EUROMYASTHENIA

Public Health

Second Meeting

Friday 14 December 2007

Maastricht School of Management, The Netherlands

Second Year Meeting

Friday 14 December 2007

Maastricht School of Management, The Netherlands

Programme

14:00-14:15	*A short tribute to John Newsom-Davies*
14:15-14:30	**Introduction.** *EuroMyasthenia Coordinator* ***Sonia Berrih-Aknin*** *(Paris)*
14:30-14:50	***WP1:*** *Our achievements in network coordination and communication* ***Nicole Kerlero de Rosbo*** *(Paris)*
14:50-15:10	***WP2 and 3****: Dissemination of the results and evaluation of the project: results of the pilot questionnaires.* ***Socrates Tzartos*** *(Athens)*
15:10-15:40	***WP4:*** *MG European database: where are we ?* ***Fulvio Baggi*** *(Milan)* *Reports on the MGFA Clinical Research Standards Meeting* ***Renato Manteggaza*** *(Milan)*
15:45-16:00	*Coffee break*
16:00-16:15	***WP6:*** *Psycho-socioeconomical determinants: first results of the survey* ***Angelina Maniol*** *(Oslo)*
16:15-16:40	*How can we help or be helped by the collaborating Partners ?* *The French MG card, an example for the European MG Card – AFM* ***Marguerite Friconneau*** *(Paris)* *Situation of MG patients in Romania. Romanian MG Association.* ***Nadia Radulescu*** *(Bucarest)* *An overview of MG in Poland.* ***Anna Kostera-Pruszczyk*** *(Warsaw)*
16:40-17:00	*General Discussion including comments from the Advisory Board* ***Don Sanders*** *(Durham, USA)*
17:00-17:15	*Concluding Remarks: the future of the Euromyasthenia network* ***Sonia Berrih-Aknin*** *(Paris)*

List of the participants
Euromyasthenia Meeting
Friday 14 December 2007
Maastricht, The Netherlands

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Advisory Board

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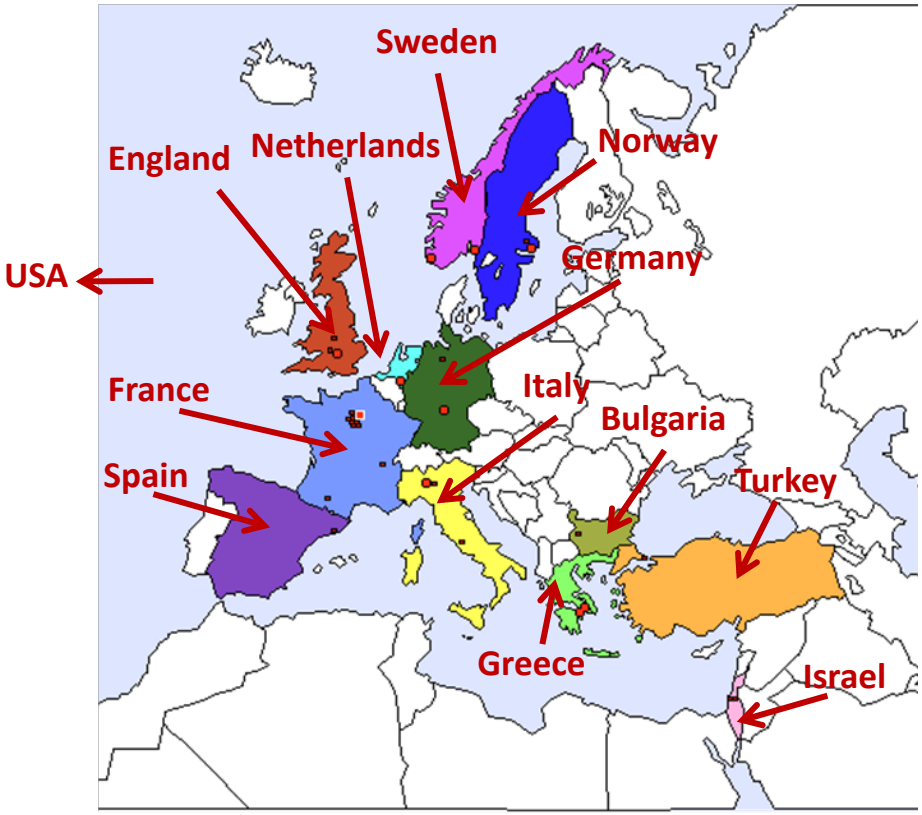
Coordination and Communication of the project

Partner UPS

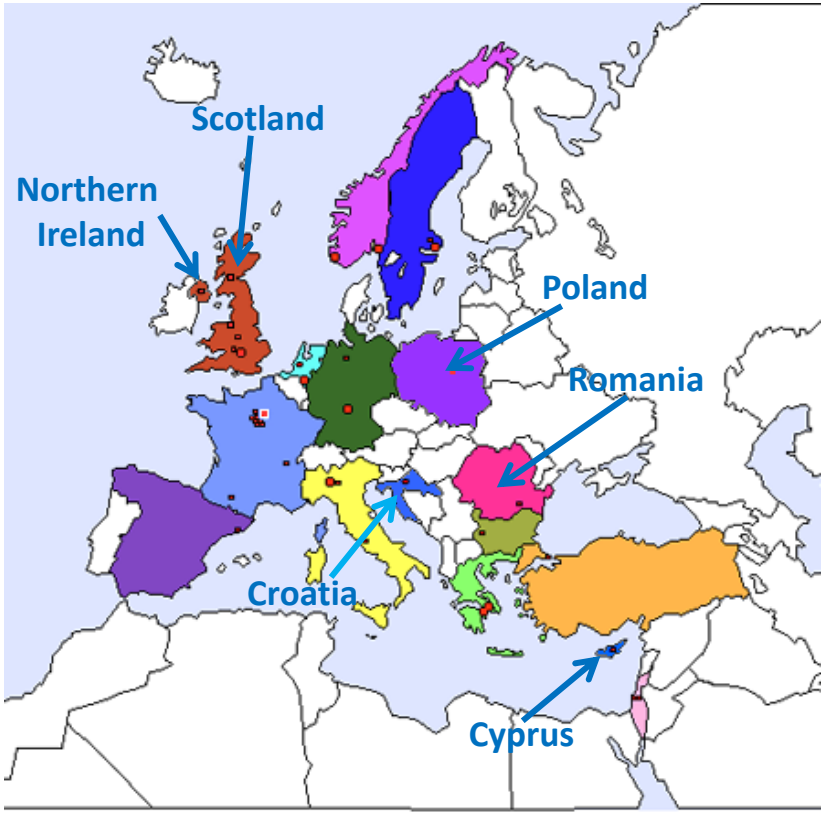
Incorporation of new Collaborating Partners

2006
13 countries



10 Associated and 21 Collaborating Partners

2007
19 countries

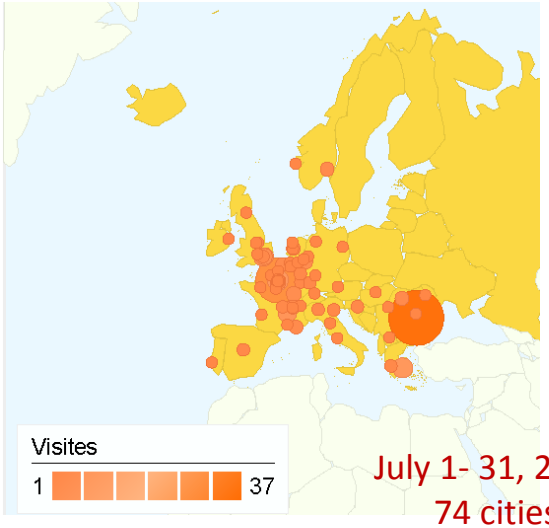


10 Associated and 33 Collaborating Partners

Analytics of the EuroMyasthenia website

1. How many visits?

2. From where?



July 1- 31, 2007
74 cities

3. Accessed how?

	% Access through:		
	Direct	Search engine	Referring site
July	28.08	34.93	36.99
August	21.79	32.96	45.25
September	30.80	34.95	34.26
October	22.76	37.31	39.93
November	39.40	32.27	28.29

4. Looking for?

Key words used: EuroMyasthenia
Names of MG specialists
Myasthenia
Names of patient associations
Others, i.e. John Newsom-Davies

Average No. pages loaded/visit :
4.5 for the period June-November 2007

Questionnaires (-MG patients -Neurologists)
Information booklet on MG for patients

Partner HPI

For EuroMG

Partner: Hellenic Pasteur Institute (HPI). Responsible: Socrates Tzartos
(Main collaborators: Konstantinos Poulas and Anastasia Sideri)

During the second year we performed the following:

1. **Questionnaire to MG patients**. A Questionnaire with 20 carefully chosen questions about the current status and the expectations of the MG patients from this network was formed, improved by several partners, tested on a few patients, and sent to all partners for delivering it to MG patients after translation into local languages. 199 replies from 3 counties have been collected and their preliminary analysis will be presented. Patients expect more information on their disease from EuroMG and 88% of them are willing to provide blood for research purposes. Significant variations between countries exist on the management of the disease.
2. **Questionnaire to neurologists**. A Questionnaire with 19 carefully chosen questions about the difficulties and problems of the clinicians while working with MG patients was formed, tested on a few neurologists, improved by several partners, and was sent to all partners for delivering it to the doctors. Preliminary data will be presented. Doctors seem interested for EuroMG.
3. **Booklet for MG patients**. The booklet with useful information on MG appropriate for the MG patients is at the final stages of finishing. It has been reviewed and improved by several partners. Recently it was decided that the booklet should include a group of questions and answers of practical use for the patients.
4. **Newsletter of EuroMG**. Five Newsletters have been delivered with MG-relevant information, including minutes of the 11th International Conference on MG and obituaries for the two major loses of the MG community, Professors John Newsom-Davis and Ann Kari Lefvert.
5. **Evaluation and Advisory Board of EuroMG**. Four eminent scientists with interest on MG were invited and kindly accepted to participate in the Board: Professor Donald Sanders, Professor Harmut Wekerle, Dr. Matilde Leonardi; the forth was the late Professor John Newsom-Davis
6. **Research** towards the development of an antigen-specific therapy for MG, towards the development of a very sensitive diagnosis, and towards understanding the mechanisms of action of the anti-AChR antibodies has been progressed.

