

# Myasthenia Gravis Association



## INFORMATION PACK Volume 1 A Medical Guide for Patients with Myasthenia Gravis



3rd Edition  
Revised November 2011

### **Acknowledgements**

The MGA is grateful to the authors, who write impartially, give their services totally free and have no conflicts of interest.

We are also grateful to all the MGA members and friends who volunteered to proof-read this Volume.

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*The Association does its best to ensure that the information contained in its series of publications is complete and up to date at the time of publication, but cannot accept any legal liability whether for any inaccuracy or otherwise.*

[<sup>1-4</sup> Deceased 2005, 2009, 2007 and 2008, respectively]

# THE INFORMATION PACK

The Board of Trustees of the Myasthenia Gravis Association has approved the following publications for supply, free of charge, to anyone with one of the Myasthenias or their families, and to the medical practitioners and professionals who look after them. Copies may be obtained from the MGA Headquarters at the address on the back cover. The pack comprises six volumes:

## **Volume 1 - A Medical Guide for Patients with MG**

Medical Information on Myasthenia Gravis for patients and families.

## **Volume 2 - A Medical Guide for Patients with LEMS**

Medical Information on LEMS for patients and families.

## **Volume 3 - Myasthenia for Complete Beginners**

A simple guide to the Myasthenias and their treatment.

## **Volume 4 - General Information for Myasthenic Patients**

Information of general assistance to people with Myasthenia, including Driving and the DVLA, the DSS, prescription charges, insurance and other helpful organizations and charities.

## **Volume 5 - Medical Information (Medical Professionals)**

Information for people working in the medical and allied professions. Details of Myasthenia Gravis, LEMS and Congenital Myasthenias, with a greater emphasis on the neurological effects and drug information (in lay language).

## **The Congenital Myasthenic Syndromes**

Information for children and adults diagnosed with Congenital Myasthenic Syndromes (CMS).

## **Medical Articles**

Medical articles published in MGA News can be viewed directly on the MGA website: [www.mga-charity.org](http://www.mga-charity.org)

# **INFORMATION ABOUT MYASTHENIA GRAVIS AND RELATED DISORDERS**

## **Foreword to first edition**

“The Myasthenia Gravis Association (MGA) has now updated the leaflets providing information about the different types of Myasthenia: Myasthenia Gravis, the Lambert-Eaton Myasthenic Syndrome and the Inherited (congenital) Myasthenias. Many patients want to be fully informed about the nature of their disorder, and such knowledge can be very helpful not only to the patient themselves but also to their families. It also makes it easier for the patient to understand what the doctor is trying to do to help them.

Although information about the Myasthenias is available on the internet, it is not always presented in a form that is easily understood by a lay person. A number of us have contributed to this new edition, and we hope that the information in these leaflets will be easy to understand. But I am sure there will be room for improvement, and for this reason we would be very grateful for feedback that will be used when we come to prepare the next edition.

For those of you who have not heard about MGA, you might like to know that the Association was formed in 1968, became independent in 1976, and was incorporated as a company in 1995. The aims of the Association are to provide a care and support network for Myasthenia patients and their families, and to promote both awareness and research aimed at understanding what causes these disorders and at developing better treatments.

The Association wants to foster close links within the patient/member community, and also with the caring professions and the researchers. We do that through our local Branches, through Branch and Regional meetings (often with an expert speaker), through MGA News and through our information leaflets. Our membership is now nearly 1,500.

We hope you find the information helpful, and please let MGA have your views.”

**John Newsom-Davis MD, FRCP, FRS (1932-2007)**  
**Late President**

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**Please note:** Some items are mentioned many times throughout this booklet; however, the contents list indicates the main area of focus for each item.

# Volume 1

## A Medical Guide For the Patient with Myasthenia Gravis

### **ABOUT THIS GUIDE**

As each person's experience of Myasthenia Gravis (MG) is unique, this guide can approach the topic only in a general way. It is one view of a complicated subject that we don't fully understand. It has been written to provide information and guidance, not only to those suffering from MG, but also their families, friends and anyone interested in finding out more about the condition. It is one team's most up-to-date view as of January 2012, but is not the only one possible.

This volume deals mainly with Myasthenia Gravis. The Lambert Eaton Myasthenic Syndrome and the Congenital Myasthenias each have Volumes of their own.

If you find the science and medical terms unfamiliar, then you could start with Appendix 1 'Some simple science for the terrified beginner' (page A1), and use the Glossary in Appendix 2 (page A3).

This revised edition now includes sections on Dentistry (section 10 page 22) and Ocular Myasthenia (section 9, page 19).

# AN INTRODUCTION TO MG

## 1.1 What is MG?

The term 'myasthenia gravis' comes from Greek (myasthenia = muscle weakness) and Latin (gravis = severe). Mercifully, the myasthenias are rare and the muscle weakness is **painless**. They are caused by problems with nerve → muscle transmission – ie in the '*ignition system*' of our muscles (see section 2, page 6). The myasthenias come in three quite separate forms:

- **Myasthenia gravis (MG)** is by far the commonest. Here, an immune attack damages the ignition locks of our 'voluntary' muscles only. The weakness typically fluctuates and is '*fatiguable*' – the more you try, the worse it gets. So patients are often strongest in the mornings and get weaker during the day.
- **Congenital myasthenias** (less than one in twenty of all myasthenias). Here, inherited genetic faults make the ignition system less efficient (see separate Volume).
- **The Lambert-Eaton Myasthenic Syndrome (LEMS)** (around one in ten of the total). Here, a similar immune attack damages the nerve endings in both the voluntary and the 'automatic' muscles (e.g. in the blood vessels, bowels and bladder; see Volume 2).

None of these directly affects sensation (e.g. sense of touch or temperature) or causes pain, though overstrain can cause aches (e.g. in the neck or the back).

## 1.2 For the new patient; what it means to have MG

We don't want you to find the next few pages scary.

### Starting on the bright side:-

- MG can nearly always be brought under such good control that most patients can lead a full life.
- If you must have one of these 'autoimmune' disorders, MG is one of

the most treatable, with the least pain and the fewest major long-term snags. Very few people actually die of their myasthenia.

- Treatments are improving all the time; with your help, we are determined that this should continue.
- Many myasthenic patients become their own best managers, and work out their own ways of keeping their myasthenia in its place.
- Try not to let it take over your life.

**On the other hand, you should be forewarned that:-**

- Your MG may well be with you for many years. Don't wait around hoping for a remission; without treatment, they happen in only about one MG patient in 20 per year.
- You will probably have to plan your day to make the most of prime time when your strength is greatest.
- MG often affects the muscles of the face and the voice, so people may not always understand you, especially at the first meeting, e.g. misreading even your best efforts at a smile (a myasthenic smile can come over more like a snarl, despite your best efforts).
- You will almost certainly need some drugs. You may well have to adapt to their side-effects, but those are far outweighed by the benefits in most people.

