - b) IVIG is administered as daily infusions over 2–5 days (Juel & Massey, 2007; Saperstein & Barohn, 2004; Trouth et al., 2012).
 - c) Onset of benefit begins about 3–10 days after beginning treatment and may last for up to 4 months, with 21–45 days being average (Gold et al., 2008; Keeseey, 2004).
 - v. IVIG may be combined with immunosuppressive medications.
 - vi. IVIG is costly, and supply may be limited (Gold et al., 2008).
 - vii. IVIG may be administered via a central venous implanted port, percutaneously inserted central catheter line, or large-bore peripheral IV catheter.
 - viii. Each infusion takes approximately 4–6 hours, depending on the dosage and infusion rate. The usual dose is 1–2 g/kg. The rate of infusion may be gradually increased over the course of a single dose to lessen risk for side effects. (Keeseey, 2004). The frequency is individualized (Vassar et al., 2008).
 - ix. Adverse reactions have been seen in fewer than 10% of patients receiving IVIG (Gold et al., 2008) and include circulatory overload, renal failure, nausea and vomiting, headaches, aseptic meningitis, thrombosis, stroke, seizures, retinal vasculitis, skin rashes, and alopecia (Gold et al., 2008; Juel & Massey, 2007; Keeseey, 2004).
 - x. Hypersensitivity reactions present in about 1 of 300 patients receiving IVIG. These patients typically have a selective immunoglobulin A (IgA) deficiency and then develop anti-IgA antibodies. Symptoms include those of anaphylaxis, such as respiratory distress, chest tightness, tachycardia hypotension, angioedema, erythema, fever, chills, and urticaria (Keeseey, 2004).
 - xi. In the case of hypersensitivity reactions, appropriate agents for treatment (e.g., epinephrine, diphenhydramine, oxygen, vasopressors) should be readily available (Gahart & Nazareno, 2012).
 - xii. Pretreatment with an antipyretic, antihistamine, and/or corticosteroid to prevent chills and fever may reduce the frequency and severity of hypersensitivity reactions (Gahart & Nazareno, 2012; Juel & Massey, 2007).
 - xiii. IVIG should be used with caution in the older adult population with multiorgan disease because of risk for complications (Gold et al., 2008).
- Nursing recommendation:** Nurses must understand the rationale for the use of IVIG in the management of MG and its reported benefits and limitations (Level 2). Nurses must be knowledgeable of different brands of IVIG and institution-specific protocols regarding dosage and rates, which may include a test dose and then a gradual increase in rate as tolerated to lessen risk for adverse effects. Action plans for adverse effects must be followed (Level 2).
- c. Thymectomy
 - i. Surgical removal of the thymus gland has been found to decrease MG symptoms in as many as 70% of patients who have thymomas or dysplasia of the thymus gland (Gold et al., 2008).
 - ii. The benefit of thymectomy in seronegative MG, nonthymomatous MG with exclusively ocular MG, or seronegative MG with MuSK antibodies is less likely and not