The Euro Myasthenia Network

(www.euromyasthenia.org)

What is Euro Myasthenia;: It is a recently created Network funded by the European Union with the aim to enhance knowledge on Myasthenia Gravis (MG) and disseminate information towards improved classification, diagnosis, and therapy of the disease.

Who is included in the network;: More than 30 collaborating partners from at least 14 countries, including researchers and clinicians with special interest in MG, as well as associations of MG patients.

What is the objective of Euro myasthenia;: The development of strategies and mechanisms for exchanging information between the participating network partners and promoting the results of their research to MG patients and medical personnel.

What are the tasks of Euro Myasthenia;

1) **Creation of a website (www.euromyasthenia.org)** open to all citizens that will promote the exchange of data. **Electronic newsletters** regularly sent to all members of the network, and which can be freely downloaded from the website, will provide insight in latest research results and the progress of the Network towards its goals.
2) **Collection of epidemiological data** from patients of the many participating countries, taking into account relevant aspects, for the identification of health indicators associated with MG-causing mechanisms.
3) **Creation of a European database** containing all relevant data for epidemiological studies.
4) **Establishment of guidelines** for the diagnosis and clinical management of MG.
5) **Establishment of a European Card** for MG patients describing their clinical status and detailing which drugs may be hazardous or forbidden.

This program should result in **improved healthcare quality for the patients.**

To help in this endeavor,

EuroMyasthenia needs your opinion

Please complete the following questionnaire and return it in the envelope provided as soon as you can. You can also download this questionnaire from the EuroMyasthenia website (www.euromyasthenia.org) or request it by e-mail from ……@…….

We thank you for taking the time to complete this questionnaire.

Questionnaire for Patients with Myasthenia Gravis

1. Patient Number:

2. Sex Male □ Female □

3. Age (in years):

4. Country

5. Is your diagnosis of MG definite;

Yes □ No □ Not sure □

6. By which criteria;

Antibody □ If present, do you know which: Anti-AChR □ Anti-MuSK □
Electromyography □ Clinical examination □

7. Has Myasthenia Gravis affected your work or other daily activities;

No □ Little □ Moderately □ A lot □

If yes, please specify:

8. What is your view of the quality of healthcare you are receiving;

Excellent □
Very good □
Good □
Moderate □
Poor □

9. Do you have any realistic suggestions for improvement of the relevant healthcare;

10. Have you received sickness/disablement benefits since you were diagnosed with Myasthenia Gravis;

Yes □ No □

11. Do you think there has been progress in the diagnosis and clinical management of Myasthenia Gravis patients since you have become myasthenic;

No □ Yes, some □ Yes, a lot □
If yes, please specify (if possible)

12. Are you a member of a patient association;
No □ Yes □

If not, would you like to join an association; Do you need help in finding an association;

If yes, which association;

13. a) How do you keep yourself updated on information and treatment regarding Myasthenia Gravis; (*Please mark <u>more than one</u> if needed)*

Doctor □ Internet □ Medical periodicals □
Patient groups/organisations □ Other □_____

b) Are you satisfied with the information you are receiving;

No □ Partially □ Yes □

c) What are your preferred tools for getting information;

Internet □ Meetings □ Newsletters □

14. What are your expectations from the present network for Myasthenia Gravis (EuroMyasthenia)**;**

Better communication □
More information on my disease □
A list of neurologists taking care of MG in my region □
Information on the local association of patients □
Practical advice □
Regular updates of recent developments, at the research and treatment levels and information on clinical trials □
Others….

15. Would you be ready to answer a questionnaire on psycho-socio-economical factors or other topics in relation to your disease;

Yes □ No

16. Is there any topic you think would be important to address in relation to your disease;

17. Would you be ready to participate to research in MG by giving some blood samples;

Yes □ No

18. Do you wish to receive more relevant information on myasthenia gravis;
Yes □ No

Thank you for completing this survey!

Questionnaire to MG patients

Country	No of Patients	2. Sex		3. Age	5. Years with MG?	6. By which criteria?				7. Has MG affected your work or other daily activities?				8. What is your view of the quality of healthcare you are receiving?					9. Sugge+Y111stions for improvement of the healthcare?	10. Have you received sickness/ disablement benefits
						Antibody		EMG	Clinical											
		Male	Fem			AChR	MuSK			No	Little	Moderately	A lot	Excell	Very good	Good	Moderately	Poor	Yes	Yes
	Patients	%	%	Age	Durati	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%
Greece	43	26	74	40	5	86	12	30	60	19	23	23	35	9	42	30	14	2	14	23
Romania	62	15	85	40	?	27	0	65	77	2	8	19	68	6	6	27	39	21	53	60
Sweden	94	37	63	57	15	89	0	97	100	13	29	26	33	62	26	7	1	3	0	50
Average of																				
3 countries	199	26	74	46	10	68	4	64	79	11	20	23	45	26	25	22	18	9	22	44
Males	55	26		61	10	75	2	82	85	13	24	22	42	47	22	13	15	4	15	42
Females	144		144	44	19	67	3	69	84	10	20	24	45	28	24	21	16	10	22	49

Country	11. Has there been progress in the diagnosis and clinical management of MG patients since you have become myasthenic?			12. Are you a member of a patient association?		13a. How do you keep yourself updated on information and treatment regarding MG?				13b. Are you satisfied with the information you are receiving?			13c. What are your preferred tools for getting information?			14. What are your expectations from EuroMG?							15. Would you answer a questionnaire on psycho-socio-economical factors in MG	16. Is there any topic you wish to address?	17. Would you participate to research in MG by giving blood samples?	18. Do you wish to receive more relevant information on MG?
	No	Yes, some	Yes, a lot	Yes	If not, would you like to join one?	Doctor	Internet	Medical periodicals	Patient Associations	No	Partially	Yes	Internet	Meetings	Newsletters	Better communication	More information on my disease	A list of neurologists	Information on associations	Practical advice	Regular updates	Others	Yes	Yes	Yes	Yes
	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%	%
Greece	23	42	23	16	65	77	49	2	2	21	40	33	60	23	63	33	65	51	33	58	70	5	81	14	86	98
Romania	55	31	15	65	0	48	66	11	71	10	45	45	68	35	50	47	84	50	39	81	85	15	100	32	89	100
Sweden	31	24	19	15	12	80	34	6	7	9	24	60	37	38	49	20	63	32	20	50	70	2	74	0	90	78
Average of																										
3 countries	36	32	19	32	26	68	50	7	27	13	36	46	55	32	54	33	71	44	30	63	75	7	85	15	88	92
Males	29	27	24	18	22	84	35	5	18	11	22	60	35	31	55	24	62	29	20	49	67	9	76	7	87	84
Females	40	31	17	35	26	64	52	8	29	12	39	45	58	35	51	34	73	47	32	66	78	6	87	15	90	91

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Although we ask your name and address, these will remain with the person who collects the questionnaires, whereas only the anonymous part of the questionnaire will be available to the EuroMG network.

We thank you for taking the time to complete this questionnaire.

