Myasthenia Gravis Association

INFORMATION PACK
Volume 2
A Medical Guide for Patients with LEMS

3rd Edition

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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.

[1-4 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*

INFORMATION ABOUT MYASTHENIA GRAVIS AND RELATED DISORDERS: foreword to first edition

"The Myasthenia Gravis Association (MGA) has 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

CONTENTS

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 2
A Medical Guide for Patients with LEMS

About this Guide

The Lambert-Eaton Myasthenic Syndrome (LEMS)

The Myasthenias come in three types. The main problem is painless weakness of voluntary muscle caused by ***faults in nerve → muscle triggering*** (see Figure 1 on page 4) in each of them. Beyond that, they are very different. Much the commonest of the three is Myasthenia Gravis (MG), which is covered in Volume 1. The subject of this Volume is the **L**ambert-**E**aton **M**yasthenic **S**yndrome (**LEMS**), caused by an immune attack by **antibodies**, this time against the nerve endings.

As each person's experience of LEMS 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 patients but also to their families, friends and anyone interested in finding out a little 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.

To assist the reader, italics have been used to *emphasise important points* and useful recurring **names** have been set in bold.

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

1
FOR THE NEW PATIENT: WHAT IT MEANS TO HAVE LEMS

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

Starting on the bright side:-

- most patients' LEMS symptoms can be brought under good control;
- if you must have a neurological disorder, LEMS is among the more treatable ones, with the least pain and the fewest major long-term snags; it very rarely causes death by itself;
- treatments are improving all the time; with your help, we are determined that this should continue;
- patients often become their own best managers, and work out their own ways of keeping their LEMS in its place.

Try not to let it take over your life.

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

- your LEMS may well be with you for many years. Don't wait for a remission – see an expert Neurologist and get treated soon;
- you will probably need some drugs to treat your LEMS. They all have side-effects, but these are greatly outweighed by the benefits in the vast majority of patients;
- in some patients, the LEMS is an early sign of a lung tumour; close/ ongoing monitoring for that raises the chances of early treatment – if any is needed.

NB The symptoms of LEMS vary so much from patient to patient that it is difficult to give general rules.

2

THE LAMBERT-EATON MYASTHENIC SYNDROME (LEMS)

The LEMS is at least five times less common than MG, so there are barely 2,000 patients in the whole UK. Although muscle weakness is the main problem, it fluctuates less than in MG. Whereas MG particularly weakens movements of the eyes, face, neck and chest, the LEMS shows a more '**bottom** ↑ upwards' pattern; the legs feel heavy – almost like walking through treacle. It can affect the arms, but less commonly the muscles of speech, swallowing, eyes or breathing. Very often, there are also problems with 'automatic' bodily functions (see ii below).

LEMS patients fall into two groups. About half of them have a 'small cell' lung cancer, which is found only in smokers; their LEMS is caused by an unusual immune reaction against the tumour cells (see below), and typically starts after age 40 years. In the others, there is no tumour; their LEMS can even start as young as 9 years old, but more often after the age of 30, and the reasons are completely unknown.

What goes wrong?

Like MG, LEMS is also caused by immune auto-**antibodies**, but these *ones cut down the release of ACh* from nerve endings (see Fig 1, page 4). As a result, muscle triggering does not work as it should.

LEMS also differs from MG in two other ways:-

i) LEMS patients often get a bit stronger as they first try harder.

ii) Because the nerve endings are similar in the guts and the bladder etc, they too get attacked by the same antibodies, so there is usually also some trouble with 'automatic' bodily functions, for example causing a dry mouth, constipation or impotence (in men), again unlike in MG.

Diagnosis can be confirmed by electrical testing of nerve → muscle triggering (electromyography; **EMG**) and by a blood test for the damaging antibodies. These are directed against calcium channels in the nerve endings and are found in around 90% of cases. It is also very important to check for lung tumours, especially in smokers. The cancer