### **1.3 What are the symptoms?**

No two patients show exactly the same symptoms, either in kind or severity. The onset can be sudden; much more commonly it starts so gradually and insidiously that it is easily missed or diagnosed only after a delay of some months.

Very often it starts in muscles that we use all the time – e.g. with drooping eyelids and double vision – i.e. affecting the movements (but not the focusing) of the eyes. Sometimes these eye muscles are the only ones affected. Frequently also, weakness of the face muscles



causes a 'snarling' smile, and/or the voice becomes nasal, and may even fade or become slurred and hard to understand. MG often affects the muscles of the throat, neck and trunk; sometimes also the hands, arms and legs, weakening the grip or, less commonly, the gait. MG has a 'head downwards' bias – the nearer the feet, the milder it is and the less likely those muscles are to be affected.

If the weakness affects swallowing or chewing, eating may be slow and there is a risk of choking or inhaling small bits of food, which can cause chest infections. Still more seriously, the patient may have difficulty in breathing and even become gravely ill – hence the 'gravis': MG used to cause many deaths until the 1930s. If the breathing troubles are serious (e.g., during an infection), the patient is in 'crisis' and needs mechanical ventilation in a hospital.

Now, with greatly improved treatments, MG rarely shortens life and most patients can lead an active life, despite a few side-effects from the treatments. It usually reaches its worst within three to five years and then levels off. Unfortunately, only around one patient in five 'grows out' of their MG (i.e. goes into long-term **remission**), and most have to learn to keep it in its place.

#### **1.4 What makes MG worse?**

Many things increase the weakness, including infections (such as colds, pneumonia, or a tooth abscess), fever, heat, over-exertion and emotional stress. Some women notice worsening of their MG during a particular time of the monthly cycle, during pregnancy or after delivery. Either too little or too much thyroid activity can worsen MG; so can salt depletion brought on by diuretic drugs or frequent vomiting; also the stress of surgery or radiation therapy.

#### **1.5 Who gets MG?**

MG can occur from the cradle to the grave, affecting all races and both sexes. While it often affects young females (aged 10 - 40), the number of elderly myasthenic patients, particularly men, has increased, and so

has our awareness of them. 'Autoimmune' MG is **not** inherited, though some risk factors do run in families. Even when one identical twin develops MG, the chances of the other getting it too are less than 1 in 5. There is absolutely no sign that MG can be caught from another person with MG. While it may seem to start after infections, no one germ is under strong suspicion.

MG occurs in all races, but the pattern of the disease can vary. For example, MG confined to eye muscles ('ocular MG') is more frequent in young Chinese and Japanese patients, especially before the age of 10 – when it is very uncommon in Europeans.

**Patient subgroups:** About 10% of patients have persistently pure 'ocular' MG. Those with generalised weakness are usually further subdivided into about 10% with a thymic tumour ('thymoma'), 25% with 'early-onset MG' (starting before age 40, mostly female) and 50% with 'later-onset' (with a slight male bias). The thymus looks abnormal in 'early-onset MG', but there is no tumour (see section 2).

Finally, the babies of about one in eight mothers with MG may be weak for the first 2 to 3 weeks after birth (see section 6); they usually respond well to treatment and soon get back to normal.

**Why do only some people get these disorders?** We know very little. However, some of the inherited risk factors for 'early-onset MG' also predispose to other autoimmune disorders, so thyroid disease and 'young-onset' diabetes are commoner in myasthenic patients – and also in their blood relatives – than in the national average. But autoimmune MG itself only strikes twice in the same family in about 1% of cases.

We suspect there must also be other inherited and external risk factors such as infections, but very few are known. Occasional patients taking the drug D-penicillamine for rheumatoid arthritis get typical myasthenic antibodies plus MG; both usually fade away when the drug is stopped. Internal factors include thymic tumours ('thymomas') in about one MG patient in ten, and the thymic changes in 'young-onset' MG patients (see section 2).

## 2

# WHAT GOES WRONG AND WHY ?

## 2.1 Normal muscle 'ignition' and how it goes wrong

When an electrical impulse arrives from the brain, the nerve endings release a shower of a chemical transmitter – acetylcholine (**ACh**) – the 'ignition keys' (the black triangles ▼ in Figure 1). These travel across a narrow gap and latch into the tailor-made 'locks'– the ACh receptors (AChRs) on the muscle surface – which then trigger the muscle to contract via complicated electrical and biochemical mechanisms. The surplus ACh is destroyed by a special protein – AChE (ACh Esterase) – which allows the muscle to relax again. The drugs neostigmine and **pyridostigmine** (Mestinon<sup>®</sup>) block this **AChE**, so that the ACh lasts longer and has a better chance of triggering. As it also normally stimulates the

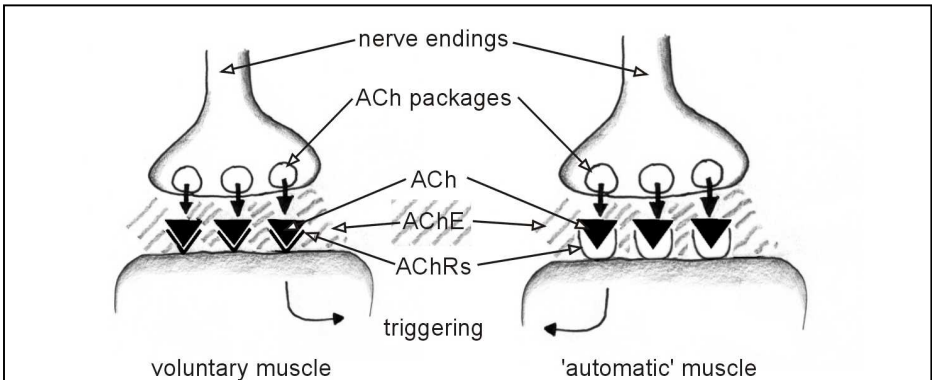


Figure 1: **Diagram of nerve → muscle junctions:**

In the two muscle types, the AChRs are completely different (V and U shapes). Luckily therefore, the immune attack on the AChRs in the voluntary ones does not affect the 'automatic' muscles in the guts, heart, blood vessels, bladder and glands. **But** the nerve endings and the AChE are similar in both, so pyridostigmine soups up ignition in both types by blocking their AChE.

**Key** ACh = acetylcholine;  
AChR = ACh Receptor;  
AChE = ACh Esterase (which destroys spare ACh).

‘automatic’ muscles and glands in the guts, these drugs often make them over-active, causing bowel looseness. To prevent that, these ‘automatic receptors’ can be blocked with the drug propantheline.

In typical **autoimmune MG**, there are too few AChRs because they have been destroyed by antibodies. These are produced by over-enthusiastic immune cells as if the AChRs were invading germs (see next section). These antibodies against the AChR are found in most (but not all) typical MG patients (see section 3).