Questionnaire for Neurologists and other Specialists caring for patients with Myasthenia Gravis

1. **Name:**

   Country & City:

   Tel.: **Fax:** **E-mail:**

2. **How many different MG patients do you see on average, per year?**

3. **What is the percentage of your MG patients above the age of 60 years?**

4. **How often does your average MG patient consult you in the context of his/her myasthenic condition?**

   Number of times per year: _____

5. **Please provide approximate percentages of your MG patients whose quality of life you would consider:**

   - Not or slightly affected: %
   - Significantly affected but tolerable (and able to work satisfactorily) %
   - Seriously affected %

6. **Please provide approximate percentages of your MG patients whose disease condition you would consider:**

   - Only ocular symptoms: %
   - Mild generalised disease: %
   - Moderate generalised disease: %
   - Severe disease: %

7. **How many of the MG patients you have managed over the past 3 year required intensive care treatment?**

8. **Which diagnostic tools do you use in addition to clinical examination?**

		Never	Occasionally	Usually	Always
a.	Anti-cholinesterase drugs (Tensilon, Mestinon, etc)	□	□	□	□
b.	Repetitive nerve stimulation	□	□	□	□
c.	Single fibre EMG	□	□	□	□
d.	Thymic examination (e.g. by CT scan or MRI)	□	□	□	□

e.	Anti-AChR antibodies	□	□	□	□
f.	Anti-MuSK antibodies	□	□	□	□
g.	Other Please specify:	□	□	□	□

9. In the case of seronegative (AChR and MuSK antibody negative) MG what test/intervention do you mostly rely on to confirm the diagnosis?

a. Repetitive nerve stimulation □
b. Single fibre EMG □
c. Tensilon/Mestinon response □
d. Immunosuppressive response □
e. Response to Plasma exchange □
f. Response to Immunoglobulin □

10. Which treatment(s) do you prescribe for your MG patients?

	Never	*Occasionally*	*Usually*	*Always*
a. Cholinesterase inhibitors	□	□	□	□
b. Prednisone	□	□	□	□
c. IVIG	□	□	□	□
d. Plasma exchange	□	□	□	□
e. Azathioprine (Imuran)	□	□	□	□
f. Cyclosporin A	□	□	□	□
g. Mycophenylate	□	□	□	□
h. Cyclophosphamide	□	□	□	□
i. Methotrexate	□	□	□	□
j. Rituximab	□	□	□	□

k. Thymectomy

i) In absence of thymoma:
Do you recommend thymectomy especially to patients with generalized MG?: (you may mark more than one)

	Never	*Occasionally*	*Usually*	*Always*
- early onset (under 45 years)	□	□	□	□
- late onset (over 45 years)	□	□	□	□
- anti-AChR antibodies	□	□	□	□
- anti-MuSK antibodies	□	□	□	□
- Double negative (both anti-AChR and anti-MuSK)	□	□	□	□

ii) In presence of thymoma:
Do you recommend thymectomy to patients with thymoma?

	Never	*Occasionally*	*Usually*	*Always*
	□	□	□	□
l) Other treatments	□	□	□	□

Please specify:

11 What is your view of the quality of healthcare your patients are receiving?

Excellent □
Good □
Moderate □
Poor □

What would you wish to improve?

12. What are the most frequent problem(s) you face in the clinical management of your MG patients?

Treatment availability □
Patients do not take therapies □
Difficulties in diagnosis □
Other □
Please specify:

13. Can you provide any suggestions for overcoming these problems?

14. **a) How do you keep yourself updated on information and treatment regarding MG?** (You may *mark more than one if needed)*

Conferences/Meetings □ Internet □
Medical Journals □ Health organisations □
Other □ Please specify:

b) Are you satisfied with the information you are receiving?

No □ Partially □ Yes □

15. What are your main expectations from the EuroMyasthenia network?
(Tick as many options as required)

- Better standardisation of MG □
- Better diagnosis of MG □
- A European MG database □
- Information on MG and current progress □
- Information on relevant meetings □
- Contact with relevant clinicians and researchers □
- Other, please specify: _____

16. **Would you be interested in receiving further information on the activities of the EuroMyasthenia network?**

No □ Yes □ Possibly, if time permits □

17. **Would you be willing to help the EuroMyasthenia Network by reading through and validating guidelines for patient management and pamphlets dedicated to informing patients about MG?**

No □ Yes □ Possibly, if time permits □

18. **Would you be interested in visiting any of the partners of the present project? <u>Or</u>: Would you be willing to attend educational and training visits to expert scientific centres?**

No □ Yes □ Possibly, if time permits □

If yes, what would you be most interested in (e.g. antibody assays, thymus pathology, other…):

19. **Do you think that an important question is not included in the questionnaire? Please specify**

……

We thank you for completing this survey!

EUROMYASTHENIA

Information on Myasthenia Gravis
for Patients and their Families

Sponsored by:

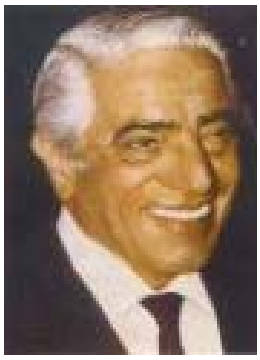
Euro Myasthenia

MYASTHENIA GRAVIS FOR THE NON-SPECIALIST

HISTORY OF MYASTHENIA GRAVIS

The term "Myasthenia gravis" (MG) comes from the Greek (myasthenia = muscle illness) and Latin (gravis = grave) languages. The first description of myasthenia gravis dates back to the 17th century when Dr Thomas Willis wrote about 'a woman who spoke freely and readily enough for a while, but after a long period of speech was not able to speak a word for one or two hours.' It became clear in the 1930s that MG is due to a defect in nerve→muscle triggering. In the 1960s, it was predicted to be an autoimmune disease, suggesting an immune attack on the person's own muscles. This hypothesis was confirmed in the mid-1970's by Drs J. Patrick and J. Lindstrom by the discovery of specific immune **autoantibodies** in most patients that damage key targets at the junction between the nerve and the muscle. The normal job of antibodies is to destroy infectious bacteria or viruses. This makes MG one of the family of autoimmune diseases, which also include thyroid disease, diabetes in the young, multiple sclerosis, rheumatoid arthritis and lupus erythematosus.

WHO IS SUSCEPTIBLE TO MG?



Aristotle Onassis: one of the famous people with MG.

MG can affect anyone, from infants to the elderly, men and women. In terms of age of onset, there appear to be two incidence peaks; in women between 20-40 years old- termed early onset MG, and in men above 40 years old- termed late onset MG. It is not inherited and occurs in about 1 out of 10,000 people. However, about 2% of all myasthenics have inherited faults in nerve→muscle triggering. In this case, the disease is named 'congenital myasthenia' and does not involve the immune system, so immunosuppressive treatments (like steroids) are completely unsuitable unlike in autoimmune MG.

Newborn babies of MG mothers can also have short-term weakness caused by the transfer of **autoantibodies** from the mother to the baby via the placenta and/ or milk. That is not common: only about 10-15% of newborns from MG mothers show symptoms, which usually improve spontaneously after about 1-3 weeks and soon disappear. The MG in the mother normally helps to rule out the presence of inherited myasthenia.

WHAT ARE THE SYMPTOMS OF MG?

The main symptom is weakness of the voluntary muscles without sensory symptoms or pain. The weakness increases the more the muscles are used (as the day progresses), i.e. it is fatiguable, but gets better after resting. It often varies from day to day/ month to month. It can also get worse quite quickly, e.g. with infections. The first muscles affected in many MG patients are usually those that move the eyes, causing eyelid drooping or diplopia (double vision). Other patients experience weakness in the face, in chewing, swallowing or speaking and/or in the neck, trunk or limb muscles. In severe cases, breathing may be so weak that the patient needs a ventilator.

Three serial pictures to demonstrate fatigue of eyelid muscles and slight squint as the patient keeps looking up. After a few minutes of rest, the eyelids have returned to near-normal position (fourth picture).

HOW DOES MG PROGRESS?

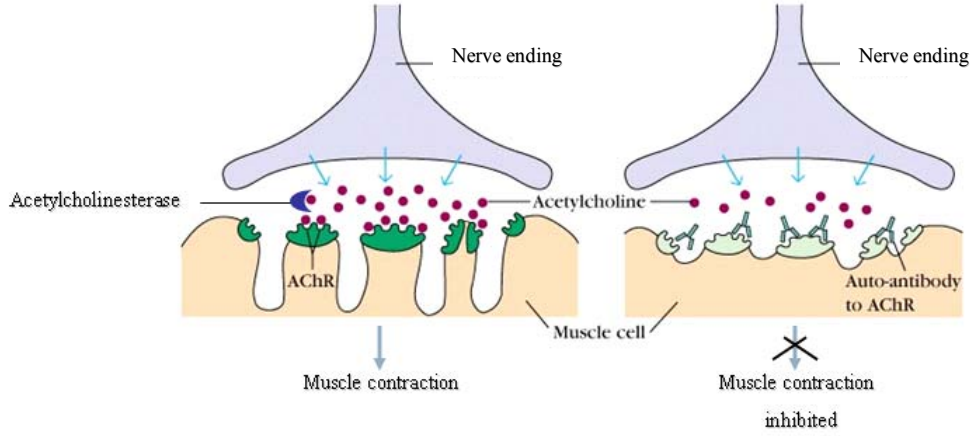
MG very often starts with eye muscle weakness. In 10-20% of patients, the weakness remains confined to eye muscles only for many years (ocular myasthenia). In the others, it starts to affect other muscle groups (listed above), usually within the first three years (generalised myasthenia). As in other autoimmune diseases, the symptoms may vary from time to time, or even go into remission in around 5% of patients per year. It was labelled 'gravis' because many patients used to die before better treatments were found in the 1930s - 1950s.

WHAT GOES WRONG?

Normal muscle function: When the brain sends an electrical signal along the motor nerves to the muscle to make a movement, a chemical transmitter – **acetylcholine (ACh)** – is released from the nerve endings. It instantly crosses to the muscle where it locks onto the **ACh receptors** (**AChR**), causing the muscle to contract. The spare ACh is broken down by ACh esterase, allowing the muscle to relax. Pyridostigmine (Mestinon®) blocks that breakdown, so that the ACh lasts longer and has a better chance of triggering.

In MG muscle, the presence of **autoantibodies** that bind to AChR causes loss of functional AChRs. Because we have very few AChRs in reserve, there are not enough of them for efficient nerve→muscle triggering. Some patients have autoantibodies to other molecules nearby the AChR in the NMJ which may indirectly act on the AChR (see below).

Normal situation **In case of Myasthenia Gravis**



Structure of the neuromuscular junction in normal and MG patients.

