ANAESTHESIA AND MYASTHENIA GRAVIS
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INTRODUCTION

Myasthenia Gravis (MG) is an autoimmune disease characterized by weakness and fatigability of skeletal muscles, with improvement following rest. It may be localized to specific muscle groups or more generalized. MG is caused by a decrease in the numbers of postsynaptic acetylcholine receptors at the neuromuscular junction, which decreases the capacity of the neuromuscular end-plate to transmit the nerve signal. Initially, in response to a stimulus resulting in depolarization, acetylcholine is released presynaptically which results in a muscle action potential being generated. In MG, the number of activated postsynaptic receptors may be insufficient to trigger a muscle action potential. Further, with repeated stimulation, the decline in release of acetylcholine correlates with the characteristic fatigability.

PATHOPHYSIOLOGY

Auto-antibodies develop against acetylcholine (ACh) nicotinic postsynaptic receptors. Cholinergic nerve conduction to striated muscle is impaired by a mechanical blockage of the binding site by antibodies and, ultimately, by destruction of the postsynaptic receptor. Patients become symptomatic once the number of ACh receptors is reduced to approximately 30% of normal. The antibodies to the acetylcholine receptor reduce the number of functional receptors by blocking the attachment of acetylcholine molecules, by increasing the rate of degradation of receptors and by complement induced damage to the neuromuscular junction. The cholinergic receptors of smooth and cardiac muscle have a different antigenicity than skeletal muscle and are not affected by the disease.
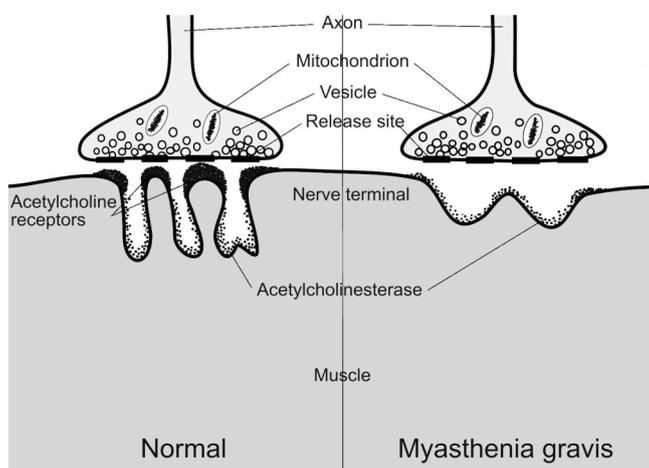
MG may be associated with other disorders of autoimmune origin such as thyroid hypofunction, rheumatoid arthritis and systemic lupus erythematosus. The role of the thymus in the pathogenesis of MG is not entirely clear, but 75% of patients with MG have some degree of thymus abnormality (eg, hyperplasia in 85% of cases, thymoma in 15% of cases). However, the stimulus that initiates the autoimmune process has not been identified.

An immunoregulatory defect has been postulated, and there is evidence of genetic predisposition. Using the most sensitive assays, AChR antibodies are detected in the sera of 85-90% of myasthenic patients. The great majority of AChR antibodies belong to the IgG class. Antibody-negative patients are those with mild or localized myasthenia, and may represent one end of the spectrum of myasthenia gravis.

Most of the antibodies bind to the main immunogenic region of the alpha subunit of the endplate receptors. Thus, MG is largely a post-junctional disorder characterized by a reduction of functional AChRs.

EPIDEMIOLOGY

The prevalence of MG is approximately 100 per 100 000 population with incidence of 2-4 per 100 000 per annum.

Mortality/Morbidity.   In the past, untreated MG had a mortality rate of 30-70%, now most patients with MG have a near-normal life expectancy. Morbidity results from intermittent impairment of muscle strength, which may cause aspiration, increased incidence of pneumonia and falls. In addition, the medications used to control the disease may produce adverse effects. With prompt diagnosis and treatment, the mortality rate of myasthenic crisis is less than 5%.

Race. The onset of MG at a young age is slightly more common in Asians than in other races.