## 2.2 The immune system and how it goes wrong

Two groups of white blood cells help to protect us against ‘invaders’ such as bacteria and viruses. The ‘B cells’ come from the bone marrow, and make **antibodies**. These proteins are tailor-made for each target. For example, if you are immunised against tetanus, you make antibodies that only recognise tetanus and not ‘flu virus (and *vice versa* if you have a ‘flu jab). Antibodies travel around in the body fluids and latch onto their particular target. They then activate other amplifying cells and proteins to destroy that target.

Other white cells called ‘T cells’ come from the thymus and are the ‘control freaks’ of the immune system. They too are tailor-made for each target; when they recognise it, they turn on any ‘specific’ B cells that recognise the same target to make their antibodies. T cells can also switch on other cells to fight infections. Because both T and B cells include thousands of different ‘families’ – each recognising different targets – the immune system is a hugely complicated mix.

In MG, alas, a few immune families start to attack their own AChRs just as if they were foreign invaders. These autoimmune ‘vandals’ are probably only a tiny minority, and the many other T and B cell families continue trying to fight infections. Their great specificity offers hope of devising smart weapons for selectively turning off only the damaging families without clobbering the whole defence system with steroids etc.

**The thymus** is where the T cells first develop, and it sits just behind the

breastbone. It is most active in early childhood, when it exports T cells in vast numbers which then go on patrol looking for invaders to attack. When they find them, many settle in lymph glands where they multiply and send some of their offspring away on further travels.

In 'early-onset MG', the thymus gets colonised by lymph gland-like 'factories' for antibody production. This may be sparked off by rare muscle-like cells, which are found in the normal thymus too. In these factories, the antibodies evolve to bind and attack the AChR even more strongly. Removing the thymus (thymectomy) **may** cut this evolution short, but there are other theories to explain its apparent benefits in MG.

**Thymomas** are tumours of the 'framework' cells of the thymus. Mercifully, many are benign, but they do need to be removed because they can invade locally (e.g. into the lungs). What is more, having MG is a valuable early warning to check for a thymoma; thanks to the usual X-rays and scans, they are often nipped in the bud. However, some thymomas have already started spreading before they are diagnosed. Even at worst, most respond much better to radio- and chemo- therapy than many other tumours. Unfortunately, removing thymomas doesn't improve the myasthenia much. Conversely, they **can** sometimes grow back again *even while the MG remains under good control*, so repeat scans are often advisable over the following years.

Thymomas often look a bit like normal thymus gone crazy, generating *vastly* too many T cells, for example. Roughly one thymoma patient in three gets MG, and another few get autoimmune bone marrow failures. We *think* thymomas must somehow immunise against AChR, but that is less clear than in the lung tumours in some LEMS patients (see section 11, page 23, also Volume 2, A Medical Guide for Patients with LEMS). These are fascinating clues to processes that are otherwise very hard to study in humans.

### 3

## HOW IS MG DIAGNOSED?

Whereas MG is quite rare, weakness and fatigue are so common, and have such varied causes, that MG is easily missed, especially if it is mild, variable or localised. However, the patient's account of the symptoms, and the visible tell-tale pattern of weakness, will ring bells with most doctors who know about MG. Once suspected, it can be confirmed in these ways:-

One way is to test muscle *stamina* or *fatigue* (eg, while holding up the arms or legs, or staring in one direction), which needs no equipment. Also, specialists can test electrically by recording the responses of a muscle to stimulation of its nerve with harmless electrical needles – electro-myography (**EMG**). In MG, the response typically gets smaller over the first few stimuli; 'single fibre EMG' provides the most sensitive test. EMG also helps to sort out confusions with LEMS and congenital myasthenias that may need different treatments.

Another test is to inject a short-acting anti-cholinesterase drug like '**Tensilon**'<sup>®</sup> ('edrophonium' – a cousin of pyridostigmine) and measure strength beforehand and afterwards in the worst affected muscle groups (usually two of them). This '**Tensilon test**' is used less often nowadays because it carries slight risks and needs to be done in a hospital with equipment ready in case of emergency. Alternatively, the patient's general improvement on anti-cholinesterase drug treatment is useful supporting evidence.

The most specific diagnostic test is a blood test for the typical antibodies to the AChR (see above); around 85% of all MG patients have them, whereas patients with other muscle diseases almost never do. Another 5 - 10% of typical MG patients have other antibodies to a different target next to the ignition lock called MuSK; they can now be detected in a similar test. These patients are more prone to respiratory crises. Their thymus is not removed; from experience, it usually seems largely normal, and its removal seems not to improve the MG.

## HOW IS MG TREATED?

There are five main sorts of treatment; most patients end up with their own individual blend of them.

### 4.1 Common sense things

Many common-sense things can be very effective in coping with MG. Plenty of rest and a well-balanced diet actually help. If possible, one should try to avoid exposure to infections, some drugs and all forms of stress, though, of course, that's easier said than done. Patients should try to pace their activities so that they don't exhaust themselves, and tackle the harder jobs when they expect to be at their strongest (e.g. mornings). While that may sound obvious, fellow-sufferers in MGA have lots of other valuable hints along similar lines.

### 4.2 Pyridostigmine

Pyridostigmine is a front-line weapon (see Fig 1, page 6; its trade name is Mestinon<sup>®</sup>); a bit like the choke in a car, it gives the handicapped ignition system a better chance of firing, so providing a temporary boost; it may strengthen some muscles much more than others. ***But it doesn't clean the plugs – i.e. it doesn't cure the under-lying immune or inherited faults in MG*** (see pages 11 - 14).

Since pyridostigmine's effects last only a few hours, it is more important to take it often than to worry about the exact dose, which varies a lot between patients and from time to time in the same one. Generally it helps to keep the dose between a half and one and a half of the 60 mg pyridostigmine tablets (i.e. 30 - 90 mg) every three or four waking hours; always keep on the low side to avoid both side-effects on the one hand and tolerance on the other (when it becomes less effective with time). These medicines sometimes cause stomach cramps and diarrhoea, so they should be taken with bland food such as crackers or milk to minimise that. These side-effects can be prevented by taking propantheline about 30 minutes in advance.

**Overdosing with pyridostigmine can lead to a ‘cholinergic crisis’**, with worsening of the myasthenic weakness. That almost never happens in people taking **six** 60 mg tablets per day or fewer. **Obviously, it is important to distinguish that from a myasthenic crisis**, which needs completely different treatment (e.g. **more** pyridostigmine). If you suspect that either type is coming on, you should seek immediate advice from your GP or Consultant. Too much pyridostigmine can cause muscle twitching; also excess sweating, salivation (drooling) and lung secretions (→ phlegm), and/ or tightening of the pupils.

