

Myasthenia Gravis Association



Facts about MG for Patients and Families

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FACTS ABOUT MG FOR PATIENTS AND FAMILIES

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). The term ‘myasthenia gravis’ comes from Greek (myasthenia = muscle weakness) and Latin (gravis = severe). It was recognised as a problem in nerve → muscle (nerve to muscle) triggering early in the twentieth century, and the benefits of drugs like neostigmine (a cousin of Mestinon[®]) were first shown in 1934. Thymectomy (removing the thymus gland) came into general use from about 1940, but we still don’t fully understand why it works.

In 1960, Prof. Ian Simpson suggested that there is an immune attack on the patients’ own nerve → muscle junctions. Only in 1973-5, however, did Drs Jim Patrick and John Lindstrom (in the USA) first find the damaging immune ‘antibodies’ against the muscle ‘ignition system’, a finding confirmed by many others since then. Steroids first became regular treatment in the 1960s, as for other ‘autoimmune’ disorders, and plasma exchange from the mid-1970s.

WHO GETS MG?

MG can start from the age of one year to extreme old age; it may be getting more common in the elderly. It rarely strikes twice in the same family; even the identical twin of an MG patient has only about a 1 in 5 risk of getting it too.

All races are susceptible to MG, but the pattern of the disease can differ. For example, MG confined to eye muscles (‘ocular MG’) is more frequent in very young Chinese and Japanese patients.

WHAT ARE THE SYMPTOMS?

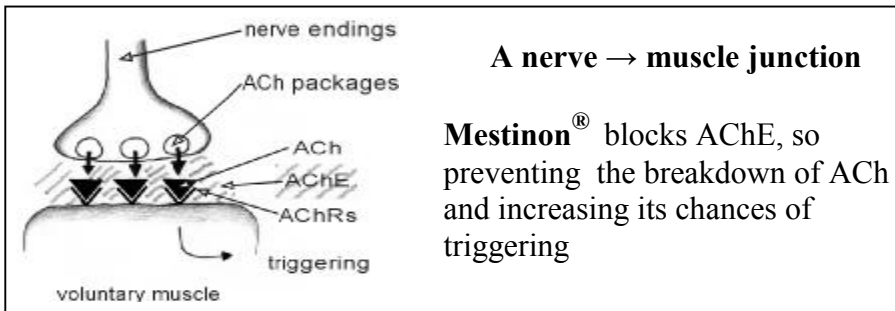
The classic symptom is weakness of the ‘voluntary’ muscles; it increases the more the muscles are used, and is painless. Strength improves after a period of rest. Any muscle that is under voluntary control can be affected. In many patients, muscles that move the eyes or hold the eyelids open are the first affected, causing double vision and drooping of one or both eyelids, but not trouble with focussing. In others, the first symptom may be weakness when smiling, speaking, chewing, swallowing or holding the head up or even of the limbs.

Sometimes it remains purely ocular, but more often it spreads to weaken other muscles. In more severe cases, breathing muscles can be affected, demanding use of a ventilator. The weakness often varies during the day and is usually worse in the evening.

Patients may find their weakness gets worse at times of emotional stress, for example when they are anxious or angry (or before a woman's monthly period). That does not reflect any underlying change in the disease process itself – but this **can** happen during infections. If so, it may affect swallowing or breathing and even cause a myasthenic crisis – which requires immediate admission to hospital.

WHAT CAUSES THE WEAKNESS?

The problem in MG is in nerve → muscle ‘ignition’. When we decide to make a movement, the brain sends electrical signals along the motor nerves right down into the relevant muscles. When these reach the nerve → muscle junction, a chemical transmitter - acetylcholine (ACh), the ‘*ignition key*’ (the black triangle ▼ in the diagram) - is released from the nerve endings. It immediately crosses to the muscle surface, where it latches into special ‘ACh receptors (AChR)’ – ‘*ignition locks*’. That, in turn, causes electrical changes in the muscle that make it contract. The spare ACh is broken down by ACh esterase (AChE), which allows the muscle to relax (see diagram).



In MG, the muscles have fewer receptors (AChRs) due to a faulty immune system, and are less easily triggered, causing weakness. Our defence or immune system protects us against ‘invaders’ like viruses and bacteria, partly by making antibodies that destroy them. Normally, it does not attack our own tissues. For unknown reasons, a few ‘autoantibodies’ in MG patients turn against their own muscle AChRs

and destroy them. So MG is one of the family of ‘autoimmune’ diseases – which also includes ‘young-onset’ diabetes, thyroid disease and rheumatoid arthritis.

WHAT CAUSES THE PRODUCTION OF AUTOANTIBODIES IN MG?

There is a lot we don’t know, but there are some clues. Our immune systems are inherited just like the colour of our eyes, for example. Similarly, just as eye colour differs between individuals, so does the immune system. Some people are particularly prone to make autoantibodies, and other autoimmune diseases are a little more common in MG families than in others. The few rogue ‘immune genes’ so far identified only raise the risk of MG rather modestly.

So what else has to happen? Many of us suspect there must be outside provoking factors such as an infection. In fact, the clearest example is the drug D-penicillamine that is sometimes used to treat rheumatoid arthritis. Around 1 treated patient in 20 develops myasthenic weakness with typical antibodies to the AChR: both disappear when the drug is stopped. But about 10% of MG patients have a tumour of the thymus gland (a thymoma), which also seems somehow to trigger an immune reaction. In others whose MG begins before age 40, the thymus is invaded by lymph gland-like nests of antibody-producing cells, but whether their MG is actually kick-started there is still not clear.