Sex. The male-to-female ratio in children and adults is 2:3.   A female predominance exists in the young adult peak (ie, patients aged 20-30 y), and a slight male predominance exists in the older adult peak (ie, patients older than 50 y).   The male-to-female ratio in children with MG and another autoimmune condition is 1:5.

Age. The onset peaks in neonates because of the transfer of maternal autoantibodies, in those aged 20-30 years, and in those older than 50 years.

ASSOCIATED AUTOIMMUNE CONDITIONS

Thyroid abnormalities (15%), systemic lupus erythematosis, rheumatoid disease, ulcerative colitis, pernicious anaemia, vitiligo, pemphigus, polymyositis/dermatomyositis

CLASSIFICATION OF MG (OSSERMAN)

- grade I – only eyes affected,
- grade IIa – mild generalised MG responding well to therapy,
- grade IIb – moderate generalised MG responding less well,
- grade III – severe generalised disease,
- grade IV – myasthenic crisis requiring mechanical ventilation

ELECTROPHYSIOLOGICAL STUDIES

Microelectrode studies indicate that the miniature endplate potential (MEPP) frequency is normal but the MEPP amplitude is reduced in myasthenia gravis, suggesting that the neuromuscular transmission defect is due to a reduction in the postsynaptic response. The presynaptic synthesis, packaging and release of ACh are normal. In MG, a large proportion of the EPPs are subthreshold, i.e., do not trigger an action potential, while the remainder are barely threshold. Repetitive nerve stimuli evoke successively smaller muscle action potentials indicating an increasing block of neuromuscular transmission. The most commonly used electrodiagnostic test of neuromuscular transmission is repetitive stimulation of a motor nerve while recording compound muscle action potentials (CMAPs) from an appropriate muscle. The amplitude of the initial CMAP is normal, though the average value of this measurement is less than the normal average. Repetitive stimulation at frequencies between one and five per second results in a decremental response. The decrement usually increases with increasing stimulation rate. The tested muscle must be warmed and the decrement must be measured after exhaustion to obtain the maximum diagnostic yield. However nerve conduction velocity measurements are normal.

CLINICAL FEATURES

The incidence is age and sex-related, with one peak in the second and third decades affecting mostly women and a peak in the sixth and seventh decades affecting mostly men.

The cardinal features are weakness and fatigability of skeletal muscles, usually occurring in a characteristic distribution. The weakness tends to increase with repeated activity and improve with rest. Ptosis and diplopia occur early in the majority of patients. Weakness remains localized to the extraocular and eyelid muscles in about 15 percent of patients.

When the facial and bulbar muscles are affected, there may be a characteristic flattened smile, "mushy" or nasal speech, and difficulty in chewing and swallowing.

Generalized weakness develops in approximately 85 percent of patients; it may affect the limb muscles, often in a proximal distribution, as well as the diaphragm and the neck extensors. If weakness of respiration becomes severe enough to require mechanical ventilation, the patient is said to be in crisis.

On physical examination, the findings are limited to the motor system, without loss of reflexes or alteration of sensation or coordination. The patient's base-line strength should be

documented quantitatively for later evaluation of the results of treatment. The most useful quantitative measures include timed forward-arm abduction, vital capacity, and dynamometry of selected muscles. The clinical severity of myasthenia gravis is usually graded functionally and regionally, as devised by Osserman.

Most patients who present to the A&E have an established diagnosis of myasthenia gravis (MG) and are already taking appropriate medications. The activity of the disease fluctuates, and adjustments in medication dosages must be made accordingly. Non-compliance with medications, infection, and other physiologic stressors may result in a fulminant exacerbation of the disease. Many other factors influence cholinergic transmission, including drugs, temperature, and emotional state.

The adverse effects of many medications may provoke exacerbations; therefore, obtaining a careful medication history is important.

Some of the **medications reported to cause exacerbations of MG** include the following:

Antibiotics - macrolides, fluoroquinolones, aminoglycosides, tetracycline, and chloroquine

Antidysrhythmic agents - beta-blockers, calcium channel blockers, quinidine, lidocaine, procainamide, and trimethaphan

Miscellaneous - diphenylhydantoin, lithium, chlorpromazine, muscle relaxants, levothyroxine, adrenocorticotropic hormone (ACTH), and, paradoxically, corticosteroids

Rarely, a patient may present with undiagnosed MG. Typical complaints are of generalized weakness and reduced exercise tolerance that improves with rest. Patients with MG do not present with primary complaints of sleepiness or muscle pain. The patient may also complain of a specific weakness of certain muscle groups (eg those used when climbing stairs).