Problems with the immune system: It is not yet clear why the body produces these autoantibodies. There may be outside provoking factors, such as infections or drugs, but we still know very little about how and why the disease starts. Around 10% of MG patients, often between the ages of 40-60, have tumours in the thymus (**thymomas**). Thymomas are confined within the thymus gland (non-invasive) and tend to grow very slowly, but can rarely become malignant and may reappear locally many years after resection. It is therefore important that patients with thymomas have a regular follow up and worsening of myasthenic symptoms should warrant immediate examination. Furthermore, about 2/3 of the patients have milder abnormalities in the thymus, such as thymic hyperplasia in early onset MG and thymic atrophy in late onset MG. The link between thymic changes and MG is still not completely clear. Many researchers are striving to understand these processes more deeply so that they can devise better targeted treatments or even prevent susceptible individuals from getting MG in the first place.

HOW IS MG DIAGNOSED?

Clinical examination

MG can be diagnosed from the clinical history and the patient's muscle weakness, which is usually evident on examination. However, in mild cases, it may only be made obvious by testing muscle stamina, e.g. by lifting the arms time after time, or sustained up-gaze (for about 1 min) making the eyelids droop. Because MG is uncommon – and fluctuates – the diagnosis can easily be missed, especially in older people.

Presence of auto-antibodies

The diagnosis is confirmed by a blood test for anti-AChR antibodies in most patients. However, these antibodies are not found in about half of the patients with purely ocular MG and about 15% of those with typical generalised weakness; their MG nevertheless improves after plasma exchange that is used to wash antibodies away that are not detected in standard tests. We now know that, in about 1/3 of the patients who do not have anti-AChR antibodies, these other antibodies instead recognise the nearby target called **muscle-specific kinase** (**MuSK**), which is involved in clustering AChRs at the

nerve-muscle junctions. Their weakness affects the face and throat even more than in typical MG. The MG can be more severe and harder to treat in anti-MuSK than anti-AChR seropositive patients, but the thymus is often almost normal.

Electromyography and other tests
Electromyography (EMG) is a useful test of the muscle response to electrical stimulation of its nerve time after time. Typically in MG, the resulting electrical discharge in the muscle decreases progressively (~10%). Finally, the increase in muscle strength after giving ACh esterase inhibitors (see Fig. 3) can be measured before and after injecting the short-acting drug *edrophonium* (*Tensilon*® or *Camsilon*®) intravenously or by giving *pyridostigmine* (*Mestinon*®), a longer-acting version, by mouth. Once MG is diagnosed, scanning of the chest should be carried out to look for an associated thymoma. Special lung function testing that measures breathing strength can help to predict whether respiration may fail and lead to a myasthenic crisis.

HOW IS MG TREATED?

There are two kinds of treatments:

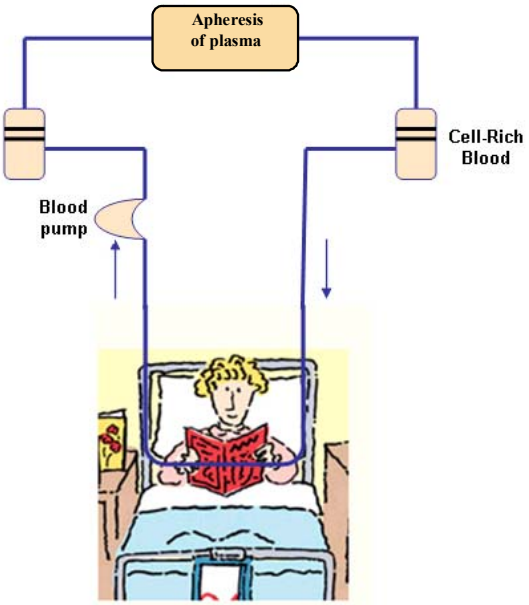
1. <u>Boosting nerve→muscle triggering,</u> mainly with *pyridostigmine* or *neostigmine*; these front-line drugs block ACh esterase, so that the ACh survives longer and has a better chance of triggering. These drugs only boost muscle triggering; many patients need something more to reduce the underlying immune reaction (see 2 below).

2. <u>Restoring AChR numbers by immune treatments by</u>:

I. Removing the damaging antibodies.

(a) **Plasmapheresis:** The simplest is plasma exchange (plasmapheresis), which is used to wash the patient's antibodies out of the bloodstream, while the blood cells are given back. It means being in hospital for about 5 days, after which the MG begins to improve. The benefits last only about 4-6 weeks because new antibodies are again produced in the patient. Plasmapheresis is especially useful when improvements are needed urgently, e.g. just before and after thymectomy, as well as while steroid treatment is being started (or sometimes while it is being continued in difficult cases). Plasmapheresis combined with steroids is recommended in severe forms of MG.

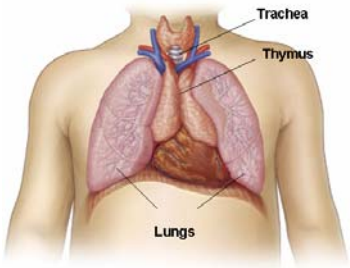
(b) **Intravenous Immunoglobulins (IvIg).** In the last few years, plasmapheresis has largely been overtaken by IvIg which means a transfusion of the antibody fraction pooled from thousands of healthy donors. That seems to work in MG by diluting or diverting the damaging antibodies. It may be used in combination with immunosuppressive drugs or when vascular access for plasma exchange is problematic. It takes longer to act than plasmapheresis, but its benefits can last several weeks. However, IvIg is very expensive and difficulties with immunoglobulin supply have been reported.



Plasmapheresis is used to remove the damaging MG antibodies.

II. Reducing antibody production.

(c) **Thymectomy.** The thymus gland plays an important role in the development of the immune system. Removing the thymus gland (thymectomy) has been used since 1940 for the long-term treatment of MG patients by re-balancing the immune system, and may lower antibody levels very slowly. Some neurologists feel that it helps patients with MG onset before the age of 45 years, especially if done early in the course of the MG, though that still awaits firm proof. Yet, when a thymoma is present, doctors agree that it should be removed to prevent spread, although its removal usually does not improve MG.



Thymus gland removal may play a role in MG treatment.

(d) **Immunosuppressive and anti-inflammatory drugs.** Such drugs, are the current standard for the treatment of moderate-to-severe MG. The most commonly used is prednisolone, especially in ocular MG. Corticosteroids are effective in decreasing the levels of anti-AChR autoantibodies, but can also cause complications, such as weight gain, high blood pressure, diabetes, anxiety/ depression/ insomnia, bone thinning, cataracts and gastrointestinal perforations. In the long-term, patients can often 'cruise' on lower doses by combining them with other immunosuppressive drugs such as *azathioprine* (*Imuran*®) or *cyclosporine A* (for *azathioprine*-intolerant patients). Alternatives that have proved successful in other immune-related diseases, such as rheumatoid arthritis and systemic lupus erythematosus, or in suppressing graft

rejection, are now undergoing clinical trials in MG, including Mycophenolate mofetil, Tacrolimus and Rituximab®.

HOW TO DEAL WITH MG?

There is no reason to find the next bits scary. **Starting on the bright side**:

- MG can nearly always be brought under good control, so most patients lead a pretty full life; very few people actually die of their myasthenia.
- The treatments for MG work better than for many other 'autoimmune' diseases; there is less pain and fewer serious long-term snags.
- These treatments are getting better all the time; with your help, we are trying to make sure that continues;
- Every MG patient should become their own 'special nurse' and work out their own ways of keeping their MG in its place. *Try not to let it take over your life*.

On the other hand, you should be warned that:

- Your MG may well be with you for years. It *can* fade away even without treatment, but only in about one patient in about 20-30 each year; so do not wait around – get treated;
- You will probably have to plan your day to make the most of the prime time when your strength is best;
- Other people may not always notice any weakness, especially when first meeting you; e.g. they may not realise that you are trying to smile.
- You are pretty sure to need some drugs, and they all have side-effects. Patients with MG usually manage on lower doses of steroids, taken every other day, than those with many other diseases.

It is also wise to avoid:

- Overexertion and unnecessary fatigue,
- Emotional stress,
- Catching infections (e.g. by staying out of crowds in the winter), and
- Certain drugs that directly affect nerve→muscle triggering, such as aminoglycoside (e.g. gentamicin) and especially ketolide antibiotics (e.g. telithromycin: Ketek®). Curiously, over-dosing with anti-cholinesterase drugs such as *pyridostigmine* or *neostigmine,* can increase the weakness or even cause cholinergic crises (overflow of saliva, tears, sweat and/ or vomiting) as well as increased weakness.

Eating a balanced diet, taking plenty of rest and some exercise (moderate, such as walking or ballroom dancing), and especially avoiding stress or infections, can help patients lead a fairly full life.

WHAT IS THE FUTURE?