- recommended (Howard, 2008; Jacob, Viegas, Hilton-Jones, & Wilcox, 2007; Magee & Mack, 2009; Sanders, El-Salem, & Massey, 2003; Skeie et al., 2010).
- iii. No published randomized controlled trials regarding efficacy exist, although a trial is in progress that compares thymectomy in nonthymomatous MG with thymectomy and thymectomy and prednisone (NINDS & National Institutes of Health, 2006).
 - iv. Different surgical approaches may be undertaken in centers with experienced thoracoscopic surgeons in collaboration with neurologists specializing in neuromuscular disease (**Figures 3a-d**)
 - a) Surgical approaches include transsternal, transcervical, and video-assisted thoracoscopic surgery (VATS) or video-assisted thoracoscopic extended thymectomy (VATET) (Magee & Mack, 2009; University of Maryland, 2008).
 - b) The transsternal approach involves making a midline incision through the sternum to expose the thymus and remove it. A chest tube is inserted (**Figure 3a**) (Magee & Mack, 2009; University of Maryland, 2008).
 - c) A partial transsternal approach is possible as well, with an incision through only half of the sternum to expose and remove the thymus (**Figure 3b**) (Magee & Mack, 2009; University of Maryland, 2008).
 - d) In a transcervical thymectomy, a horizontal incision is made at the lower part of the neck; a scope is inserted under the sternum to visualize the thymus and remove it using small instruments. This approach is less invasive than transsternal but may be more likely to result in incomplete removal of the thymus (**Figure 3c**) (Magee & Mack, 2009; University of Maryland, 2008).
 - e) When VATS is used, a small incision is made on the left or right side of the chest. Fiber-optic instruments are used to visualize and remove the thymus. In the extended form, additional incisions are made on both sides of the chest and in the neck. (**Figure 3d**) (Magee & Mack, 2009; University of Maryland, 2008).
 - f) VATS and VATET may require longer operative time, but these procedures reduce the length of the hospital stay, postoperative pain, and blood loss and result in a better cosmetic result than transsternal thymectomy (Zahid, Sharif, Routledge, & Scarci, 2011).
 - v. Complications of thymectomy include respiratory failure related to myasthenic crisis (6%), infection (11%), and laryngeal or phrenic nerve injury (Juel & Massey, 2007; Watanabe et al., 2004).
 - a) For the patient with preoperative respiratory or bulbar symptoms, treatment with one of the rapid immunotherapies, plasmapheresis, or IVIG may be warranted prior to surgery or during the postoperative period.
 - b) Bulbar symptoms, a preoperative history of myasthenic crisis, and a preoperative serum AChR antibody value higher than 100 nmol/L is associated with a higher likelihood of postoperative MG (Watanabe et al., 2004).
 - vi. Age
 - a) There is no official age-related contraindication for thymectomy (Saperstein & Barohn, 2004).
 - b) The patient more than 60–65 years of age does not usually undergo thymectomy, except those with thymoma (Gold,

Figure 3. Surgical Approaches for Thymectomy

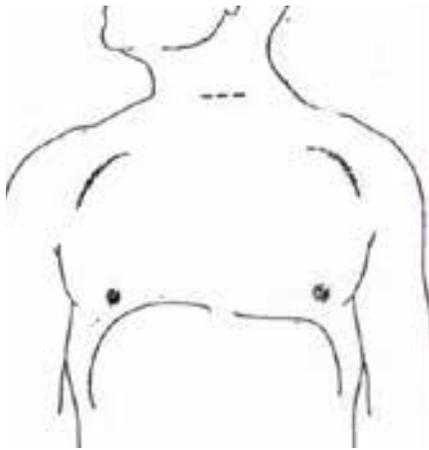
a) Transsternal Approach



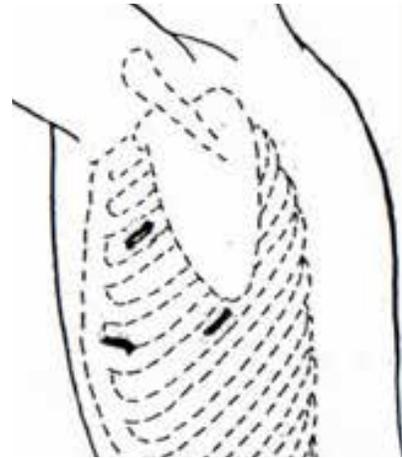
b) Partial Transsternal Approach



c) Transcervical Approach



d) VATS or VATET



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- 2008).
- c) If malignant thymoma is present, thymectomy is recommended for patients of any age (Gold et al., 2008).
 - d) In nonmalignant thymoma, surgical thymectomy is usually performed on patients 10–50 years of age (Gold et al., 2008).
 - e) A thymectomy in the patient older than age 60 may not be as beneficial because of atrophy of the thymus gland (Saperstein & Barohn, 2004).
 - f) Thymectomy benefits patients at all stages of MG (Durieux, Radermecker, Dekoster, & Limet, 2008).
- vii. Prognosis after thymectomy
- a) A better prognosis is likely for patients receiving thymectomy early after initial symptom onset (Gold et al., 2008; Gronseth & Barohn, 2000).
 - A better prognosis has been reported at less than 1 year of disease duration (Aghajanzadeh, Khoshrang, Mohammadzadeh, Roudbari, & Ghayeghran, 2007).
 - A better prognosis has also been reported within 5 years since first manifestation (Gold et al., 2008).
 - b) The average daily dose of an anticholinesterase drug may decrease after thymectomy. (Durieux et al., 2008).
 - c) Improvement in the MG may not occur immediately and may take up to several months or years to reach maximal benefits (Juel & Massey, 2007; Keesey, 2004; Saperstein & Barohn, 2004).
 - d) The degree of improvement may be related to preoperative

MG status and rate of decrease in AChR antibody titer (Aghajanzadeh et al., 2007; Hase et al., 2006).