HOW IS MG DIAGNOSED?

The patient’s account of their symptoms and the typical weakness found on testing their strength both usually ring bells for any doctor familiar with MG. But you may well be your GP’s first-ever case of MG, because it is quite rare. So it is easily overlooked, especially as it varies so much with time.

A blood test for antibodies to the AChR confirms the diagnosis, although it may take 1 - 2 weeks to get the result. However, about 15% of typical MG patients have antibodies to other targets, including one called ‘MuSK’. These somehow cause a similar loss of AChRs, and can now be tested too.

Another very useful test is electromyography (EMG), where the muscle response to electrical nerve stimulation is recorded. In MG, it

typically gets smaller over the first few stimuli. ‘Single fibre EMG’ is the most sensitive test for sorting out the various possible defects in nerve → muscle ignition.

Finally, we can measure the increase in muscle strength after giving anti-myasthenic drugs (see below) – either injecting a short-acting form (Edrophonium = ‘**Tensilon**[®]’) or giving a longer-acting version (Pyridostigmine = ‘**Mestinon**[®]’) by mouth.

SOME SPECIAL ISSUES

During pregnancy, few MG women notice any increase in their weakness, though some may do so for a few months afterwards.

The babies born to about one MG mother in eight have MG weakness at birth. This ‘neonatal myasthenia’ is caused by transfer of the damaging (anti-AChR) antibodies to the baby along with all the others that protect it from infections. As these antibodies gradually disappear, the babies recover, usually in 3 weeks or so. Neonatal myasthenia may be less common now, because of improved treatment.

WHAT ARE THE TREATMENTS?

The first-line drug is Mestinon[®]. It blocks the AChE that normally destroys ACh, so that the ACh lasts longer and has a better chance of triggering. It can also cause over-activity of the ‘automatic’ muscles in the guts and glands (e.g. drooling, diarrhoea and stomach cramps). In even larger doses, it can actually make the MG worse.

When there is a thymoma, it should usually be removed to prevent local invasion; luckily, these tumours are usually **not** highly malignant. Alas, removing them seldom improves the MG. On the other hand, thymectomy does seem to help patients with generalised MG beginning before the age of 45 years who have detectable antibodies in their blood and who do not have a thymoma. About a quarter can expect to recover fully over the next 1-3 years, a half to improve and a quarter to be unchanged, after thymectomy.

If the MG still hasn’t improved, or thymectomy is not suitable (e.g. for older patients, or those without antibodies to AChR), immune-suppressive drugs are often prescribed. Prednisolone (a ‘steroid’) is sometimes given alone, especially in ocular MG. In patients with

generalised MG, it is quite often combined with another immunosuppressive drug, azathioprine (Imuran[®]), to help us get away with lower doses of steroids. Steroids can take a few weeks – and azathioprine many months – to kick-in, especially in severe cases. Once the MG is controlled, the dose can often be cut down in steps.

Two treatments are used to tide over acute bouts of weakness. First, plasma exchange (‘plasmapheresis’) washes the antibodies out of the blood stream (while the red cells are given back). It usually improves the MG for four to six weeks. So do intravenous infusions of immunoglobulin (‘IvIg’), the antibody fraction pooled from healthy donors. IvIg is often used now, but we don’t know how it works.

WHAT IS THE OUTLOOK?

The current treatments for MG are so effective that most patients can now expect a marked improvement in their symptoms. These may even disappear, though most patients need some drugs to keep them away. These drugs can have side-effects, but, overall, they do much more good than harm.

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 seem to be getting more common in older people, especially men? Ideally, we need more selective treatments to target only the damaging immune cells without clobbering all the others that are protecting us against infections. The answers to such questions demand further research, but the enormous advances in understanding and treating MG over the last 25 years encourage us to believe that the future for people with myasthenia is bright.

Acknowledgements

Our thanks to Professor John Newsom-Davis who wrote the original text in 1999, to Professor Nick Willcox for bringing it up to date in 2003 and to Dr Ian Spreadbury for providing the Diagram.

Whilst the MGA is unable to endorse any product or company, it is grateful to Valeant Pharmaceuticals Ltd for sponsorship of this leaflet. We are also grateful to our authors who write impartially, give their services totally free and do not receive any funding from Valeant, or other pharmaceutical companies.

The Information Pack

The Board of Trustees of the Myasthenia Gravis Association has approved the following publications, for supply, free of charge, to sufferers of Myasthenia Gravis 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 those people who have been diagnosed with the condition.

Volume 2 - A Medical Guide for Patients with LEMS or Congenital Myasthenia

Medical Information on LEMS and Congenital Myasthenia for those people who have been diagnosed with these conditions.

Volume 3 - Additional Information for Myasthenic Patients

Information on complementary treatments.

Volume 4 - General Information for Myasthenic Patients

Information of general assistance to people with myasthenia, including Driving and the DLA, the DSS, prescription charges, insurance and other helpful organizations and Charities.

Volume 5 - Medical Information (Medical Professionals)

Information for people working in the medical profession. Details of Myasthenia Gravis, LEMS and Congenital Myasthenia with a greater emphasis on the neurological effects and drug information.

Volume 6 - Medical Articles

Extracts from medical articles published in the MGA Newsletters.

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



Myasthenia Gravis Association
First Floor, Southgate Business Centre
Normanton Road, Derby,
DE23 6UQ

Tel: 01332 290219, Fax: 01332 293641,
Freephone: 0800 919922 (UK)
1800 409672 (Eire)
Web Site: www.mgauk.org.uk
Email: mg@mga-charity.org

MGA is a Registered Charity No. 1046443

April 2005