### **4.3 Plasma exchange and Ivlg**

Plasma exchange and Ivlg are two short-term measures to treat the underlying *immune faults* in MG. In the first, the damaging antibodies are simply washed out of the bloodstream; during a thorough plasma exchange (‘plasmapheresis’), several litres of blood are removed one by one, and the red blood cells are separated and then returned in an artificial substitute (human albumin and saline solution) without the antibodies. After about three days, that reliably improves strength for up to 6 weeks, but then the benefits slowly wear off as the antibodies are gradually replaced. It is used most when benefits are needed *urgently*, e.g. if a respiratory crisis is looming, before surgery, or to cover the start of steroid treatment. It is very safe.

Plasma exchange must be done under close medical supervision, which means being in a special hospital ward for 5 days connected by an intravenous line (usually in the groin) to and from the separator, for up to 4 hours per day.

Nowadays, an alternative is ‘**Iv Ig**’, which means infusing the total antibodies (**Ig**), pooled from huge numbers of healthy blood donors, into a **vein (Iv)**. It clearly does help, though again *only for 6 to 8 weeks*. We don’t know *how* it works; there are more theories than hard facts. (It may simply water-down the damaging MG antibodies or side-track the bystander damaging mechanisms they recruit).

It costs slightly more than plasma exchange, but again it means being in



a special hospital ward for 5 days running. The Ig has to be given very slowly into a small arm vein for up to 5 hours each day. Patients may get a headache, a rash or rise in blood pressure; blood tests are used to monitor for possible effects on the kidneys.

Human blood products inevitably carry low-level risks. Despite very careful screening for the known viruses (hepatitis and HIV), there is obviously a remote possibility of some new unsuspected agent.

## 4.4 Thymectomy

Thymectomy *seems* to help around a quarter of ‘early onset’ MG patients to go into complete drug-free remission, and another half to improve – and / or to get away with lower doses of steroids than they would otherwise need. These benefits may take up to 2 years to reach their maximum\*. Alas, we can’t predict beforehand who will improve after thymectomy – or not (as in the final quarter)\*. Whether it helps patients over 45 is far less clear\*. It seems not to improve the MG in thymoma patients, but is almost always done to prevent spreading.

Thymectomy is a safe operation (for details, see section 5.6, page 16). Even with keyhole surgery, it is a major operation, done only when the patient’s MG is well controlled, and preferably in a specialist centre.

## 4.5 Long-term immuno-suppression

### 4.5.1 Prednisolone

The first choice drugs are usually synthetic *steroids* called ‘Prednisone’ or ‘Prednisolone’, which are taken by mouth. They reliably start to improve the myasthenia after a delay of around 2 - 6 weeks. They lower the damaging antibodies, and probably have many other immune-suppressing effects too.

You probably already know that steroids can be a mixed blessing. Do remember that, in most myasthenic patients, **their benefits far outweigh their snags, so don’t be put off** by what follows. Obviously, the choice between steroids and other treatments needs careful thought.

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*\*We hope that some of these queries may be answered in an on-going clinical trial.*

Only about one myasthenic patient in ten has to give them up because of the side-effects. Your doctors will tell you about them in detail, but here is a very quick run-down.

In general, as you know, *people vary greatly*: so they do in their responses to steroids – both the benefits and the side-effects. At the outset, steroids can even make the MG worse for a few days, so their dose is usually built up gradually to flatten the MG, and then lowered as far as we dare. In the end, most people reach a steady level, with a good balance between benefits and snags. Again, the ‘cruising’ dose varies a lot between patients. Unfortunately, very few manage to cut them out altogether.

### **The snags fall into three main groups:-**

i. Because they are suppressing immunity, steroids are bound to raise the risk of infections. By taking reasonable care (e.g. avoiding big crowds), you can usually keep that risk low without complete isolation.

ii. Steroids are produced naturally at carefully controlled levels by our own ‘adrenal’ glands. One of their main jobs is to tune us up for the day, and to tide us over times of physical **stress** (e.g. injury or appendicitis). Because the doses given to patients are so unnaturally high, they shut our adrenal glands off. So we are no longer cushioned against these stresses, and may collapse suddenly in a crisis. Hoping to prevent that, many patients take their steroids every other day, to ‘keep their adrenals on their toes’. Even so, whenever we drop the dose, it has to be done in very gradual steps. Therefore, everyone on steroids must carry a card to alert others.

iii. Steroids lower activity in many cells. For this and other reasons, they can also cause many other side-effects including:- weight-gain, mood changes, sleeping troubles, diabetes and high blood pressure; skin changes including thinning, easy bruising and unwanted hair growth; bone-thinning and stomach ulcers, which can each be prevented with other drugs; glaucoma and lens cataracts.

More detailed information on steroids may be found in Volume 5.

### 4.5.2 Azathioprine (Imuran®)

This drug also reduces antibody production, but that takes at least a year to 'kick in'. It is sometimes used by itself in patients who can't quite manage on pyridostigmine alone. More often, it is given to enhance the benefits of steroids / allow cruising on lower doses thereof.

Its side-effects include allergies, liver damage and bone marrow suppression, for which regular blood tests are needed around every week at the start and every 2 months for ever more (done by the GP). Some patients react to it in the first few weeks, with fever, nausea, vomiting, loss of appetite or stomach pain, and the drug must then be stopped. In pregnancy, one should ideally avoid most drugs as far as possible; however, many healthy babies have been born to mums who needed to take azathioprine and/or steroids to keep up their strength while pregnant. *As with steroids, the benefits usually far outweigh these hazards.*

### 4.5.3 Other immunosuppressants

People who can't take the above front-line drugs nearly always find another immuno-suppressant that suits them, such as Ciclosporin, Methotrexate or Mycophenolate Mofetil. These are less well tried-and-tested in MG, and have their own side-effects too, partly because they are more powerful immuno-suppressants. Like azathioprine, they increase the risks of skin warts/ tumours in the long-term, so patients should be careful about sun exposure. As with steroids, the benefits usually far outweigh these modest risks.

## 5

### ANAESTHETICS AND MG

Myasthenia used to pose challenges for anaesthetists. Nowadays, they are so well aware of them that that it rarely causes problems any more. Thanks to better awareness, preparation, monitoring and treatment, you can forget all the out-of-date horror stories, ***as long as the anaesthetist knows in advance about your MG.***

#### 5.1 Local and general anaesthetics

As you know, you can have either a **local** or a **general anaesthetic**.

**Local anaesthetics** (e.g. lignocaine, bupivacaine, mepivacaine) are

injected around the nerves and 'freeze' them by blocking their electrical conduction. So all feeling from their territory is wiped out for some hours. That works just the same whether they are injected near the nerve endings (e.g. into the jaw nerve) or around their spinal cord roots, as for spinal and epidural anaesthetics, which are suitable for many operations below the waist, e.g. on hips, knees, varicose veins, hernias, and even some in gynaecology. Many of you prefer them – both to avoid the feeble breathing caused by some general anaesthetics, and also to allow your MG treatment to continue normally. Light sedation given in advance helps you to 'chill out' – a bit like a sleeping tablet or an extra tipple!