The outlook for MG patients has improved dramatically in the last 30-40 years, with mortality rates currently near zero. As a result, the myasthenia is not "gravis" any more. Most present-day treatments evolved by trial-and-error, and some have serious side-effects. As we learn more about autoimmune diseases, it should soon be possible to target treatments so that they selectively block only the damaging immune response in

MG and not the whole immune system. With the knowledge accumulated on the immunopathology of MG and the role of the thymus and defects in immunoregulation, prospective antigen-specific therapies and novel technologies have been developed and are undergoing trials.
However, a lot still needs to be done. Since very few inherited or environmental risk factors are known for MG, we know almost nothing about how to prevent it. It is also interesting to know why some people are particularly susceptible to MG and others are not. Further research and optimisation of ongoing experimental approaches are therefore promising for the treatment of MG in the future.
Since MG is a rather rare disease, funding of relevant research is limited and therefore the research groups working towards understanding its mechanisms and developing more efficient treatments are very few in each country (often only one laboratory per country). This problem necessitates the coordination of efforts of the individual labs at a European level. The present European network has the aim of putting the efforts of various European research institutes together, in order to achieve faster progress in the understanding and treatment of the disease.

FAQs to be added soon

USEFUL CONTACTS

- http://pages.prodigy.net/stanley.way/myasthenia/
- **The Myasthenia Gravis Association**
  Southgate Business Center, Normanton Rd,
  Derby DE23 6UQ, UK.
  Tel: (0044) 01332-290219, Fax: (0044) 01332-293641
  http://www.mgauk.org/
- **Myasthenia Gravis Foundation of America**
  1821 University Ave. W., Suite S256,
  St. Paul, MN 55104.
  Tel: (651) 917-6256 or (800)541-5454
  Fax: (651) 917-1835
  http://www.myasthenia.org/
- **Association Francaise Contre Les Myopathies**
  Rue de l'Internationale 91 000, Evry.
  Tel: (0033) 01 69 47 28 28
  http://www.afm-france.org/
- **The Australian Myasthenic Association**
  108 Bantry Bay Road, Frenchs Forest NSW 2086.
  Tel: (02) 4283 2815
  http://www.myasthenia.org.au/

This leaflet is supported by EU (project EuroMyasthenia, http://euromyasthenia.org).
It used as starting material a similar leaflet of MGA of UK.

EUROMG DB structure

Patient		
IDPatient	Automatic	
InsertionDate	Automatic	
Local ID1	**Mandatory**	
Local ID2		
BirthDate	**Mandatory**	
BirthPlace		
Country of residence	**Mandatory**	
Ethnic origin	**Mandatory**	**List: Caucasian,...**
First Name Coded	Automatic	
Last Name Coded	Automatic	
Informed consent	**Mandatory**	**List: Yes, No, not known**
Diagnosis	**Mandatory**	**List: MG, MG Ocular, MG probable, ...**
Death	**Mandatory**	**List: Yes, No, not known**
Death date		
Death causes		List: MG, not MG
IDContact	Automatic	
Contact	Automatic	
Institute code	Automatic	

Diagnostic criteria		
ID Patient	Automatic	
InsertionDate	Automatic	
Gender	**Mandatory**	**List: Male, Female**
Onset date	**Mandatory**	
Onset age	Automatic	
Diagnosis date	**Mandatory**	
First Cllinical Record date		
Last Observation date		
Fup time	Automatic	
Age now	Automatic	
Fatiguability / Weakness	**Mandatory**	**List: Yes, No, not known**
Description Fat/Weak		
AChR Ab	**Mandatory**	**List: Done, Not Done, Positive, Negative, Unkn.**
Result AChR	Ab value	
MuSK Ab	**Mandatory**	**List: Done, Not Done, Positive, Negative, Unkn.**
Result MuSK	Ab value	
Other AutoAb 1	**Mandatory**	**List: Done, Not Done, Positive, Negative, Unkn.**
Other AutoAb details		
EMG Repet Stim	**Mandatory**	**List: Yes, No, not known**
Description EMG RS		
SF-EMG	**Mandatory**	**List: Yes, No, not known**
Description SF-EMG		
AChE-Inhib Test	**Mandatory**	**List: Yes, No, not known**
Description AChE-Inhib		
MGFA Score at onset	**Mandatory**	
Result MGFA		

FollowUp

IDPatient	Automatic	
InsertionDate	Automatic	
MGFA Score at entry	**Mandatory**	
MGFA Score at nadir	**Mandatory**	
MGFA Score at last observation		
Treatment(s):		
Cholinesterase inhibitors		List: Yes, No
Corticosteroids		List: Yes, No
Immunosupressor drugs		List: Yes, No
Plasmapheresis		List: Yes, No
IVIG		List: Yes, No
Side effects		
Hospital stays (duration)		
Description		

Thymectomy

IDPatient	Automatic	
InsertionDate	Automatic	
Imaging date		
Imaging type		
Imaging result	**Mandatory**	
Thymectomy	**Mandatory**	**List: Done, Not Done, Unkn**
Thymectomy Date	**Mandatory**	
Technique		
Where		
Histology	**Mandatory**	**List: Normal, Hyperplasia, Involuted, Thymoma, ...**
Thymoma	**Mandatory**	**List: Yes, No, not known**
WHO type		
Stage		
Therapy		

Biological Sample

IDPatient	Automatic	
InsertionDate	Automatic	
ID Sample	Automatic	
Sample Date		
Sample Type		List: DNA, PBL, Serum, ...
Local Sample Number		
Availability		List: Yes, No

Other Diseases

IDPatient	Automatic	
InsertionDate	Automatic	
Disease		
Diagnosis date		
Where/Who		
Therapy		
Comment		

Referring contact

IDContact	Automatic from LogIn info
InsertionDate	Automatic from LogIn info
Title	Automatic from LogIn info
FirstName	Automatic from LogIn info
LastName	Automatic from LogIn info
Department	Automatic from LogIn info
Institute	Automatic from LogIn info
Institute code	Automatic from LogIn info
Address	Automatic from LogIn info
City	Automatic from LogIn info
Country	Automatic from LogIn info
Phone2	Automatic from LogIn info
Phone1	Automatic from LogIn info
FAX	Automatic from LogIn info
e-mail	Automatic from LogIn info

Questionnaire Psycho-socioeconomical

Partner VU

QUESTIONNAIRE FOR PATIENTS WITH MYASTHENIA GRAVIS

INSTRUCTIONS

On following pages you will find questions and assertions regarding your background, health, lifestyle and aspects around Myasthenia Gravis.

Please answer **all** questions to your best ability.

BACKGROUND

1. Sex: **Male** □ **Female** □

2. Age (in years):_____

3. Do you live alone? **Yes** □ **No** □

If <u>No</u>, do you live with.. (*Tick one box for <u>each</u> line and fill in the number)*

Husband/wife/partner	**No** □	**Yes** □
Persons of the age 18 or older	**No** □	**Yes** □ **Number:**____
Persons under the age of 18	**No** □	**Yes** □ **Number:**____

4. Do you have children? **No** □ **Yes** □ **Number:**___

5. Country of birth?_____

6. In which country were your parents and grandparents born?

Mother:_____ **Grandmother**_____
Grandfather_____

Father:_____ **Grandmother**_____
Grandfather_____

7. How many people live in your town/city? *Tick <u>one</u> box only*

> 500.000 □ **100.000-500.000** □ **10.000- 100.000** □
1000- 10.000 □ **< 1000**

8. Approximate distance to the nearest hospital?

0-10 km □ **10-50km** □ **>50km** □

9. Education: ***Please mark the <u>highest</u> level achieved.*** *Tick <u>one</u> box only*

Pre-primary education (less than 7 years education)……..…….□
Primary and lower secondary education (7-10 years)…….. □
Upper secondary education (10-13 years)……..□
Tertiary education, short (4 years or shorter higher education)…□
Tertiary education, long (more than 4 years)…….□

10. Do you work or have you worked previously?

Yes □ **No** □ (If **no**, please jump to question **17**)

11.What is (was) your occupation or title of the place of work? *Please tick on only <u>one</u> box that describes your last occupation/ type of work.*

Administrative leaders and politicians…..…… □
Academic professions.…….. □
Occupation with shorter college education and technicians…… □
Office and customer service occupation…… □
Business, service and caretaking occupation……... □
Farming, forestry and fishery……..…… □
Craftsmen and related trade workers…… □
Process-and machine operaterr and transport workers etc…….. □
Occupation without any demand of education……... □
Armed forces/ military education…… □

12.

a) Has Myasthenia Gravis had any influence on your choice of occupation?

Yes □ **No** □ **Don`t know** □

b) Have you changed your occupation due to Myasthenia Gravis?

Yes □ **No** □

13. Were you employed ***before*** the diagnosis of Myasthenia Gravis was made?

Yes, full time □ **Yes, part-time** □ **in %**_____ **No** □

14. Are you ***currently*** employed?

Yes, full time □ **Yes, part-time** □ **in %**_____ **No** □

15. Have you ever thought about changing your occupation or place of work during the last **12 months**?

Yes □ **No** □

16. Have you been absent from work in the past **12 months** due to Myasthenia Gravis?

Yes □ **No** □

If ***yes,*** approximately for how long in summary? *Tick only <u>one</u> box.*

2 weeks or less..... □
2-8 weeks..... □
More than 8 weeks..... □

17. Are you receiving any of the following benefits? *Tick one box for <u>each</u> line.*

	Yes	**No**
Sickness benefit.....	□	□
Old-age pension, early retirement pension	□	□
Rehabilitation allowance.....	□	□
Disablement pension.....	□	□
Unemployment insurance.....	□	□
Social assistance/ insurance.....	□	□

MYASTHENIA GRAVIS

18. a) At what **age** did you first notice symptoms of Myasthenia Gravis?