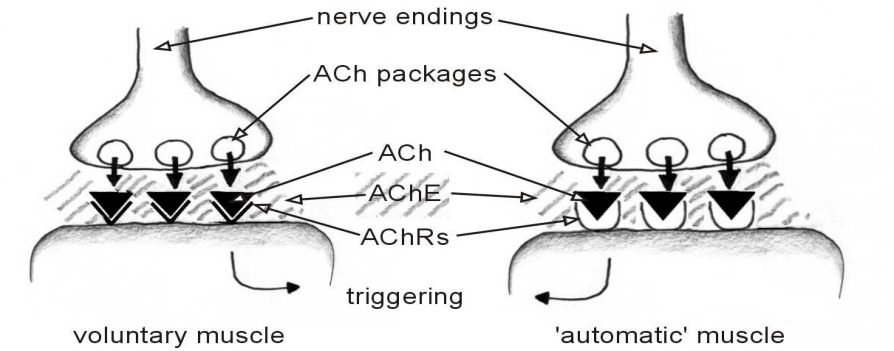
cells have rather similar calcium channels and somehow immunise the patients against their own nerve endings. When they do, the LEMS is often a valuable early warning of the tumour: what's more, its growth seems to be slowed by the immune reaction, so having the LEMS isn't all bad.

Antibodies are immune proteins that travel from the blood into the tissues, and are tailor-made by clones of 'B cells' to destroy germs or neutralise toxins. In the LEMS, for unknown reasons, rare rogue clones start making antibodies that attack your own calcium channels.

Figure 1
Diagram of nerve → muscle junctions

Electrical impulses arriving from the brain stimulate the nerves to release packages of ACh – the *ignition keys*. These cross the short gap and latch into the special *ignition locks* – the ACh receptors (AChR) on the muscles – which they then trigger. The spare ACh is broken down by AChE and then re-cycled in the nerve terminals. By blocking AChE, drugs like pyridostigmine give the ACh a longer life-span and a better chance of triggering.

The AChRs are totally different in the voluntary and 'automatic' muscles (so we've given them V and U shapes). However, the nerve endings (and AChE) are similar. Their calcium channels – which are attacked by the auto-antibodies in LEMS patients – are located right at the point of ACh release on the nerve endings.



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

Treatment

Two front-line drugs help to soup-up nerve → muscle triggering in the short-term, but without treating the underlying disease process. **Pyridostigmine** (mestinon®) blocks the breakdown of ACh, so that it lasts longer and has a better chance of triggering. Another drug – '3,4-diamino-pyridine' (**DAP**) acts by boosting the feeble ACh release – the key defect in LEMS. Each can have side-effects, but they are usually minor.

Used alone or together, these drugs may be enough to treat mild LEMS. However, many patients need more radical treatment to remove the damaging antibodies or cut down their production.

These antibodies can simply be washed out of the blood stream by **plasma exchange**, or watered-down with **IvIg**. The benefits of plasma exchange take longer to kick-in (best after 2 - 3 weeks) than in MG (3 - 5 days). With both, they gradually tail off after 6 - 8 weeks. In the longer term, you can take immune-suppressing drugs like steroids and/ or azathioprine (see pages 9 - 10). Thymectomy is not used, because the thymus isn't involved in the LEMS. In patients with tumours, treatment of the cancer must take priority; if it can be removed or destroyed, the LEMS may get better or even disappear.

3
HISTORY

Breakthroughs in MG have often paved the way for subsequent progress for the other Myasthenias. MG was first clearly described in the 17th century but it has probably always affected human beings. Indeed, it must be ancient since it also occurs in dogs and cats.

The term 'myasthenia gravis' comes from Greek (myasthenia = muscle weakness) and Latin (gravis = severe). It was recognised as a disorder of nerve → muscle ignition in the early part of the 20th century; only in the mid 1930s did (British) doctors discover the benefits of physo-stigmine (an early version of pyridostigmine). [Thymectomy was first used in MG from 1940 onwards; we still don't fully understand why it works].

An 'autoimmune' origin for MG was suggested by our late Vice-

President, Prof. Iain Simpson, in 1960. It was only proved 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 how their production is controlled. Steroids began to be prescribed regularly as treatment in the 1960s and plasma exchange was first used in the mid-1970s (see section 5).

The differences between the LEMS and MG were clearly recognised only in the 1950s, when the American physiologist **Dr Ed Lambert** (at the Mayo Clinic) noted that too little ACh is released from the nerve endings – sometimes in about half-normal amounts. However, it can build up with repeated stimulation; as many patients notice, the harder they try, the stronger they get – the exact opposite of MG.

Noting that LEMS patients often also have other auto-immune disorders, Prof John Newsom-Davis and his team tried **plasma exchange** in about 1981; to general delight, the LEMS got better. Moreover, the plasma produced similar electrical and structural defects in the muscle ignition system when transferred to mice; the damaging antibodies were first shown to recognise calcium channels in the mid-1980s by Dr Bethan Lang in the same team.