In 20% of patients, MG affects the bulbar muscles alone.

Eighty-five percent of patients with bulbar weakness go on to develop generalized weakness involving the limbs.

TRANSIENT NEONATAL MYASTHENIA

Fifteen to 20% of neonates born to myasthenic mothers have transient myasthenia, due to protective effects of alpha foetoprotein, which inhibits binding of anti-AChR antibody to AChPregnancy may produce either exacerbation or remission of the disease. Signs are usually present at birth, but occasionally may be delayed for 12- 48 hr. Maternal anti-acetylcholine receptor antibody can cross via breast milk and accentuate neonatal myasthenia. Commonly associated features include difficulty in sucking and swallowing, difficulty with breathing, ptosis and facial weakness. The most likely explanation of neonatal myasthenia is the passage of AChR antibodies across the placenta, but no correlation has been found between the presence or degree of neonatal myasthenia and the concentration of the antibodies in the infant's serum.

The condition has a tendency to spontaneous remission, usually within two to four weeks, and once therapy has been tapered and stopped there is no risk of relapse. In severely affected infants, treatment should be commenced immediately by oral neostigmine, depending on the severity of response.

SEVERE EXACERBATIONS OF MG

Severe episodes may be caused by insufficient medication (myasthenic crisis) or excessive medication (cholinergic crisis) and are suggested by:

- Facial muscles may be slack, and the face may be expressionless
- Inability to support the head, which will fall onto the chest while the patient is seated
- Jaw is slack, voice has a nasal quality, body is limp
- Gag reflex is often absent, and such patients are at risk for aspiration of oral secretions

The patient's ability to generate adequate ventilation and to clear bronchial secretions are of utmost concern with severe exacerbations of MG. An inability to cough leads to an accumulation of secretions; therefore, rales, rhonchi, and wheezes may be auscultated locally or diffusely. The patient may have evidence of pneumonia (ie fever, cough, dyspnea, consolidation).

CHOLINERGIC CRISIS

One of the confusing factors in treating patients with MG is that insufficient medication (myasthenic crisis) and excessive medication (cholinergic crisis) can present in similar ways.

Cholinergic crisis results from an excess of cholinesterase inhibitors (neostigmine, pyridostigmine, physostigmine) and resembles organophosphate poisoning. In this case, excessive ACh stimulation of striated muscle at nicotinic junctions produces flaccid muscle paralysis that is clinically indistinguishable from weakness due to MG.

Myasthenic crisis or cholinergic crisis may cause bronchospasm with wheezing, bronchorrhea, respiratory failure, diaphoresis, and cyanosis.

Miosis and the SLUDGE syndrome (salivation, lacrimation, urinary incontinence, diarrhoea, GI upset and hypermotility, emesis) also may mark cholinergic crisis. However, these findings are not inevitably present.

Despite muscle weakness, deep tendon reflexes are preserved.

DIAGNOSIS

Laboratory tests. None are available in a time frame that is useful to confirm the emergency diagnosis of myasthenia gravis (MG). An arterial blood gas determination can help guide respiratory management and should be obtained early in severe cases. An elevated $PaCO_2$ suggests progressive respiratory failure and may indicate the need for emergency airway management.

Anti-AchR antibodies are detected in 80-85% of patients with MG and are pathognomonic for the disease. Other investigations exclude any associated autoimmune diseases.

Imaging. A chest Xray is indicated to determine the presence of aspiration or other pneumonias, which commonly occur in patients with MG. A CT scan or MRI of the chest is highly accurate in detecting thymoma and should be done in every new presentation.. Chest radiography is relatively insensitive in screening for thymoma, as it does not detect up to 30% of cases.

Tensilon (edrophonium) challenge test is useful in diagnosing MG and in distinguishing myasthenic crisis from cholinergic crisis. A positive response is not completely specific for MG because several other conditions (eg amyotrophic lateral sclerosis) may also respond to edrophonium with increased strength.