Nursing recommendation: In collaboration with the multidisciplinary team, nurses should educate the patient and family regarding indications, pre- and postoperative care, and prognosis for patients undergoing thymectomy (Level 3). Following thymectomy, nurses should monitor the patient closely for complications related to MG and the thymectomy procedure and manage them effectively (Level 3).

- d. Postoperative care after thymectomy
 - i. Close monitoring in an intensive care unit setting is usually needed for monitoring of respiratory status. Pulmonary function testing, specifically forced vital capacity (FVC) and negative inspiratory force (NIF), are recommended (Jacob et al., 2007; Mehta, 2006).
Nursing recommendation: Nurses should monitor respiratory status, including rate, depth, work of breathing, breath sounds, oxygenation, and ventilation tolerance. Spontaneous breathing trials, pulmonary function studies, FVC, and NIF should be ordered as available (Level 3).
 - ii. An increase in myasthenia symptoms can occur postoperatively; these symptoms are related to anesthesia, analgesia, and sedation and omission of medications administered intraoperatively, which may result in prolonged postoperative mechanical ventilation (Jacob et al., 2007; Mehta, 2006).
Nursing recommendation: Nurses must administer MG medications postoperatively as prescribed. Nurses should balance the administration of medications that may worsen MG, including opioids, with a comfort level that will allow the patient to breathe with the least amount of effort and discomfort (Level 3).
 - iii. Depending upon the surgical

approach, after thymectomy, patients may need a chest tube(s) to control and monitor thoracic drainage. Hourly chest tube drainage of greater than 100 ml is excessive (Durai, Hoque, & Davies, 2010; Jacob et al., 2007; Malone, 2010).

Nursing recommendation: Nurses should follow the manufacturer's direction for the chest tube drainage system and monitor chest tube(s) for patency, underwater seal, evidence of air leak, drainage output, and signs and symptoms of infection. Nurses should monitor for signs and symptoms of increasing pneumothorax or hemothorax (Level 3).

- e. Factors that may increase the likelihood for crisis and result in prolonged neuromuscular weakness after surgery include the following (Watanabe et al., 2004):
 - i. Preoperative vital capacity of less than 1.2 L
 - ii. Preoperative bulbar symptoms such as dysphagia, difficulty chewing, dysphonia, and dysarthria
 - iii. History of preoperative myasthenic crisis
 - iv. Preoperative AChR antibody serum level higher than 100 nmo/L.
 - v. Intraoperative blood loss exceeding 1,000 ml
Nursing recommendation: Nurses should be aware of patients who have factors that may increase the likelihood of a postoperative MG crisis that could complicate their recovery (Level 3).
- f. Patients undergoing thymectomy for MG have an impaired immune system as a result of their disease and medical management. They are at risk for postoperative infection related to invasive devices and surgical incisions (Jacob et al., 2007).
Nursing recommendation: Nurses should monitor closely for signs and symptoms of infection and minimize a patient's risk for infection by consistently complying with infection-control measures (Level 3).

XVIII. MG Crises

- A. An MG crisis occurs when there is an exacerbation of MG symptoms (myasthenia crisis) or as a result of treatment associated with excess doses of a cholinesterase inhibitor, a cholinergic crisis.
 1. Differentiation of crisis is a priority (Table 6).
- B. *Myasthenic crisis* is defined as any provoked MG exacerbation necessitating mechanical ventilation that results from weakness of the respiratory and bulbar muscles.
 1. Most patients presenting with myasthenic crisis have an identifiable risk factor such as infection, drug use, stress, endocrine disorder, or metabolic imbalance (Krob, 2008).
 2. Myasthenic crisis should be suspected in all patients with respiratory failure, particularly those with unclear etiology.
 3. Additional manifestations of myasthenic crisis include generalized increased weakness; tachycardia; pale, cool skin; and hypertension.
 4. The in-hospital mortality rate is higher in myasthenic crisis than for overall inpatient MG mortality, at 4.47% versus 2.20% (Alshekhlee et al., 2009).
 5. Acute management requires comprehensive care with attention to all systems and ventilatory support and institution of measures to minimize neuromuscular blockade.
 - a. Plasma exchange or IV immunoglobulin
 - b. Identification and removal of offending trigger(s)
- C. *Cholinergic crisis* is defined as neuromuscular weakness and respiratory failure resulting from a high dose of cholinesterase inhibitors (see Table 2) and may present with symptoms similar to myasthenic crisis.
 1. Although less common, cholinergic crisis may be associated with the use of

commercial, agricultural, military, and bioterrorism chemicals that have cholinergic properties.