Families with **inherited myasthenias** began to be noticed in the 1930s. A key breakthrough was the identification of the AChR genes, first in animals and then (by Prof David Beeson, with MGA support) in humans in the 1980s. Finding the first faults took several years, both in David's lab and by Dr Andrew Engel's team in the Mayo Clinic (USA). Luckily, the methods improved greatly in the early 1990s. Faults in other nearby proteins were first found only in the late 1990s.

4

MORE ABOUT TREATMENTS

General common-sense things can be very effective in coping with the Myasthenias. 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. It may help if patients pace their activities so that they tackle the harder jobs when they expect to be strongest (eg, after a recent dose of their DAP), and don't exhaust themselves. While that may sound obvious,

others in the MGA will have further useful hints along similar lines.

Specific treatments

Broadly, autoimmune Myasthenias can be treated by:

A. souping-up nerve → muscle ignition;

B. reducing the damaging antibodies in the **short**-term;

C. reducing the damaging antibodies or their production in the **longer**-term.

A) DAP and **Pyridostigmine** (trade name: Mestinon®) are front-line weapons; a bit like the choke in a car, they give the (handicapped) ignition system a better chance of firing by boosting it for a few hours (see Fig 1, p 4). They may strengthen some muscles much more than others, *but they don't 'clean the plugs' – ie they don't cure the underlying immune faults*. Hence many LEMS patients need more fundamental treatment to reduce the damaging antibodies.

- **DAP** acts on the nerves; it makes their electrical signals last longer so that more ACh is released, and the chances of successful muscle triggering increase. At normal doses, it can cause short-term tingling around the mouth or in the fingers and toes. At excessive doses (not recommended), it can also affect the brain, causing anxiety, over-excitement and even epileptic fits, but that is very rare below 100 mg per day. For most LEMS patients, DAP is more effective than pyridostigmine, but combining the two is sometimes even better.

- **Pyridostigmine** (Mestinon®) blocks the breakdown of the ACh, so that it lasts longer and again has a better chance of triggering the muscle. Since its effects last only a few hours, it is more important to take it often (for example 5 times daily) 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 (that is 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). Pyridostigmine sometimes causes stomach cramps and diarrhoea; to minimise that, some patients take it with bland food such as crackers or milk. These side-effects can be prevented by taking propantheline about 30 minutes in advance.

B) Short-term treatments for reducing the levels of the damaging antibodies are important in the LEMS (as in MG). Plasma exchange and IvIg are both used when benefits are needed *urgently*. That is unusual in the LEMS, but needs might arise if the weakness is rapidly getting worse, before surgery, or while waiting for steroids to take effect. While both measures are very useful for that, neither is curative; alas, the cells obstinately go on making the antibodies, so extra immuno-suppressive drugs are very often needed.

- **Intravenous Immunoglobulin (Iv Ig)** is the easier to use and is particularly effective in LEMS patients. It means infusing the total antibodies (**Ig**), pooled from huge numbers of healthy blood donors, into a *vein* (**Iv**). It clearly does help, though *only for about 8 weeks*, alas. We don't know *how* it works; there are more theories than hard facts. (It may simply water-down the damaging anti-bodies or side-track the bystander amplifying mechanisms they recruit). It costs slightly more than plasma exchange, and it also 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 about 5 hours each day. Patients sometimes get a headache, a rash or rise in blood pressure; blood tests are used to monitor for possible effects on the kidneys.

- **Plasma exchange** is a helpful alternative, but needs more complex machinery; the antibodies are simply washed out of the blood and replaced with a plasma substitute. During a thorough plasma-pheresis, several litres of blood are removed one by one, the red blood cells are separated and then returned in an artificial substitute (human albumin and saline solution) without the antibodies. That means being in a special hospital ward for 5 days connected by an intravenous line (often in the groin) to and from the separator for around 4 hours per day. After around 2 - 3 weeks, strength reliably

improves for another 6 weeks or so, but then the benefits wear off as the antibodies are gradually replaced. It is safe, if slightly uncomfortable.

By their nature, human blood products inevitably carry low-level risks. Though very carefully screened for the known viruses (hepatitis and HIV), there is obviously a remote possibility of some new previously unsuspected agent.

C) Long-term immuno-suppression (to 'clean the plugs')

- **Prednisolone.** The first choice drug is usually the synthetic *steroid* 'prednisolone', which is taken by mouth. It generally improves the LEMS after a delay of a month or more. It lowers the damaging antibodies, and probably has many other immune-suppressing effects too.