Once the patient's airway and ventilation are secured, an initial test dose of edrophonium is given. Some patients may respond noticeably to a small dose (1 mg). If no adverse reaction occurs following the test dose, another dose (3 mg) of edrophonium should produce noticeable improvement in muscle strength within 1 minute. If no improvement occurs, an additional dose of 5 mg can be administered to total no more than 10 mg.

Patients who respond generally show dramatic improvement in muscle strength, regaining facial expression, posture, and respiratory function within 1 minute.

During this procedure, the patient must be monitored carefully because edrophonium can cause significant bradycardia, heart block, and asystole. The return of muscle weakness after edrophonium wears off combined with residual increased oral secretions can exacerbate respiratory distress and the risk of aspiration.

Patients with a cholinergic crisis may respond to edrophonium challenge by increasing salivation and bronchopulmonary secretions, diaphoresis, and gastric motility (SLUDGE syndrome). These changes should be managed expectantly, as the half-life of edrophonium is short (approximately 10 min).

If muscle strength fails to improve following the maximum dose of edrophonium, the patient is having a cholinergic crisis, or has another cause of weakness that is unrelated to MG.

The effects of edrophonium are brief, and repeated doses may be required before oral anticholinesterase medication can take effect.

In patients with less severe exacerbations, the degree of improvement with edrophonium may be subtle. Many authors recommend having several blinded observers assess the patient's response in these cases.

Ice pack test. Cooling may improve neuromuscular transmission. In a patient with MG who has ptosis, placing ice over an eyelid will lead to cooling of the lid, which leads to improvement of the ptosis. Lightly placing ice that is in a surgical glove or that is wrapped in a towel over the eyelid will cool it within 2 minutes. A positive test is clear resolution of the ptosis. The test is thought to be positive in about 80% of patients with ocular myasthenia.

Standard electromyography, single-fiber electromyography, assays for acetylcholine receptor antibody [ARA]) are used to confirm the diagnosis of MG, but these tests usually are not available on an emergency basis.

EMG testing shows similar characteristics to a small dose of non depolarising relaxant given to normal subjects during anaesthesia - a reduced compound muscle action potentials (CMAP) to single supramaximal twitch and decrement (fade) of > 10% on tetanic stimulation. EMG findings not exclusive to MG.

TREATMENT

In general, four methods of treatment are currently in use: enhancement of neuromuscular transmission with anticholinesterase agents, surgical thymectomy, immunosuppression, and short-term immunotherapies, including plasma exchange and intravenous immune globulin.

Anticholinesterase agents continue to be used as the first line of treatment for myasthenia gravis. Pyridostigmine (Mestinon) is the most widely used anticholinesterase. Its effect begins within 30 minutes, peaks at about 2 hours, and gradually declines thereafter, with a half-life of 4 hours. The dosage and schedule of administration must be tailored to the patient's needs. The maximal useful dosage of pyridostigmine rarely exceeds 120 mg every three hours. Higher doses may produce increased weakness. A sustained-release preparation is available but should be used only at bedtime if necessary to treat weakness occurring at night or in the early morning. Although anticholinesterase drugs benefit most patients, the improvement is usually incomplete and often wanes after weeks or months of treatment. Most patients therefore require further therapeutic measures.

Surgical thymectomy is indicated for its therapeutic effect in myasthenia gravis or to prevent the spread of a thymoma. The goal of thymectomy as a treatment for myasthenia gravis is to induce remission, or at least improvement, permitting a reduction in immunosuppressive medication. There is now a broad consensus that patients with generalized myasthenia gravis who are between the ages of puberty and about 60 years should have surgical thymectomy. Although no adverse effects have been reported as a consequence of thymectomy in children, it is preferable to delay thymectomy until puberty if possible, because of the established role of the thymus in development of the immune system. Thymectomy has been advocated for elderly patients with myasthenia gravis, but there is uncertainty about the persistence of thymic tissue in such patients after the age of 60.