Years:_____

b) Did the **first** symptoms of Myasthenia Gravis occur at the same time as any of the following? *Tick one box for <u>each</u> line.*

Other disease/illness	**Yes** ☐	**No** ☐
Pregnancy/ birth	**Yes** ☐	**No** ☐
Medical treatment/ surgery	**Yes** ☐	**No** ☐

Other:_____

19. At what age were you **diagnosed** with Myasthenia Gravis?

Years:_____

20. Which **Medical Centre <u>or</u> Neurologist** diagnosed your Myasthenia Gravis? *Tick <u>one box or more</u> and write the name.*

Medical Centre ☐ **Name:**_____

Neurologist ☐ **Name and city:**_____

21. Which of the following symptoms did you have in the **early stages** of Myasthenia Gravis? *Tick one box for <u>each</u> line.*

	None	**Mild**	**Severe**
Muscle weakness of eyelids.....	☐	☐	☐
Double vision.....	☐	☐	☐
Muscle weakness affecting the arms and hands	☐	☐	☐
Muscle weakness affecting the legs.....	☐	☐	☐
Muscle weakness affecting neck flexion.....	☐	☐	☐
Muscle weakness in face, jaw, lips.....	☐	☐	☐
Difficulties with talking.....	☐	☐	☐
Difficulties with chewing.....	☐	☐	☐
Difficulties with swallowing.....	☐	☐	☐
Difficulties with breathing.....	☐	☐	☐

22. Which of the following symptoms have you had in **the past 3 months**? *Tick one box for <u>each</u> line.*

	None	Mild	Severe
Muscle weakness of eyelids.....	□	□	□
Double vision.....	□	□	□
Muscle weakness affecting the arms and hands	□	□	□
Muscle weakness affecting the legs.....	□	□	□
Muscle weakness affecting neck flexion.....	□	□	□
Muscle weakness in face, jaw, lips.....	□	□	□
Difficulties with talking.....	□	□	□
Difficulties with chewing.....	□	□	□
Difficulties with swallowing.....	□	□	□
Difficulties with breathing.....	□	□	□

23. Have you ever experienced **a worsening** of Myasthenia Gravis? *Tick one box only.*

No □ (jump to question **25**)

Yes □ (please answer question **24**)

Don`t know □ (jump to question **25**)

24. Which of the following symptoms did you experience during a **worsening** of Myasthenia Gravis? *Tick one box for <u>each</u> line.*

	None	**Mild**	**Severe**
Muscle weakness of eyelids..……	□	□	□
Double vision…….	□	□	□
Muscle weakness affecting the arms and hands	□	□	□
Muscle weakness affecting the legs…..…..……	□	□	□
Muscle weakness affecting neck flexion…….	□	□	□
Muscle weakness in face, jaw, lips…..……	□	□	□
Difficulties with talking……	□	□	□
Difficulties with chewing…….	□	□	□
Difficulties with swallowing…….. ……..	□	□	□
Difficulties with breathing……..	□	□	□

25. Do you know if you have antibodies? *Tick one box for <u>each</u> line.*

a)Anti-acetylcholine receptor antibodies (AChR-ab)

Yes □ **No** □ **Don`t know** □

b)Antibodies against Muscle-spesific kinase (Anti-MuSK-ab)

Yes □ **No** □ **Don`t know** □

26. Do you know of others in your family diagnosed with Myasthenia Gravis?

No □

Yes □ If **<u>Yes</u>**; Father □
Mother □
Brothers and sisters □
Grandparents □
Cousin □

27. Have you been thymectomised?

Yes □ **No** □

28. What kind of medical treatment have you been using in **the past 3 months** for Myasthenia Gravis? *Tick one box for each line.*

No therapy □ (If no therapy, jump to question **29**)

Cholinesterase inhibitors (Mestinon)……	Yes □	No □
Prednisone……	Yes □	No □
Intravenous immunglobulin (IVIg)……	Yes □	No □
Plasma exchange therapy.……	Yes □	No □

Immunsuppression therapy other than prednisone:

Azathioprine …….	Yes □	No □
Mycophenoylate (Cellcept)……	Yes □	No □
Cyclosporine A ……	Yes □	No □

Other forms of therapy……Yes □ No □

If **yes**, please name treatment/drug:_____

29. What kind of medical treatment have you received **in the past** (any time since the diagnosis of Myasthenia Gravis)? ***Excluding new treatments in the last 3 months****. Tick one box for each line.*

No therapy □ (If no therapy ever, jump to question **31**)

Cholinesterase inhibitors (Mestinon)……	Yes □	No □
Prednisone……	Yes □	No □
Intravenous immunglobulin (IVIg)……	Yes □	No □
Plasma exchange therapy……	Yes □	No □

Immunsuppression therapy other than prednisone:

Azathioprine …….	Yes □	No □
Mycophenoylate (Cellcept)……	Yes □	No □
Cyclosporine A ……	Yes □	No □

Other forms of therapy……Yes □ No □

If **yes**, please name treatment/drug:_____

30. Have you ever had to terminate treatment for Myasthenia Gravis due to severe side effects?

No □ **Yes** □ **(*please name treatment*):**_____

31. During the last **12 months**, have you been using any medical treatment daily or regularly? *Do **not** include medications for Myasthenia Gravis.*

Yes □ **No** □ (If **No** please go to question **33)**

32. How many months have you been using the following medications? *Please mark each line whith a number and write **0** if you have not been using the medications.*

Painkillers…….. _____ Months
Sleeping pills…….. _____ Months
Sedatives…… _____ Months
Anti-depressives…….. _____ Months
Allergy medicine…….. _____ Months
Asthma medicine……. _____ Months
Heart medicine……. _____ Months

Other medicine on prescription:_____
_____

33. Do you have any of the following diseases? *Tick one box for <u>each</u> line.*

			In years
Insulin dependent diabetes	Yes □	No □	If *yes*, for how long?: ___
Rheumatoid arthritis	Yes □	No □	If *yes*, for how long?: ___
Coeliac disease	Yes □	No □	If *yes*, for how long?: ___
Lupus erythematosus	Yes □	No □	If *yes*, for how long?: ___
Crohn`s disease	Yes □	No □	If *yes*, for how long?: ___
Auto-immune hepatitis	Yes □	No □	If *yes*, for how long?: ___
Thyroid disease	Yes □	No □	If *yes*, for how long?: ___
Psoriasis	Yes □	No □	If *yes*, for how long?: ___
Asthma	Yes □	No □	If *yes*, for how long?: ___
Allergy	Yes □	No □	If *yes*, for how long?: ___
Cancer	Yes □	No □	If *yes*, for how long?: ___
Lung disease	Yes □	No □	If *yes*, for how long?: ___
Heart disease	Yes □	No □	If *yes*, for how long?: ___
Mental disease	Yes □	No □	If *yes*, for how long?: ___

Other:_____

34. Have you had an emergency admission to a hospital due to a **worsening** of Myasthenia Gravis? *Tick only one box.*

No □ **Yes, 1-2 times** □ **Yes, 3-4 times** □

Yes, more than 5 times □

35. Which of the following factors ***do you think*** **<u>worsen</u>** your Myasthenia Gravis? *Tick one or more boxes*

Infection □ **Stress (psychological/physical)** □

Season (temperature) □ **Drug therapy** □

Don`t know □ **Other factors** □_____

36. Who manages or monitors your Myasthenia Gravis?

District family doctor □

Hospital internist / general physician □

Neurologist □

Other □ _____

37. How many times did you consult your physician regarding your Myasthenia Gravis in the **past 2 years**?

Number of times:_____

38. How do you grade your physician`s follow-up regarding your Myasthenia Gravis? *Tick only <u>one</u> box.*

not relevant □ **good** □ **average** □ **bad** □

39. Are you a member of an organisation/group representing patients with Myasthenia Gravis?

Yes □ **If *yes*, please write name:**_____

No □

If no, do you wish to make contact with an organisation/group?

Yes □

No □

40. a) How do you keep yourself updated on information and treatment regarding Myasthenia Gravis? *Tick one box or more.*

Doctor □ **Internet** □ **Medical periodicals** □

Pasient groups/organisation □ **Other** □_____

b) Are you satisfied with the information you are receiving?

No □ **Yes** □

HEALTH AND LIFESTYLE

41. Weight (**in kg**):_____

42. Height (**in cm**):_____

43. Have you smoked/do your smoke daily (cigarettes, cigars, pipe)? *Tick <u>one</u> box only.*

Yes, now □ **, please write number/day:**_____

Yes, earlier □ **, please write when:**_____ **years ago**

Never □

44. Alcohol:

a) Are you total abstinent regarding alcohol?