2. Symptoms of cholinergic excess include DUMBBELL, a mnemonic for diaphoresis, urination, miosis, bradycardia, bronchial secretions, emesis, lacrimation, and loose stools (Krob, 2008). Worsening of symptoms in response to an edrophonium chloride injection is indicative of cholinergic excess. Withdrawing the anticholinesterase medication should result in improvement. Edrophonium may cause an interaction with antiarrhythmics. Respiratory management for ineffective respiratory and bulbar function is related to the weakness of intercostal muscles, diaphragm, larynx and pharynx (Barrick & Kyle, 2008).

Nursing recommendation: Nurses should be knowledgeable in the differentiation of the two different types of MG crises, myasthenic crisis or cholinergic crisis, and should recognize that both are care priorities. In either situation, nurses should perform a complete respiratory and neuromuscular assessment, which is essential to identify ineffective respiratory function and impaired gag and swallow, and initiate the appropriate airway-management strategies and oxygen delivery (Level 3) (Vassar et al., 2008).

 3. Assess and document respiratory status, rate, rhythm, and breath sounds.
 4. Assess gag and cough reflexes and quality of voice; notify the physician of changes from baseline.
 5. Obtain baseline FVC (normal > 60 mg/kg).
 6. Obtain NIF (normal > -70 cmH₂O) and continue to monitor (Mehta, 2006; Vassar et al., 2008).

Table 6. Differentiating Myasthenia Crisis and Cholinergic Crisis

Clinical Features	Myasthenic Crisis	Cholinergic Crisis
Heart rate	Tachycardia	Bradycardia
Muscles (including respiratory)	Flaccid	Flaccid and fasciculations
Pupil size	Normal or large	Small
Skin	Pale, cool	Red, warm
Gastrointestinal	No change	Diarrhea, cramps
Secretions	No change	Increased
Tensilon (edrophonium) test	Improvement	Worsening

Source: Krob, 2008

7. Notify a physician or advanced practice nurse regarding respiratory abnormalities or change in FVC and/or NIF from baseline value or NIF < -30, FVC < 1.5 liter (Mehta, 2006; Vassar et al., 2008).
 - a. Values of FVC < 1.0 liter or < 15 mL/kg body weight/NIF < -20 cm H₂O are indications for mechanical ventilation (Mehta, 2006; Vassar et al., 2008).
 8. If facial weakness is present, obtain NIF/FVC via face mask.
 9. Administer intubation, mechanical ventilation, intermittent positive-pressure breathing (IPPB), and oxygen as needed.
 10. Suction and chest physiotherapy to manage secretions
- D. Aggressive respiratory treatment (e.g., suctioning, IPPB, sighs [mechanical ventilator breaths of greater tidal volume than the set tidal volumes delivered several times each hour to lessen atelectasis], chest physiotherapy) diminishes the risk for prolonged respiratory complications, including prolonged mechanical ventilation and risk for pneumonia (Varelas et al., 2002).
- Nursing recommendation:** Nurses should assess respiratory status, including pulmonary function tests (i.e., NIF and FVC); provide pulmonary hygiene as needed; and alert the licensed independent provider regarding indications for additional respiratory therapy management to minimize respiratory complications, including prolonged ventilation and pneumonia (Level 3).

XIX. General nursing management of the patient with MG

A. Medications that may worsen MG

1. Many drugs used in the treatment of other conditions may exacerbate or have the potential to worsen MG by increasing weakness; consequently, they should be used with extreme caution and require careful monitoring. Examples include quinine, quinidine, procainamide, and lidocaine; macrolide and aminoglycoside antibiotics (erythromycin, azithromycin, gentamycin, kanamycin, neomycin, vancomycin); quinolone antibiotics (ciprofloxacin, levofloxacin, norfloxacin); beta-blockers such as propranolol and dorzolamide eye drops; calcium channel blockers; magnesium salts (laxatives, antacids, magnesium sulfate); and iodine-based contrast dye (Howard, 2008, Pascuzzi, 2007).
2. The following drugs should not be used in patients with MG: alpha-interferon,

d-penicillamine (known to cause MG), botulinum, and telithromycin (Howard, 2008; Pascuzzi, 2007).