Before any **general anaesthetic**, it is vastly better if the myasthenia is under the best possible control. That may mean tuning up with plasma exchange or Ivlg a week or so beforehand. Then, it should be just as safe in myasthenic patients as in anyone else, as long as care is taken over the following:-

## **5.2 Muscle relaxants**

These drugs paralyse all the voluntary muscles by blocking muscle ignition. They are given to help the surgeons get easier access for 'deep' operations, e.g. on gall bladders (etc). Because they also paralyse the breathing muscles, we must connect you to a breathing machine (ventilator) via a tube in your windpipe. All that is standard practice nowadays (as it avoids the deeper anaesthesia that used to depress blood pressure and breathing, and to cause longer recovery times and more vomiting). NB some operations don't need any muscle relaxants; in that case, you can breathe by yourself or with assistance.

With their lower reserve of muscle-triggering power, myasthenic patients are extra-sensitive to muscle relaxants, and need 5 or even 10 times lower doses. The resulting paralysis can easily be monitored in any operating theatre. It is normally stopped after the operation by injecting a short-acting pyridostigmine cousin, neostigmine. Very occasionally, an unsuspected myasthenic patient may need more neostigmine than expected to perk them up – that is one of the roundabout ways in which MG is sometimes first diagnosed.

### 5.3 Pyridostigmine

Should it be stopped beforehand? **No**, but it counteracts the muscle relaxants, so they may need to be given at slightly higher doses if you have recently taken your pyridostigmine. That should not be a problem, and may even help if you find it reassuring to take it regularly. Afterwards, it can be given into a stomach tube if you have trouble swallowing it.

### 5.4 Steroids

Should the doses change? **Yes**: you naturally produce extra steroids to tide you over the stress of surgery. Prior steroid treatment shuts that response off, so we normally boost your body's own efforts with extra steroids by injection before, during and after the operation.

### 5.5 Talking to the Anaesthetist

Finally, meeting the anaesthetist in advance helps both sides. (You should be able to find out who it will be from either your surgeon or the hospital anaesthetic department). If you do, the anaesthetist can explore with you the various options, assess the severity of your MG and your overall fitness for anaesthesia and surgery, and arrange for an intensive care bed for recovery if need be. Importantly, too, it gives you confidence and courage, which is ideal for everyone.

### 5.6 Thymectomy

The rules are exactly the same as above, though a general anaesthetic is essential. The thymus lies just behind the breast-bone (sternum), which can be split open to allow direct removal. That usually takes only around 1½ hours, and most patients don't need any blood transfusion. Since about 1995, 'keyhole' video-assisted thymic surgery (**VATS**; via small holes below one armpit) has become popular, because of the less obvious scars and faster recovery afterwards – 2 - 3 days instead of 6 - 7. The results seem to be as good as with the traditional method, though some surgeons think it's harder to be sure of removing all of the thymus.

## 6

### FAMILY AND WOMEN'S ISSUES

Many women notice their weakness is worse around the time of their monthly periods, and others for a few months during the menopause

(‘change of life’). There is no objection to Hormone Replacement Therapy (‘HRT’) in patients with MG, nor to the contraceptive ‘pill’. Moreover, MG very rarely affects the outcome of pregnancy; there is almost no extra risk of miscarriage or stillbirth. While MG occasionally gets worse during pregnancy, it more often does so for a few months afterwards.

Prednisone and azathioprine should only be used in pregnancy when they are essential, although historical evidence suggests that they do not harm the unborn baby. That is probably also true for cyclosporin, but **not** for methotrexate and mycophenolate which should definitely **not** be used in pregnancy.

With around one MG mother in eight, the newborn babies have a short-term weakness, but they usually recover fully in the first 3 weeks or so. This ‘**neonatal myasthenia**’ is due to transfer of the mother’s damaging antibodies across the placenta (along with her protective ones) which then affect the baby’s muscles (just like its mum’s). Unfortunately, the antibodies are also transferred through the milk, so, if the baby is affected, breast-feeding should be avoided. Mercifully, since the babies do not make anti-AChR antibodies of their own, they recover as those from the mum gradually decline, and their muscles get back to normal. Each mum tends to stick to the same pattern – i.e. later babies usually show similar weakness (or not) to that in the first. Neonatal myasthenia may be getting rarer with improved treatments for MG. Very rarely, babies can have joint deformities (‘arthrogryposis’). If so, that is because the mum’s antibodies particularly attack the baby’s AChR (which is slightly different from the adult’s); subsequent pregnancies can be protected by prior immunosuppression.

## 7

### WHAT IS THE OUTLOOK?

With improved treatments, MG rarely shortens life and the outlook now is good. Most patients can expect a marked improvement in their symptoms, which may well disappear altogether, though they may have to continue to take some drugs. However, these treatments sometimes have troublesome side-effects that can lessen their usefulness.

In general, it is very important to keep your MG in its place, and try not to let it take over your life. Also, there is a lot of truth in the old saying that

everyone is their own best doctor, because they can usually find ways of handling their own MG, some of which may not suit other myasthenic patients.

For the researchers, a lot remains to be done. We need to know why some people get MG and, perhaps more importantly, why others don't. What triggers it? Why does it appear to be getting commoner in older people, especially men? How, exactly, do steroids help? We need to find more selective ways of treating the disorder, ideally stopping only the damaging immune reaction in its tracks and avoiding any side-effects. To answer such questions, we need further research, which the MGA is striving hard to fund and encourage. Valuable clues may well come from observant patients, so we welcome your queries, however much some of them may fox us. As the enormous advances in understanding and treating MG over the last 80 years strongly suggest, the future is bright for myasthenic patients.

## 8

### HISTORY

Myasthenia gravis (MG) was first clearly described in the 17th century, although it has probably always affected human beings. Indeed, it also occurs in dogs and cats, for example. The term 'myasthenia gravis' comes from Greek (myasthenia = muscle weakness) and Latin (gravis = severe). It was recognised as a disorder of the nerve-muscle junction in the 1930s; only then did the (Scottish) Dr Mary Walker discover the benefits of physostigmine (an early version of pyridostigmine). Thymectomy was pioneered in the UK by a previous MGA Vice-President, Sir Geoffrey Keynes (brother of JM Keynes), from 1940 on; we still don't fully understand why it works.

An 'autoimmune' origin for MG was suggested by another former Vice-President, Prof. Iain Simpson, in 1960. It was only proved, however, in 1973, when Drs Jim Patrick and John Lindstrom (in the USA) showed that antibodies *can* cause MG. Much subsequent research has focussed on how they cause weakness, and on the control of their production. *Steroids* began to be prescribed regularly as treatment in the 1960s and plasma exchange was first used in the mid-1970s (see section 4, p 11).