  You probably already know that steroids can be a mixed blessing. Do remember that, in most 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. Only about 1 patient in 10 has to give them up because of the side-effects. You can find out more about them and other immuno-suppressants in Volume 5 or from your doctors, but here is a very quick run-down.

  In general, as you know, *people vary greatly*: so do their responses to steroids – both the benefits and the side-effects. The normal procedure for LEMS patients is to start with a relatively high dose and then, when the weakness has been brought under control, to cut down to the minimum needed to keep up the patient's strength. 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. Alas, very few manage to cut it down to zero.

  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 (for instance by avoiding big crowds), you can usually keep that risk low without spoiling your social life.

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** (for example injury or appendicitis). Because the doses given are so unnaturally high, they shut the adrenal glands off; hoping to avoid that, many doctors give them every other day. Even so, patients may no longer be cushioned against these stresses, and may collapse suddenly. So *cutting down the dose always has to be done in small steps*. For all these reasons, everyone taking 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, many of which can be prevented or treated. They include: weight-gain, mood changes, sleeping troubles, diabetes and high blood pressure, skin changes (including thinning, easy bruising, slow healing and unwanted hair growth), glaucoma and lens cataracts; especially also bone-thinning and stomach ulcers, which can each be prevented with other drugs.

- **Azathioprine (Imuran®)** This drug also reduces antibody production, but takes about a year to 'kick in'. It is sometimes used by itself for patients who can't quite manage on DAP or pyrido-stigmine alone. More often, it is used to enhance the benefits of steroids, and/or to use them at lower doses ('steroid-sparing'). After that, the dose of azathioprine itself is tapered down to the minimum needed to control the symptoms. For several reasons, steroids may be used alone, without azathioprine, in patients with lung tumours.

  Azathioprine's side-effects include allergies; also liver damage and bone marrow suppression, for which regular blood tests are needed around every week at the start and every 3 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 the long-term, skin cancers are

somewhat more common in people taking Azathioprine, *so they should be careful about sun-exposure. Usually the benefits far outweigh these hazards.*

- **Other immuno-suppressants** can be used if need be. Ciclosporin may help if Azathioprine hasn't been a success even after being given a fair chance (ie after at least one year). Other alternatives include mycophenolate mofetil, methotrexate and cyclophosphamide, which are usually kept in reserve for people who can't take the above front-line drugs. These others are less well tried-and-tested than steroids, especially in the LEMS, and have their own side-effects too, partly because they are stronger immuno-suppressants.

Drug interactions

The target for the damaging antibodies in LEMS is a calcium channel in the nerve endings; drugs like Verapamil and Diltiazem block these channels. They are used often to treat high blood pressure, and occasionally by anaesthetists, but they should be avoided in LEMS as they can make it worse.

Vaccines

Two warnings for people taking significant amounts of immune-suppressing drugs (more than 20 mg prednisone on alternate days):-

i. Remember always to mention what you are taking before you are given any vaccines; a good rule of thumb is that live attenuated vaccines should be avoided, while the other (killed) types are safe:

ii. It may be wise to discuss with your doctor whether you should be immunised against 'flu each autumn (and even pneumonia).

5

SPECIAL ISSUES (SEE ALSO VOLUME 5)

Some issues arise only rarely in the LEMS – especially if it is well controlled – because it seldom affects either young women or the muscles used in the mouth, in the throat or in breathing.

It is vital that your doctors/ midwives are told in advance about your LEMS, in case it affects any of the items listed below. If needed, ***there is more information on each of them in Volume 5***.

A Pregnancy

In pregnancy any drugs should ideally be used as little as possible. However, it is important for mums to keep strong. If necessary, pyridostigmine, steroids and azathioprine are safe. The baby may be weak for 1 - 3 weeks after delivery, but can also be treated with pyridostigmine if necessary.

B Dentistry

It helps to book appointments for whenever you expect your strength to be greatest, and to keep them short. If there are difficulties in opening or closing the mouth, in holding the head up, or in swallowing, the dentist can provide helpful props. In general, **infections** can aggravate the LEMS, so it's important to keep the teeth well cleaned/ flossed to prevent tooth abscesses.

C Anaesthetics

The myasthenias rarely cause problems nowadays; that's partly because anaesthetists are much more aware of them; it's also thanks to better preparation, monitoring and treatment.