Thymectomy has also been carried out in patients with purely ocular manifestations, with good results reported. Thymic tumours must be removed surgically since they may spread locally and become invasive although rarely metastasize. The tumour and the remaining thymus gland should be removed as completely as possible.

Thymectomy should be performed in institutions that have extensive experience not only with the surgery but also with preoperative and postoperative management of myasthenia gravis. Thymectomy is not an emergency procedure. Preoperative preparation should optimize the patient's strength and especially respiratory function, but immunosuppressive agents should be avoided if possible due to the increased risk of infection.

The requirement for anticholinesterase medication may be decreased for a few days after thymectomy; therefore, postoperative anticholinesterase medication is given intravenously at a dose equivalent at about 75% of the preoperative requirement. The benefits of thymectomy are usually delayed for months to years after surgery.

The mechanism by which thymectomy produces benefit in myasthenia gravis is still uncertain. In general, acetylcholine-receptor antibody levels fall after thymectomy, although there are conflicting reports. There are several possible mechanisms - removal may eliminate a source of continued antigenic stimulation, remove a reservoir of B cells secreting acetylcholine-receptor antibody or in some way correct a disturbance of immune regulation in myasthenia gravis.

Immunosuppressive therapy is indicated when weakness is not adequately controlled by anticholinesterase drugs and is sufficiently distressing to outweigh the risks of possible side effects of immunosuppressive drugs. Prednisone, azathioprine, and cyclosporin are the agents now used for long-term immunosuppression in myasthenia gravis. In general, treatment must be continued for a prolonged period, most often permanently. Because of the risks inherent in prolonged immunosuppressive treatment, conscientious medical follow-up and the patient's compliance with therapy are essential for safe and effective management.

Table 1: Immunosuppressive agents used to treat MG

DRUG	ADULT DOSE	TIME TO ONSET OF EFFECT	TIME TO MAXIMAL EFFECT	VARIABLES TO MONITOR EFFECT
Prednisolone	15-20mg/day gradually increasing to 60mg/day and gradually changed to every other day	2-3 weeks	3-6 months	Weight, blood pressure, blood glucose, electrolytes, Ophthalmic changes, bone density, 24 hr urinary calcium
Azathioprine	2-3 mg/kg/day (total dose 100-250 mg/day)	3-12 months	1-2 years	White cell count $< 3500/mm^3$ Differential count <1000 lymphocytes/mm^3 MCV, platelets, Liver function
Ciclosporin	5mg/kg/day in 2 divided doses (total dose 125-200 mg twice daily)	2 -12 weeks	3 – 6 months	Blood pressure, serum creatinine, BUN, trough plasma ciclosorin level

Steroids are the most commonly used and most consistently effective immunosuppressive agents for the treatment of myasthenia gravis. They also have significant side effects. Patients with moderate-to-severe generalized weakness are hospitalized for the initiation of steroid therapy because of the risk of transient steroid-induced exacerbation of disease, which may occur during the first weeks of treatment.

The risk of exacerbation is minimized by increasing the dose gradually. The rate of increase must be guided by the patient's clinical response, and the end point is either a satisfactory clinical response, or a dose of 50 to 60 mg per day. Improvement usually begins in 2 to 4 weeks, with maximal benefit realized after 6 to 12 months or more. Few patients are able to do without prednisone entirely.

In myasthenia gravis, steroid treatment may reduce acetylcholine-receptor antibody levels and diminish the anti-acetylcholine-receptor reactivity of peripheral-blood lymphocytes. In addition, corticosteroids are reported to have certain direct neuromuscular actions.

Experimentally, steroids increase the synthesis of acetylcholine receptors in cultured muscle cells and may enhance neuromuscular transmission, but the clinical relevance of such effects in myasthenia gravis has not been established.

Azathioprine is metabolized to the cytotoxic derivative 6-mercaptopurine. Its action is predominantly on T cells, and its effectiveness in myasthenia gravis may be due to the fact that the production of acetylcholine-receptor antibody is T-cell-dependent. It is most useful in patients with myasthenia gravis for whom corticosteroids are contraindicated, in those with an insufficient response to steroids, or as an adjunct to permit a reduction in the steroid dose. It is one of the easiest immunosuppressive agents to use, but it has two drawbacks.