## 9

### EYE WEAKNESS IN MG (OCULAR MYASTHENIA)

MG can affect one group of muscles much more than others, for example, just one small muscle that moves one eyelid or one eye in one direction; or just one of the larger muscles involved in face, limb or breathing movements, sometimes only on one side. Weakness of eye movements is particularly common in MG: indeed, it may be the only problem in some patients, whereas it is often an early sign of a more general picture in others. So optometrists and eye specialists are important allies for the MG community; that's partly because they are often the first to suspect MG; also, in both community and private practice, they are increasingly involved in the shared care of MG patients and can sometimes offer them practical help.

Strictly speaking, we only label myasthenia as '*Ocular MG*' if the weakness is *still* restricted to eye movements *at least two years* after the very first symptom. We do that because *generalised MG begins with ocular weakness* in around three quarters of all myasthenics (and affects about 9 in 10 eventually); it may start to affect other muscles only after 6 months (in about a quarter of them), or even longer (in about an eighth). So, if the MG remains purely ocular for two years, there is only about a 1 in 20 chance that it will 'generalise' after that.

Like any muscles in MG, those that move the eyes may be quite strong when you are well rested. However, they can tire easily as you use your eyes or when you are subject to emotional strain. For example, after looking upwards or sideways for a long time, your eyelids may gradually start drooping or you may see double as one of the muscles weakens. Your eyes may even refuse to move altogether. These signs can easily be mistaken for other medical conditions with similar effects, e.g. strokes, tumours, thyroid eye disease, infections or multiple sclerosis.

Why are the eye muscles so commonly involved in MG? As you know from watching people nodding off, *the eye muscles are especially prone to tiredness*, probably for several reasons:-

**a)** they need to be much more precise than most other muscles;



- b) they are very small and have less reserve capacity;
- c) there are subtle differences (from other muscles) in their nerve endings and possibly in their AChRs;
- d) they get less rest, even during sleep.

What makes eye weakness worse? Bright sunlight, emotional stress, viral illness, surgery, menstruation, pregnancy, immunisations and other factors may all provoke changes in the ocular weakness, although not in predictable directions.

## DIAGNOSIS

The diagnosis depends on your story and physical condition, and on a blood test for the anti-AChR antibodies (positive in about 60% of patients with pure Ocular MG). If it is negative, a very sensitive electrical test (single fibre EMG) can be done on the eyelid muscles. In a few cases, we need to test the response to an injection of Tensilon<sup>®</sup> (edrophonium), which would be carried out in a hospital.

## DRUG TREATMENTS

As with most forms of MG, pyridostigmine (mestinon<sup>®</sup>) is usually the first-line treatment. With careful use, it often helps, but it may not eliminate all ocular weakness. Again, if it is not enough, then immunosuppressive drugs may be tried.

## OTHER MEASURES

**For double vision (diplopia)**, you can tilt your head or turn your face to bring your relatively stronger eye muscles into play. If looking upwards is the main problem, then you can tilt your head back, thus bringing your gaze downwards out of the area of the weakened muscle.

If drugs work poorly or cause side-effects, other methods may help to relieve your double vision. Fresnel (stick-on) prisms, for instance, can be attached to your eyeglasses to relieve double vision; if helpful, they can then be incorporated into the lenses. By optically 'bending light', they enable you comfortably to look straight ahead or downwards and read with both eyes open. Sometimes, a pirate's eye patch, a frosted

lens, or simply sticking a piece of tissue paper over one lens in the spectacles is an easy short-term way of stopping double vision to allow more comfortable reading or TV-watching. Very rarely, surgical correction can be useful for long-term deviations that don't vary.

For droopy eyelids (**ptosis**), some patients use sticky tape to hold them up. **Ptosis props** are sometimes useful if drug treatments are not successful, but are not widely used. They come in two forms:-

a) **Lundie Loops** act as a spring-based support for the upper lid and are fitted to the spectacle frame, which needs to be thick enough along its top rim to support them. Details of the loop can be obtained from the MGA.

b) Traditional **bar ptosis props** can be fitted by most glazing houses; their projection, length and size are specified by the optometrist. Rubber tubing can be used to cushion the bar. A few patients find them a tolerable long-term solution.

Rarely, surgical correction may be considered if the ptosis is stable and other measures are not working. NB before recommending either surgery or props, it is particularly important *to ensure a good capacity for eye closure*, which is often weak in MG. Otherwise, defects in the normal protective reflexes may confer a risk of damage to the cornea.

## 10

### DENTISTRY AND MYASTHENIA GRAVIS

As explained below, taking good care of your teeth, and preparing yourself for dentistry, may save you a lot of trouble.

*Excellent home care habits are crucial*, however difficult they may be. They include *regular* brushing, daily flossing, cleaning between teeth, and oral cleanliness; also regular dental visits and cleaning, to keep your teeth free of plaque.

**Prevention is vital to avoid dental emergencies**; they are most stressful and can aggravate your myasthenia.

Your gums are liable to infections – which you may not always be aware of. If severe, they can have knock-on effects on your myasthenia and / or lower your resistance, so proper care is vital. With immuno-suppressants, infections are more likely, and healing may take longer

than expected. Finally, weakness of jaw muscles can affect closing of the teeth. That, in turn, can create extra stresses or even pain.

If your myasthenia is under good control, there is no reason why you can't have normal dental care. Excellent communication between you and your dentist is vital, so that you know exactly what is the plan. The dentist needs to know what your limitations are, and to be prepared for them. That should help you to relax and co-operate more fully. It is vital that the dentist consults with your Neurologist at the planning stage if surgery is necessary, and it may also help even for normal care.

It helps to book appointments for the morning or whenever your strength is greatest, and to keep them short. If you have difficulties in opening and closing your mouth, in holding your head up, or in swallowing, ***the dentist needs to know*** so as to prevent problems. A mouth prop may help for keeping your mouth open; thorough suction (perhaps controlled by you) helps to avoid drooling or choking.

Even root canal work need not be traumatic. A rubber dam may be needed to prevent worries about choking. If you can't close off your throat, or tend to regurgitate fluids into your nose, you may prefer to sit more upright in the dental chair.

If you have to have an anaesthetic, local anaesthetics are preferable to general. The latter should **never** be used outside the hospital setting.

## 11

### THE OTHER MYASTHENIAS

This Volume focusses on Myasthenia Gravis: the following brief description of the two other forms of Myasthenia is included for completeness. **Their own individual Volumes each give more detail.**

#### 11.1 The Lambert-Eaton Myasthenic Syndrome (LEMS)

The LEMS was first recognised in the early 1950s. The damaging antibodies (which are different from those in MG) were first identified in the early 1980s.