Yes □**, if yes please jump to question 45.**

No □

b) How many times ***a month*** do you consume alcohol? *Low alcohol beer and non-alcoholic beer are* ***not*** *included. Write* ***0*** *if you do not drink any alcohol.*

Number of times:_____

c) How many glasses of beer, wine or spirits do you usually consume in a period of 2 weeks? *Please write <u>number of glasses.</u> Low alcohol beer are not included. Write* ***0*** *if you do not consume any alcohol.*

Beer:_____ glasses

Wine:_____ glasses

Spirits:_____ glasses

45. How many cups of coffee/or tea do you consume per day? (*Put the number" 0" if you do not drink coffee or tea)*

Number of cups coffee:___ **Number of cups tea:**___

46. Do you regularly take vitamins?

Yes, daily □ **Sometimes** □ **No** □

47. What kind of phsyical activity have you undertaken in your **spare time** in the course of **the past year**? *Estimate a **weekly** average for the year. The distance between home and work is regarded as spare time. Please answer both questions.*

	Hours pr. Week			
	None	**Less than 1**	**1-2**	**3 or more**
Light exercise……. (You do not sweat or feel out of breath)	□	□	□	□
Hard physical activity (You sweat and feel out of breath)	□	□	□	□

48. Physical activity and work. *Please answer if you do paid or unpaid work.*

How will you describe your work? *Tick one box only.*

I sit a lot when I work (sitting behind a desk….)……. □
I walk a lot in my work (industrial work, shopassistent)….. □
I walk a lot and carry heavy things (messenger, nurse,)…. □
I do heavy physical work (heavy gardening…..)…….. □

49. Were you vaccinated as a child (standard vaccination program)?

Yes □ **No** □ **Don`t know** □

50. Have you had any vaccinations **after** the age of 18?

Yes □ **No** □

This part of the questionnaire (SF-36) asks for your views about your health. This information will help us keep track of how you feel and how well you are able to do your usual activities.

Please answer every question by setting a circle (O) around the number that best describes your answer

51. In general, would you say your health is:

(please mark a number)

Excellent	1
Very good.....	2
Good.....	3
Fair.....	4
Poor.....	5

51. **Compared to one year ago**, how would you rate your health in general **<u>now</u>**?

(please mark a number)

Much better than one year ago	1
Somewhat better now than one year ago.....	2
About the same as one year ago	3
Somewhat worse now than one year ago.....	4
Much worse than one year ago	5

52. The following questions are about activities you might do during a typical day. **Does your health now limit you in these activities?**

If so, how much?

(please mark a number on each line)

ACTIVITIES	**Yes, limited alot**	**Yes, limited a little**	**No, not limited at all**
a. Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports	1	2	3
b. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	1	2	3
c. Lifting and carrying groceries	1	2	3
d. Climbing several flights of stairs	1	2	3
e. Climbing one flight of stair	1	2	3
f. Bending, kneeling, or stooping	1	2	3
g. Walking more than a mile	1	2	3
h. Walking several hundred yards	1	2	3
i. Walking one hundred yards	1	2	3
j. Bathing or dressing yourself	1	2	3

53. During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of your physical health**?

(please mark a number on each line)

	YES	NO
a. Cut down on the **amount of time** you spent on work or other activities	1	2
b. **Accomplished less** than you would like	1	2
c. Were limited in the **kind** of work or other activities	1	2
d. Had difficulty performing the work or other activities (for example, it took extra effort)	1	2

54. During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of any emotional problems** (such as feeling depressed or anxious)?

(please mark a number on each line)

	YES	NO
a. Cut down in the **amount of time** you spent in work or other activities	1	2
b. **Accomplished less** than you would like	1	2
c. Did work or activities **less carefully** than usual	1	2

55. During the **past 4 weeks**, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups)

(please mark a number)

Not at all	1
Slightly.....	2
Moderately.....	3
Quite a bit	4
Extremly.....	5

56. How much **bodily** pain have you had during **the past 4 weeks**?

(Please mark a number)

None.....	1
Very mild.....	2
Mild	3
Moderate	4
Severe	5
Very severe	6

57. During the **past 4 weeks**, how much did **pain** interfere with your normal work (including both work outside the home an housework)?

(please mark a number)

Not at all	1
A little bit	2
Moderately.....	3
Quite a bit	4
Extremely	5

58. These questions are about how you feel an how things have been with you **during the past 4 weeks.** For each question, please give **one** answer that comes closest to the way you have been feeling. **How much of the time during the past 4 weeks….**

(Please mark a number on each line)

	All of the time	**Most of the time**	**Some of the time**	**A little of the time**	**None of the time**
a. Did you feel full of life?	1	2	3	4	5
b. Have you been very nervous?	1	2	3	4	5
c. Have you felt so down in the dumps that nothing could cheer you up?	1	2	3	4	5
d. Have you felt calm and peaceful?	1	2	3	4	5
e. Did you have lot of energy?	1	2	3	4	5
f. Have you felt downhearted and depressed?	1	2	3	4	5
g. Did you feel worn out?	1	2	3	4	5
h. Have you been happy?	1	2	3	4	5
i. Did you feel tired?	1	2	3	4	5

59. During **the past 4 weeks**, how much of the time has your **physical health or emotional problems** interfered with your social activities (like visiting friends, relatives, etc.)?

(please mark a number)

All of the time	1
Most of the time	2
Some of the time.....	3
A little of the time.....	4
None of the time.....	5

60. How **TRUE** or **FALSE** is <u>each</u> of the following statements for you?

(please mark a number on each line)

	Definitely true	**Mostly true**	**Don`t know**	**Mostly false**	**Definitely false**
a. I seem to get sick a little easier than other people	1	2	3	4	5
b. I am as healthy as anybody I know	1	2	3	4	5
c. I expect my health to get worse	1	2	3	4	5
d. My health is excellent	1	2	3	4	5

QUESTION FOR MEN ONLY

61. At what **age** did you reach puberty (changes in body hair/ breaking voice etc)?

_____**Years**

QUESTIONS FOR WOMEN ONLY

62. Age at first menstruation: *Write **0** if you never have had a menstruation*_____**years**

63. Age reaching menopause: *Write **0** if you still have your menstruation*_____**years**

64. Are you **currently** pregnant?

Yes □ **No** □ **Don`t know** □ **Not relevant** □

65.a) How many children have you given birth to? *Write **0** if you not have given birth*

Number:_____

b) Age when you gave birth to your first child:_____**years**

c) Age when you gave birth to your last child:_____**years**

66. Have you ever had a miscarriage? *Write **0** if you have not had any miscarriages*

Number of miscarriages:_____

67. Have you ever had assisted conception/ IVF-treatment?

Yes □ **No** □

68. Are you using or have used any of the following? *Tick one box on <u>each</u> line*

	Current	**Used before**	**Never**
Oral contraceptives …….…….……..	□	□	□
Hormon coil……..	□	□	□
Hormone replacement therapy (HRT)….	□	□	□

69. If you are using or have previously used Hormone replacement therapy (HRT), please specify for how long in months. *Write* **0** *if you never have used HRT*

Months:_____

70. In which way have the following **factors** affected the <u>clinical course</u> of Myasthenia Gravis? *Tick one box on <u>each</u> line*

Menopause improved □ unchanged □ worse □ don`t know □ not relevant □

Menstruation improved □ unchanged □ worse □ don`t know □ not relevant □

Pregnancy improved □ unchanged □ worse □ don`t know □ not relevant □

First 6 months after pregnancy
improved □ unchanged □ worse □ don`t know □ not relevant □

HRT improved □ unchanged □ worse □ don`t know □ not relevant □

THANK YOU FOR COMPLETING THIS SURVEY!

Collaborating partners

-Romanian MG Association

Romanian MG Association

How we started

Romanian MG Association

Our mission

OUR MISSION = improvement of MG patients lifes

Patient services

- imperious need = medication - Mestinon
- information ,communication
- support - patients and families
- psychological, legal counselling
- public information about Mg ers problems