3. Agents commonly used for surgical and dental procedures may also exacerbate or have the potential to worsen MG; consequently, they should be used with extreme caution and require careful monitoring. Examples include certain neuromuscular blocking agents (e.g., succinylcholine vecuronium), local anesthetics, analgesics, and anxiolytics, sedatives, and hypnotics (Howard, 2008; Pascuzzi, 2007).

Note: The above lists are not all-inclusive, are current at the time of this publication, and may change in the future. Numerous additional medications are reported to increase weakness in some patients with MG. Refer to all current drug information as it relates to the patient with MG.

Nursing recommendation: Nurses should administer drugs that may worsen MG with caution. Review medication profiles with the pharmacist and licensed independent provider (Level 3).

B. Nursing management of swallowing and chewing impairment (Butler, 2008; Vassar et al., 2008).

1. Adjust the patient's eating schedule to optimize medication efficacy. Typically, meals should be taken during periods of optimal strength (such as during the earlier part of the day, 30 minutes after administration of cholinesterase inhibitor medications, or after rest periods).
 - a. Because muscle fatigue impairs chewing and swallowing, the following will facilitate maintaining nutritional status and decreasing the risk for aspiration:
 - i. Allow the patient to rest before eating and drinking.
 - ii. Provide foods that are soft, tender, and not sticky and do not require a lot of chewing.
 - iii. Provide highly viscous foods and thickened liquids that are easy to chew and swallow.
 - iv. Offer the patient small bites and instruct him or her to chew well, eat slowly, swallow after each bite, and swallow frequently.
 - v. Allow the patient to rest while chewing and in between bites to restore strength.
 - vi. Allow the patient to take small sips of liquids.

- vii. Provide frequent, small meals that include high-calorie and high-protein foods.
 - viii. Offer large meals in the morning and small meals in the evening.
 - a) Offer softer consistencies and moisten dry food.
 - b) Position the patient upright with his or her head slightly forward when eating and drinking, using compensatory maneuvers (chin tuck, head turn) as necessary.
 - c) Discourage talking and eating at the same time and avoid distractions while eating.
 - d) Review principles of nutrition and basic food groups so patients can select foods that provide a balanced diet.
 - b. Consult with a dietitian to determine nutritious food choices.
 - c. Consult with a speech pathologist to determine the safest, most effective swallowing technique.

Nursing recommendation: Nurses should adopt the previous protocols to facilitate swallowing, avoid aspirations, and optimize nutritional and fluid status (Level 3).
- C. Nursing management of fatigue
1. Assess a patient's abilities and restrictions to carry out daily activities including ADLs. Assess for weakness and/or visual impairment associated with self-care deficits and the need for assistive devices.
 2. Collaborate with licensed independent providers to adjust medication dosage and schedule to maximize effectiveness.
 3. Use consistent routines, allowing for sufficient time. Use optimal positioning, and offer positive reinforcement.
 4. Plan activities to provide periods of rest.
 5. Consult with a physical therapist and/or occupational therapist (Holmes, 2008).
 6. Consult with a psychologist or other qualified professional to screen the patient for depression. Research has demonstrated that depression, activity restrictions, and number of years since diagnosis can negatively influence fatigue (Kittiwatanapaisan, Gauthier, Williams, & Oh, 2003).
 7. Address activity abilities and restrictions.

- a. Identify self-care techniques and develop strategies to decrease activity intolerance and risk for injury and promote energy conservation at home, at work, and in the community.
- b. Fatigue worsening occurs with overexertion, physical and emotional stress, warm temperatures, high humidity, and other exacerbating factors.
- c. Mental and physical self-care interventions include stress-reduction techniques, pacing all activities, increased rest or sleep, and aerobic exercise (remaining physically active is the hallmark of fatigue management) (Grohar-Murray, Becker, Reilly, & Ricci, 1998; Vassar et al., 2008).

Nursing recommendation: Nurses should apply the above strategies in managing fatigue for the patient with MG (Level 3).

XX. Special consideration in the juvenile MG population

- A. Medication management in juvenile MG
1. Azathioprine, cyclosporine, mycophenolate, and cyclophosphamide
 2. It may be necessary to avoid these drugs in women of reproductive age because of possible teratogenic effects on the fetus (Ciafaloni & Massey, 2004).
 3. Birth control is required for sexually active women to avoid birth defects.