The LEMS is rare and usually starts after age 30 years. It is also caused by auto-antibodies, but these ones cut down the **release of ACh** from nerve endings. So it differs from MG in several ways. LEMS patients briefly get *stronger* as they try harder. Their weakness also affects the

limbs more than the head, neck and trunk. Because the nerve endings are similar in the guts and the bladder etc (see Figure 1, page 6), these too get attacked by the same antibodies, so there is usually also some trouble with 'automatic' bodily functions, e.g. a dry mouth, constipation or impotence (in men).

We can confirm the diagnosis by checking for the typical changes in the electromyogram (EMG), and for the damaging antibodies in a blood test. It is also very important to watch any smokers for lung tumours, which are found in around half of LEMS patients. The cancer cells somehow immunise the patients against their own nerve endings. If they do, the LEMS is often a valuable early warning of the tumour; what is more, the immune reaction even seems to slow its growth, so having the LEMS isn't all bad (see Volume 2).

**Treatment** with pyridostigmine often helps less than in MG, but another drug – '3,4-diamino-pyridine' (**DAP**) – may work better in LEMS patients; it acts by boosting ACh release. As it has its own side-effects, it has to be used cautiously.

Being autoimmune, the LEMS responds well to the same plasma exchange, IvIg and immune-suppressing treatments as MG, though plasma exchange takes longer to kick-in (2-3 weeks) than in MG. Thymectomy is not used, partly because the patients are older. In patients with tumours, treatment of the cancer must take priority, but it may help the LEMS too.

## **11.2 Congenital Myasthenic Syndromes (CMS)**

These account for about one myasthenic patient in 40 (2 - 3%) and are caused by **inherited genetic faults** in nerve → muscle triggering. In general, faults can occur at random in any gene, so they can affect any system in the body, and they vary greatly. So congenital myasthenic patients are a mixed bunch, ranging from mild cases, mainly with droopy eyelids, to wheelchair users. In most, the AChRs are just too few in number. In some, they are overactive and cause muscle damage that builds up over the years; sometimes these get diagnosed only later in childhood, though 'Congenital' strictly means evident at birth. These myasthenias *do run in families*, especially in those with cousin marriages, where the same genetic fault can be passed down from both sides.

An EMG often gives useful hints of the likely fault. These rare patients need to go for assessment to one of the Specialist Centres at:- The Hospital for Sick Children, London; Newcastle-upon-Tyne; Oxford, where Prof Beeson's team\* also runs a diagnostic service for identifying the faults (in DNA from blood samples). Obviously, that can take time, as there are so many genes at risk – and still more to be found.

Specialist assessment helps for advising the parents about the chances of further children having the same problem, and about care and treatment for the present child. That is especially important because *good treatment for one subgroup may even make others worse*. For example, some need pyridostigmine or 3,4-DAP to boost ignition, whereas blocking that with quinidine or fluoxetine may help those with overactive AChRs.

Because there is no autoimmune problem in ***congenital myasthenias***, ***none of the immune treatments is suitable for them in any way.***

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## SOME SIMPLE SCIENCE FOR THE TERRIFIED BEGINNER

### The building blocks of life

Protons, neutrons and electrons are assembled into the smallest chemical units called atoms. Atoms, in turn, can assemble into molecules (e.g. table salt, consisting of sodium and chloride atoms). Many molecules in living things are much bigger than salt, indeed so big that they can be seen on the strongest (electron) microscopes.

Different kinds of molecules collect together and are built up into **cells**, which can quite easily be seen on normal (light) microscopes. In general, our cells are composed of a thin outer surface membrane made of fat, a bit like a soap bubble. Inside that is a jelly-like solution a bit like egg white, containing various salts, sugars and small building blocks that get put together into proteins and fats and sugary carbohydrates. Inside that is the nucleus, the 'brain' of the cell; here the inherited blue-prints or **genes** (made of DNA) that code for our proteins, are stored and copied. Each of us inherits one copy of each gene from our mother and another from our father. They number around 25,000 in all.

**Proteins** are incredibly variable and versatile molecules; they can be structural, as in wool and silk and ligaments; those called enzymes speed up chemical reactions as in yeast and in all our cells; others transport molecules like oxygen, as does the red protein haemoglobin in our blood; some transport food substances into our cells from outside (e.g. glucose); others act as surface receptors for outside signals, as does the AChR, the key target molecule in MG; some themselves act as messengers (as insulin does when it binds to insulin receptors); some move other cells; a few can even turn chemical energy into light. In general, they are highly specialised, and often recognise other chemicals very specifically.

Differences between proteins lie in their exact combinations of different building blocks. These come in twenty different shapes, and are strung together in a precise order (sequence); nearly every link in the chain (up to 3,000 in all) has to be just right. A single mistake at one key point can be a

## Appendix 1

matter of life or death. Inherited mistakes are called **mutations**, and can occur randomly anywhere in any gene.

### **The cells involved in the myasthenias**

Muscles and nerves consist of huge numbers of much smaller cells.

**Nerve cells** relay electrical impulses from sense organs (e.g. eyes and skin) to the brain and spinal cord or from there to muscles and glands. They relay signals to other nerves or muscles or glands at special junctions (synapses), and switch them either on or off. Sometimes, they act more like dimmer switches or thermostats, telling other cells to work harder or slower.

**Muscle cells** are long tubes of interlocking proteins (i.e. woven together); when triggered, they shorten ('contract'), so pulling bones ('voluntary' muscles), or narrowing tubes (e.g. the involuntary muscles in the guts, bladder, blood vessels and heart). In voluntary muscles, the nerve provides a short sharp trigger. In involuntary ones, different nerves may turn the thermostat up or down.

A **synapse** is a junction between a nerve and another nerve, or a muscle or a gland. Signals are usually passed by chemical transmitters like ACh, but sometimes by direct electrical triggering. It is in the nerve → muscle synapse that things go wrong in the myasthenias (see section 2, page 6).

### **The immune system**

To protect us against germs, we have several cooperating systems.

'General' ones include blood proteins that help to destroy either germs, rubbish or our own normal cells as they die (which happens all the time).

These proteins are helped by cells ('phagocytes') that eat up rubbish.

'Specific' defences include '**T cells**' and '**B cells**' which are each tailor-made to recognise only one target – usually a foreign germ, but

occasionally, alas, our own molecules or cells in auto-immune diseases like MG, thyroid disease and young-onset diabetes. The B cells' main job

is to release **antibodies**, proteins that travel around in the blood and specifically latch onto their targets so that they get destroyed quickly.

## GLOSSARY

**Acetyl-Choline (ACh)** is a chemical transmitter released from nerve endings = 'ignition key(s)' [see Figure 1, page 6]. It is far too small to be seen on any microscope.

**Acetyl-Choline Receptor (AChR)** is the 'ignition lock' on the nearby muscle surface [see Figure 1, page 6]. When ACh binds to it, it opens up channels into the muscles, allowing salt (Na<sup>+</sup>) to enter and trigger the muscle into action. Like other large proteins, AChRs can just be seen on the most powerful (electron) microscopes.