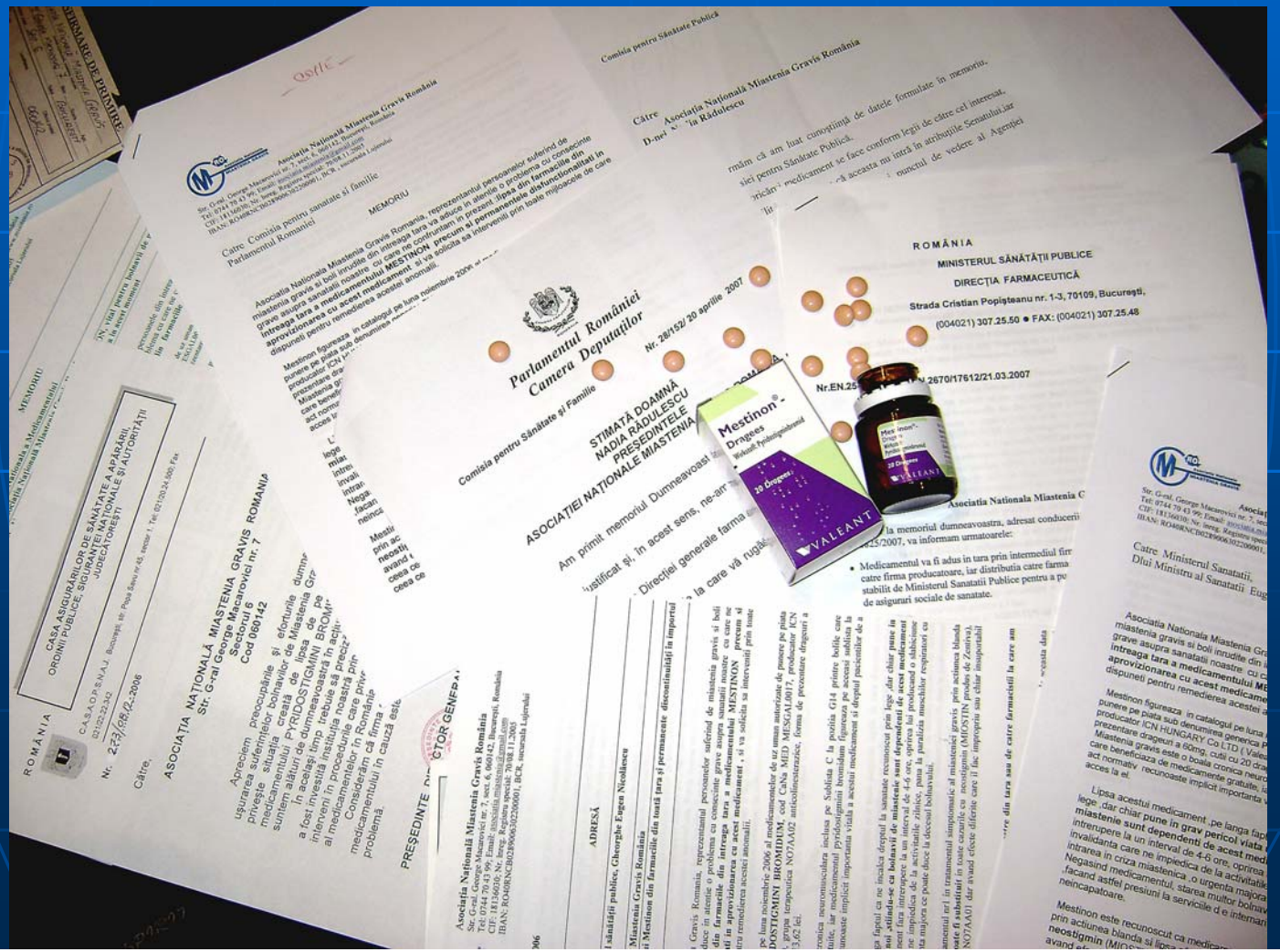
Education for

● patients	books brochures website internet forum support groups Newsletters
● families	
● medical health providers	trainings
● population	mass media, posters

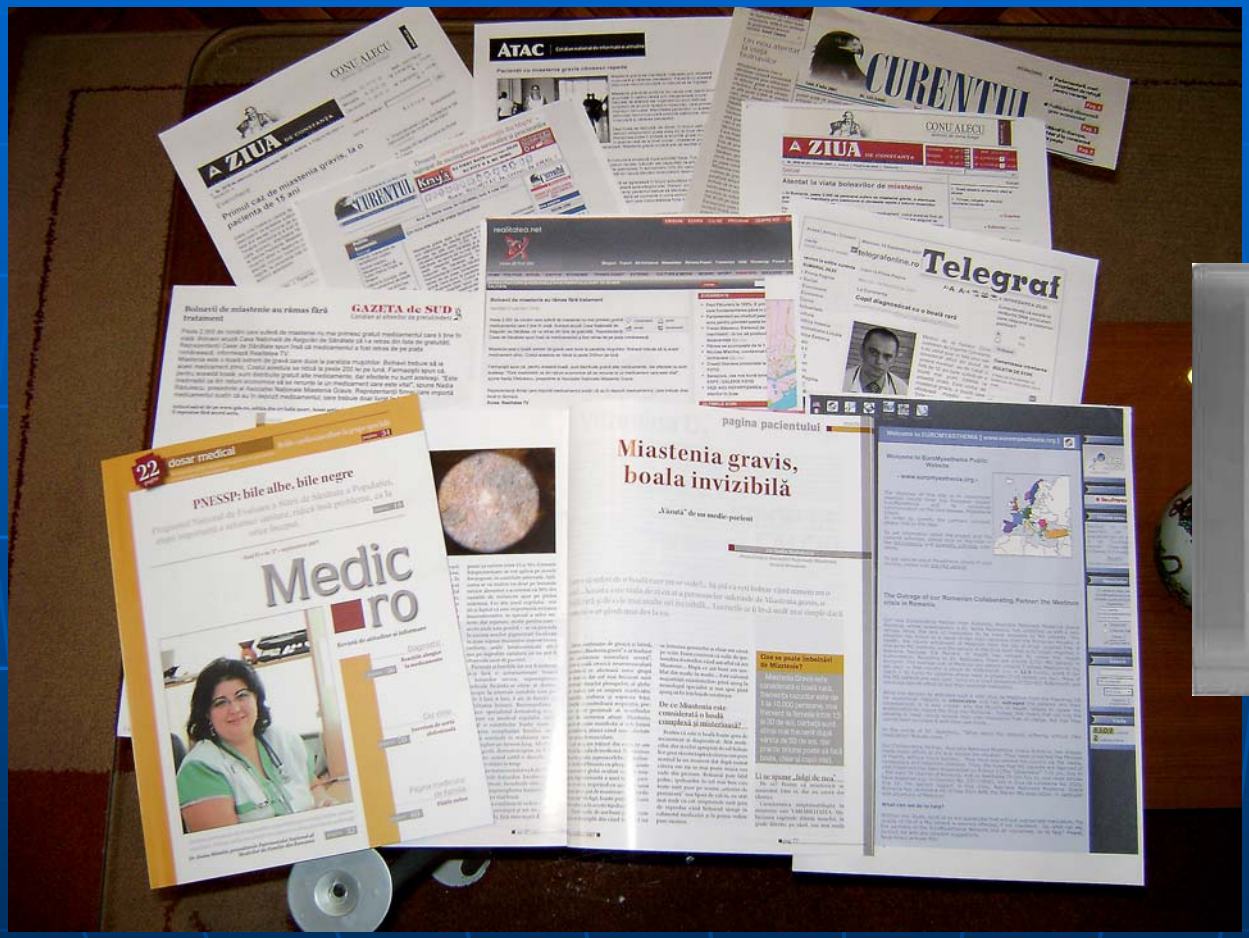
Research for -> MG cause and cure (a dream!!) ->fund raising

Mestinon crisis

Fighting against bureaucracy



Mestinon crisis



The association has made major efforts to try to solve this situation: we contacted the authorities (Minister of Health, Parliament etc) without much success. We have alerted the country via the media ,newspapers and TV channels and finally we claim for help to our friends from Europe and we found a lot of support.

Mestinon crisis

Support from Euromyasthenia partners

The Outrage of our Romanian Collaborating Partner: the Mestinon crisis in Romania.

Our new Collaborating Partner from Romania, Asociatia Nationala Miastenia Gravis Romania, whose spokesperson is Dr. Nadia Radulescu, has contacted us with a very serious issue, the lack of medication to be made available to MG patients. This situation has arisen as a result of two main decisions from the Romanian Ministry of Health: the recent withdrawal of Mestinon from the list of drugs supplied free of charge to MG patients, and the penury of the drug itself that is no longer imported in Romania because the Ministry of Health has refused to renew the import authorization.
According to Dr. Radulescu, there are around 2,000 MG patients in Romania. The average cost of Mestinon per patient (around 3 tablets Mestinon 60 mg per day) in that country is about 80 RON/month (i.e. ~ **22.5** Euros), albeit it can reach ~ 90 Euros for patients whose need is greater (7-10 tablets per day). Many of the MG patients are very poor, living on a small allowance of 300-400 RON/month and obviously cannot afford to buy their essential medication.
While the decision to withdraw such a vital drug as Mestinon from the free-drug list for economical reasons is **intolerable** and has **outraged** the patients and their spokesperson, it is also unclear why the Ministry of Health refuses to renew the authorization to import the drug into Romania… Indeed, this means that not only the patients in need cannot receive their vital medication free of charge, but also they cannot even purchase it with their own funds….

In the words of Dr. Radulescu, "What about the patients suffering without the medication? Nobody cares. What about the MG patients in myasthenic crisis? Nobody cares."

Our Collaborating Partner, Asociatia Nationala Miastenia Gravis Romania, has already made major efforts to try and resolve the situation: They have contacted the Minister of Health, without much success… They have also alerted the country via the media, newspapers and television channels. Thus, the news that MG patients are deprived of vital treatment has been broadcasted on Antena 1 (The "Observator" 7.35 pm, July 9), the main TV channel of Romania, and on Realitatea TV (on July 6), and news articles have appeared e.g. in Ziua de Constanta No. 2020, July 12. For patient support in this crisis, Asociatia Nationala Miastenia Gravis Romania has received a lot of help from AIM, the Italian MG association, in particular with donations of Mestinon.

What can we do to help?

Without any doubt, most of us will appreciate that without appropriate medication, the quality of life of a MG patient is severely affected, if not inexistent… So, what can we, the partners of the EuroMyasthenia Network and all concerned, do to help? Please, contact me with any possible suggestions…

Nicole Kerlero de Rosbo, PhD

E-mail : nicole.kerlero-de-rosbo@u-psud.fr

Romanian MG Association today

- 62 active members
- Supporters
- Professionals

354 assisted patients







Romanian MG Association local chapters

Romanian MG Association Website

Romanian MG Association Projects

Collaborating partners ->EUROMYASTHENIA
->Associations of Neurological diseases
Disabled people
MG from european countries
Volontiers
->Pharmacies

Admitance as EFNA's member

Implementation of

-> Euromyasthenia standards -> acces to same treatments as european patients (IVIG, mestinon retard)

-> ICF in Romania
-> Romanian National Registry for MG
-> National /European MG database

European Integration Equality of chances
Activities Participation

Young MG-ers group

Projects
for fund raising

Romanian MG Association

- Young
- Dynamic
- Fighting
- Disponibility
- Resources

Bringing back the the SMILE