Nursing recommendation: Nurses should be aware of the teratogenic effects of immunosuppressive medications on the fetus and provide appropriate education to women with MG of childbearing age (Level 3).
- B. Developmental issues
1. The transition from juvenile to adult requires coordination and collaboration, with a focus on transitions of care for issues such as childbearing, career, and lifestyle.
 2. Promote independence and a lifelong relationship with specialty healthcare providers.

XXI. Psychosocial and educational needs

- A. MG is characterized by relapses and exacerbations and is considered a chronic illness. Education regarding strategies to deal with disease fluctuations includes appropriate goal setting.
1. Patient organizations and their support groups that are devoted to MG are

- resources for patients and families. Encourage visits to MGFA at www.myasthenia.org and the Muscular Dystrophy Association at www.mda.org. Other unbiased reputable Internet sources include www.MayoClinic.com, WebMD, and Medline Plus.
2. General educational needs of the patient with MG and their family (Vassar et al., 2008)
 - a. Knowledge of the disease and methods to control it
 - b. An understanding of the treatments and drugs used to control and manage symptoms and disease
 - c. Awareness of all interactions that drugs unrelated to MG may have on MG or the ways in which these drugs may interfere with drugs used to treat MG (refer to the drugs identified in section XIX, General nursing management of the patient with MG)
 - d. Knowledge of the need to wear a medical alert bracelet or medallion inscribed with the words, “Myasthenia Gravis: Use Drug Precautions” and to carry an emergency alert card with an accompanying drug list card available from MGFA
 - e. Awareness of birth defects that may occur in offspring of women taking some classes of MG drugs
 - f. Adjustment of eating schedules to optimize medication efficacy (Vassar et al., 2008)
 - g. Knowledge regarding potential over-the-counter drug interactions with MG
 - h. Instructing the patient to discuss taking any newly prescribed medications or over-the-counter drugs with their physician or neurologist
 - i. Instructing the patient that if he or she is undergoing surgical or dental procedures, he or she should request that the surgeon, anesthesiologist, and/or dentist consult with the physician or neurologist
 3. Educational strategies to manage swallowing and chewing impairment (Butler, 2008)
 - a. Teach the patient the strategies to manage swallowing and chewing as outlined in sections B1 a.i through xii.
 4. Strategies to manage fatigue and conserve energy
 - a. Teach the patient the strategies to manage fatigue and conserve energy as outlined in section C 1-7.
 - b. Limit fatigue by pacing and planning, using the following guiding principles (Holmes, 2008)
 - i. Prioritize. What is the most important activity? What else do you want to do?
 - ii. Listen to your body. Know when to push, and know when to rest.
 - iii. Plan the day. Pace; know limits, strengths, and weaknesses; avoid overdoing and crashing; build in rest periods; prepare for upcoming activities; go slow/get rest earlier in the day; and recognize that exercise should not cause more fatigue.
 - iv. Teach energy conservation strategies applicable to various settings (Holmes, 2008; Thomas, 2008).
 - a) Home: Sit during chores, delegate to family members, keep objects at an appropriate height, schedule rest periods, plan activities, break an activity into parts, and use power tools/electrical appliances.
 - b) Grooming: Sit on a stool to shave or brush teeth, use an elbow prop and electric toothbrushes, take rest breaks, take shorter showers/baths with warm water, and sit to dress.
 - c) Community: Park close to your destination, ask to get dropped off, or use a disabled parking permit. Avoid peak shopping times, wear supportive walking shoes, stay balanced (use a walker, cane, etc.), use a cart for merchandise, plan according to medication schedules, unload perishables, shop by mail order, and bear in mind that small sizes weigh less.
 - d) Work: Ensure proper neck and back support, sit rather than stand, avoid eye strain, take breaks, use proper air conditioning, and consider learning more about Family and Medical Leave Act provisions.

- e) Lifestyle management to optimize living with MG: Target good nutrition, physical activity, stress management and coping skills. Observe infection control and health maintenance guidelines, medication guidelines, and emergency alerts.

Nursing recommendation:
Nurses should educate the patient with MG and their

family regarding management of the disease; influence of the disease on lifestyle, swallowing, and chewing impairment; and fatigue and energy conservation (Level 3).

XXII. Resources for patients, families, and healthcare professionals

- A. Myasthenia Gravis Foundation of America:
www.myasthenia.org

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