First, up to 10 percent of patients have an idiosyncratic influenza-like reaction, consisting of fever, malaise, and myalgias, that precludes its use. Second, its therapeutic action in myasthenia gravis begins slowly, requiring many months to one year for an adequate therapeutic trial.

Cyclosporin, is a potent immunosuppressive agent increasingly used in the treatment of patients with the disease. Cyclosporine inhibits the production of interleukin-2 by helper T cells. Its efficacy is similar to that of azathioprine, but it works more quickly, usually within one to two months. The side effects of cyclosporin include nephrotoxicity and hypertension, which limit its use in patients with pre-existing renal disease or uncontrolled hypertension.

Short term immunotherapies - plasma exchange and intravenous immune globulin

Plasmapheresis removes antibodies from the circulation and produces short-term clinical improvement in patients with myasthenia gravis. It is used primarily to stabilize the condition of patients in myasthenic crisis or for the short-term treatment of patients undergoing thymectomy. Typically, five exchange treatments of 3 to 4 liters each are carried out over a two-week period. The effect of plasmapheresis is rapid, with improvement occurring within days of treatment. Improvement correlates roughly with a reduction in the anti-acetylcholine-receptor antibody titres, but even patients with antibody-negative myasthenia gravis may improve after plasmapheresis. The beneficial effects of plasmapheresis are temporary, lasting only weeks. Repeated plasmapheresis as long-term therapy is occasionally helpful in the rare patient who does not respond to the other methods outlined above. The drawbacks of

plasmapheresis include problems with venous access, the risk of infection of the indwelling catheter, hypotension, and pulmonary embolism. The benefit must be weighed against these problems and the high cost of the procedure.

The indications for the use of **intravenous immune globulin** are the same as those for plasma exchange: to produce rapid improvement to help the patient through a difficult period of myasthenic weakness. It has the advantages of not requiring special equipment or large-bore vascular access. In responsive patients improvement begins within four to five days.

The mechanism of action of immune globulin is unknown, but it has no consistent effect on the measurable amount of acetylcholine-receptor antibody. Adverse reactions include headache, fluid overload, and rarely, renal failure. Immune globulin is very expensive.

ANAESTHETIC MANAGEMENT

The anaesthetic management of the myasthenic patient must be individualized to the severity of the disease and the type of surgery. The use of regional or local anaesthesia seems warranted whenever possible. Whenever local or regional anaesthesia is used, the dose of the local anaesthetic may be reduced in patients to decrease the possible effects of anaesthetics on neuromuscular transmission. This may be particularly important when ester local anaesthetics are administered to patients receiving anticholinesterase therapy (inhibit plasma cholinesterase). General anaesthesia can be performed safely, provided the patient is optimally prepared and neuromuscular transmission is adequately monitored during and after surgery.

Preoperative preparation. Adequate preoperative evaluation of the myasthenic patient must be carried out carefully. Age, sex, onset and duration of the disease as well as the presence of thymoma may determine the response to thymectomy. Also, the severity of myasthenia and the involvement of bulbar or respiratory muscles must be evaluated. Patients should be admitted 24-48h before surgery to allow detailed assessment of respiratory muscle and bulbar function and review of anticholinesterase and corticosteroid therapy. Respiratory reserve is best monitored by serial forced vital capacity (FVC) measurement.

Preoperative factors associated with need for prolonged postoperative IPPV include: FVC < 2.9l, history of MG > 6 years, major surgery, co-existing lung disease and grades III and IV MG. Other autoimmune diseases need to be elicited and appropriate preoperative investigations initiated.

Optimization of the condition of the myasthenic patients can markedly decrease the risk of surgery and improve the outcome. Many regimens have been recommended for preoperative treatment. It is controversial whether anticholinesterase therapy should be maintained or discontinued before and after surgery. Anticholinesterases potentiate the vagal responses and hence adequate atropinization must be ensured. Also, anticholinesterases can inhibit plasma cholinesterase activity with a subsequent decrease in the metabolism of ester local anaesthetics, and the hydrolysis of suxamethonium will be decreased.