In theory, it's possible that patients whose LEMS has not yet been diagnosed might fail to perk-up after operations in which muscle relaxants have been used – as they are extra-sensitive to them. Also, as noted above (end of Section 4), the calcium channel blockers that some anaesthetists like to use can make the LEMS worse.

Appendix 1

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** (for example table salt, consisting of sodium and chloride atoms). Many molecules in living things are much bigger than salt – 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 raw egg white, containing various salts, sugars and small building blocks that are combined to form proteins, fats and sugary carbohydrates. Inside this solution is the nucleus, the 'brain' of the cell; it is where 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, in all our cells; some can transport molecules like oxygen, as does the red protein haemoglobin in our blood; others can transport food substances (e.g., glucose) into our cells from outside; some can act as surface **receptors** for outside signals, as does the AChR, the key target molecule in MG; others can themselves act as messengers (as insulin does when it binds to insulin receptors); some can move other cells (as muscle proteins do); one can even turn chemical energy into light. In general, they are highly specialised, and often recognise other chemicals very specifically.

The difference between one protein and another lies in its exact combination – and order – of different building blocks. These come in twenty different shapes, and are strung together in an exact order (sequence); nearly every link in the chain has to be just right. A single mistake at one key point can be a 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 are made up of huge numbers of much smaller cells.

Nerve cells relay electrical impulses from sense organs (for instance 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 (ie woven together); when triggered, they shorten ('contract'), so pulling bones ('voluntary' muscles), or narrowing tubes (for example 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 just 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. Nerve → muscle synapses are where the weakness arises in the Myasthenias (see Section 2, page 4).

The immune system

To protect us against germs, we have several co-operating 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 autoimmune 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 4]. 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 4]. When ACh binds to it, it opens up channels into the muscles, allowing salt (Na+) 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 4].

Anti-Choline Esterases are drugs that block AChE, so that any ACh lasts longer and has a better chance of triggering [see Figure 1, page 4]. These drugs include pyridostigmine (long-acting; trade name Mestinon®), neostigmine and Tensilon® (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 immune cells or antibodies that sometimes attack our own tissues or cell products.

Azathioprine (Imuran®) is a drug that generally suppresses immune responses, particularly of T cells [see Section 4, page 10].

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.

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, evident from birth.

Cyclophosphamide is a drug that generally suppresses immune responses, used in patients who can't take more standard immuno-suppressants [see Section 4, page 11].

Ciclosporin is a drug that generally suppresses immune responses, especially of 'T cells' [see Section 4, page 11].

DAP, **3,4-diamino-pyridine**, is a drug that makes the nerve impulses last longer, leading to more ACh release from their endings [see Section 4, page 7].

Diplopia, double vision.

Diuretic, causing an increased output of urine.

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 experts to sort out LEMS from other myasthenias.

Gene, inherited blueprint for one of our natural proteins; genes are made of DNA.

Imuran®, see Azathioprine.

IvIg, intravenous immunoglobulin, injecting (slowly into a vein) the pooled antibody fraction from normal blood. For unknown reasons, that improves many autoimmune conditions [see Section 4, page 8].

LEMS, Lambert-Eaton Myasthenic Syndrome, caused by antibodies against nerve endings.

Mestinon® is the commercial name for Pyridostigmine, a choline-esterase inhibitor.

Methotrexate is a drug that generally suppresses immune responses, used in patients who can't take other immuno-suppressants [see Section 4, page 11].

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

Myasthenia, disorders causing weakness of voluntary muscles.

Mycophenolate Mofetil (CellCept®) is a drug like azathioprine that generally suppresses immune responses, especially of 'T cells'.

Nerves relay electrical impulses from sense organs (for example 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 guts or glands to work harder or slower.

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 (see Section 4, page 8).

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 automatic muscles and glands, e.g., in the guts.

Pyridostigmine, an anti-choline esterase drug, also called Mestinon®.

Strabismus, squint.

Synapse, any junction between a nerve and another nerve, a muscle or a gland. Signals are usually relayed by chemical transmitters like ACh, but sometimes by direct electrical triggering instead.

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

Tensilon® (edrophonium) is a short-acting anti-AChE drug; for diagnosing Myasthenia, it is injected into a vein and the resulting increase in muscle strength is measured [see AChE and Figure 1, page 4].

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 breast-bone and the heart. It may be involved in starting the immune reaction against the AChR [see Volume 5]; removing it – thymectomy – seems helpful in some patients with young-onset MG but not LEMS.

Thymoma, a tumour of the thymus found in around 10% of MG patients, that 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.

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