**Acetyl-Choline Esterase (AChE)** is a protein near the AChRs that destroys any spare ACh [see Figure 1, page 6].

**Anti-choline esterases** are drugs that block AChE, so that any ACh lasts longer/has a better chance of triggering [see Figure 1, page 6]. These drugs include pyridostigmine (long-acting; trade name Mestinon<sup>®</sup>), neostigmine and Tensilon<sup>®</sup> (short-acting; Edrophonium).

**Antibodies** are proteins tailor-made to destroy germs or block toxins. They are made by 'B cells' (from the bone marrow) and travel around in the blood and tissue fluids [see Volume 5].

**Antibody negative MG** is a bad name, because these patients do have typical MG, and it is caused by antibodies, but not against the AChR. In about half of them, antibodies instead recognise another muscle target called MuSK.

**Apnoea/apnoeic attack**, the sudden stopping of breathing.

**Autoimmune diseases** are caused by cells or antibodies that can attack our own tissues or cell products.

**Azathioprine (Imuran<sup>®</sup>)** is a drug that generally suppresses immune responses, particularly of T cells [see section 4, page 14].

**B cell(s)** are immune cells from the bone marrow [see Volume 5]. When their surface-bound antibodies recognise their particular target or germ, they release more of these antibodies to destroy it.



## Appendix 2

**Bulbar** applies to the movements of chewing, swallowing, speech and breathing controlled by the lower brain stem.

**ChAT**, the enzyme that produces ACh in the nerve endings.

**Congenital myasthenia** strictly means that it can be seen at birth. In fact, some of these inherited faults in nerve → muscle triggering can start even in the teens [see section 11 and Volume 2]. While many faults are in the AChR, others are in other genes involved in triggering.

**Cyclophosphamide** is a drug that generally suppresses immune responses, used in patients who can't take more standard immuno-suppressants.

**Ciclosporin A** is a drug that generally suppresses immune responses, especially of 'T cells' [see, section 4, page 14].

**DAP**, '3,4 diamino-pyridine' is a drug used to boost ACh release from nerve endings in the LEMS and some congenital myasthenias [see Volume 5 ].

**Diplopia**, double vision.

**Diuretic**, causing an increased output of urine.

**Dominant**, an inherited feature like brown eyes that shows itself even when you have only one copy of the gene, and is evident in about half your offspring.

**Dysarthria**, difficulty in getting words out – i.e. in the movements of speech rather than in finding the right word in your brain.

**Dysphagia**, difficulty in chewing/swallowing.

**Dyspnoea**, difficulty in breathing or shortness of breath.

**EMG = electromyography**, where nerves are stimulated electrically, and the resulting (electrical) impulses are measured in the muscles they supply. EMG helps Neurologists to sort out different congenital myasthenias and LEMS from 'immune' MG [see section 3, page 9].

**Gene**, inherited blueprint for one natural protein; made of DNA.

**Imuran<sup>®</sup>**, see Azathioprine.

## Appendix 2

**Ivlg, intravenous immunoglobulin:** i.e. injecting (slowly into a vein) the antibody fraction pooled from normal blood. For unknown reasons, that improves many autoimmune conditions [see section 4, page 11].

**LEMS, Lambert-Eaton Myasthenic Syndrome,** is caused by antibodies against nerve endings [see page 23 and Volumes 2 and 5].

**Mestinon<sup>®</sup>** is the commercial name for Pyridostigmine.

**Methotrexate** is a drug that generally suppresses immune responses, used in patients who can't take more standard immunosuppressants [see section 4, page 14].

**Muscles** are long tubes of proteins woven together; when triggered, they shorten ('contract'), so pulling bones ('voluntary' muscles), or narrowing tubes (e.g. the involuntary muscles in the guts, bladder, blood vessels and heart). Muscles and nerves are made up of huge numbers of (much smaller) cells.

**Mutation,** an inherited change in any gene.

**Myasthenia,** disorders causing weakness of voluntary muscles.

**Mycophenolate Mofetil (Cell-Sept<sup>®</sup>)** is a drug like azathioprine that generally suppresses immune responses, especially of T cells.

'**Neonatal MG**', the term used when MG in a newborn baby is caused by antibodies from its mum [see sections 1.5 and 6 and Volume 5]. Luckily, it only happens with about one in eight of MG mums.

**Nerves** relay electrical impulses from sense organs (e.g. eyes and skin) to the brain and spinal cord or from there to muscles and glands. They relay the signals to other nerves or muscles at special junctions, and switch them either on or off. Sometimes, they act more like dimmer switches, telling things to work harder or slower.

**Ocular MG** is MG affecting only the eye movements, and not other muscles (nor eye focussing).

**Plasmapheresis** or **plasma exchange**, means washing the liquid fraction out of the blood, to remove the antibodies, and then giving the red cells back in an artificial fluid.

## Appendix 2

**Prednisone, Prednisolone**, synthetic steroid drugs (like those from the adrenal glands) that generally suppress immune responses.

**Propantheline** is a drug like atropine that cuts down the side-effects of pyridostigmine on the guts.

**Pyridostigmine** is a drug that blocks the breakdown of ACh (by AChE), giving it a better chance of triggering the muscles (Fig 1, p 6).

**Quinidine** is a drug that partly blocks the AChR, and is used to limit the harmful effects of some congenital myasthenias. Related to quinine (from a tree bark), it was used to treat malaria (it's still in tonic water).

**Strabismus**, squint.

**Synapse**, any junction between a nerve and another nerve, a muscle or a gland. Signals can be passed either by chemical transmitters like ACh, or by direct electrical triggering.

**T cell(s)** are immune cells (from the thymus). Like antibodies, they also recognise foreign germs; they can either directly attack infected cells or recruit other cells to do that instead ('inflammation'). They are also needed to help switch 'B cells' on to make antibodies [see Vol 5].

**Tensilon® (Edrophonium)**, a short-acting anti-AChE drug; for diagnosing myasthenias, it is injected into a vein and the resulting increase in muscle strength is measured [see AChE and Figure 1, page 6].

**Thymus**, a 'factory' that produces immune 'T cells', especially before age 40, and exports them to the rest of the body. It lies between the breastbone and the heart. It may be involved in starting the immune reaction against the AChR [see Volume 5]; removing it – **thymectomy** – seems to improve the MG in some young-onset patients.

**Thymoma**, a tumour of the thymus found in around 10% of MG patients. It may somehow auto-immunise in MG [see Volume 5].

**Vaccine**, a germ (or germ product) made harmless. Still recognisable by 'T and B cells', it can be injected in advance, so stimulating these cells to multiply and forearm us before the real menace comes along.

**VATS**, video-assisted thoracoscopic thymectomy (via 'keyholes').



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February 2012