As in non-myasthenic patients, the duration of suxamethonium block in myasthenic patients is inversely related to the plasma cholinesterase activity. In contrast with suxamethonium, the inhibition of acetylcholinesterase by anticholinesterases may increase the need for nondepolarizing muscle relaxants in the myasthenic patient, although this has not been documented. Recently, plasmapheresis alone without immunosuppression has been used to optimize the medical status of the myasthenic patient prior to major surgery. Anticholinesterase agents are discontinued, while corticosteroid medications are maintained to be tapered and discontinued postoperatively.

Premedication. Myasthenic patients may have little respiratory reserve and hence depressant drugs for preoperative premedication should be used with caution, and avoided in patients with bulbar symptoms, but an anticholinergic may be useful. Hydrocortisone 'cover' should be given to those on long-term corticosteroid therapy.

Anaesthetic techniques. Two techniques have been recommended for general anaesthesia in the myasthenic patient, although none is superior. Because of the unpredictable response to suxamethonium and the marked sensitivity to non-depolarizing muscle relaxants, some anaesthetists avoid muscle relaxants and depend on deep inhalational anaesthesia, for tracheal intubation and maintenance of anaesthesia. These agents allow neuromuscular transmission to recover, with rapid elimination of these agents at the end of surgery. In theory, desflurane and sevoflurane may offer some advantages, due to their low blood solubility. Sevoflurane is probably superior to desflurane, due to its lower incidence of excitatory airway reflexes during inhalational induction.

However, others utilize a balanced technique which includes the use of muscle relaxants, without the need for deep inhalational anaesthesia, titrating small doses (10– 25% of the ED95) of intermediate-acting relaxants monitoring with a peripheral nerve stimulator for both intubation and surgical relaxation, if required. The decision as to whether to reverse residual neuromuscular blockade at the end of surgery is controversial. Some argue that the presence of anticholinesterases and antimuscarinics will confuse efforts to differentiate weakness due to inadequate neuromuscular transmission from cholinergic crisis in the recovery room. Some prefer spontaneous recovery and extubation when the patient has demonstrated adequate parameters for extubation (head-lift, tongue protrusion).

Similarly, the presence of fade (T4/T1 < 0.9) in the preanaesthetic period predicts decreased atracurium requirements in patients with MG. This technique, along with preoperative pulmonary function testing, may be useful in determining preoperative baseline function.

Total intravenous anesthesia (TIVA) for the management of myasthenics has been reported. Haemodynamic instability in older patients makes this approach more difficult, whereas younger patients usually tolerate it. The use of remifentanil as part of TIVA may alleviate some of the hemodynamic instability.

When possible, many clinicians prefer to utilize regional or local anesthetic techniques. Regional techniques may reduce or eliminate the need for muscle relaxants in abdominal surgery. Epidural techniques offer the advantage of postoperative pain control with minimal or no opioid use.

Postoperative management. Ventilatory function must be monitored carefully after surgery. There are few tests of neuromuscular function which correlate with adequate ventilation. It has been shown recently in normal patients that many of the recommended tests such as maintained response to tetanic stimulation of a peripheral nerve can return to normal, while the pharyngeal and neck muscles necessary to protect the airway can still be partially paralysed. The different response of peripheral versus bulbar muscles may be more evident in myasthenic patients, particularly those suffering from bulbar and/or respiratory muscle weakness. It is essential that sustained respiratory muscle strength be confirmed before extubation of the trachea and resumption of spontaneous ventilation. Myasthenic patients may be at increased risk of developing postoperative respiratory failure - following trans-sternal thymectomy, up to 50% of patients require prolonged postoperative ventilation.

Four risk factors have been identified: **(Anesthesiology 1980; 53: 26-30)**

- Duration of myasthenia gravis for longer than six years (12 points). (Duration of MG proved to have the greatest value in predicting the need for ventilatory support).
- A history of chronic respiratory disease other than respiratory dysfunction directly due to MG (10 points).
- A dose of pyridostigmine greater than 750 mg per day, 48 hr before operation (8 points).
- A preoperative vital capacity < 2.9 L (4 points)

These risk factors were weighted according to their significance as predictors; a total score of ≥ 10 points identified those patients likely to need postoperative pulmonary ventilation for more than three hours.