MYASTHENIA GRAVIS: DIAGNOSIS AND TREATMENT

Kleopas A. Kleopa, MD

Neurology Clinics
and
Neuroscience Laboratory
The Cyprus Institute of Neurology and Genetics
What is myasthenia?

*myasthenia* (= αδυναμία μυών) *gravis* (=σοβαρή)

- Chronic, autoimmune disease that affects the neuromuscular junction, causing muscle weakness and fatigability
- Not inherited (but influenced by genetic factors)
- Not contagious
- Exact cause remains unknown, but possible mechanisms have been revealed
- Rare disease (frequency < 1: 2000) but with potentially serious progression ("*myasthenia gravis*”) if not treated correctly
Organs of the immune system and their role

Maturation of T-lymphocytes

Activation of mature T & B-lymphocytes

Maturation of B-lymphocytes

Thymus gland

Bone marrow
Basic aspects of the immune reaction

Invading microbes (antigens)

Energopoíhisi lemfokuttarwn
Katastrophe twn antigónwn

T lemfokuttara
Molusmeno kúttaro
Katastrophe antigónwn krumménwn méssa sta kúttara mias

V lemfokuttara
Antiswuma
Katastrophe eléutherwn antigónwn
Autoimmunity

- Physiologically our own proteins/molecules do not activate our immune system (=tolerance)
- In the autoimmune disease, our own proteins are recognized as foreign (=auto-antigens) causing activation of lymphocytes and production of auto-antibodies

**What contributes to autoimmunity?**
- Dysregulation of lymphocytes (impaired suppression)
- Alterations in our body/tissues (incl. Cancer)
- Genetic factors (genes that play a role in the regulation of the immune system)
- Infections (?viral) may play a role in some cases by:
  - Combination of microbes with our own molecules (eg. Viral production in our cells)
  - Molecules of the microbes resemble our own (molecular mimicry)
  - Release of normally hidden molecules in the cell surface or circulation

«**Danger model of autoimmunity**»
When autoimmunity meets the neuromuscular junction (NMJ)
The Neuromuscular System

CNS
- teleodendria
- axon collateral
- axon
- dendrites
- cell body
- dendritic spines
- terminal button (end foot)

PNS
- nucleolus
- nucleus
- cell body (soma)
- dendrite
- neurilemma
- myelin sheath
- node of Ranvier

NMJ
- sensory neuron
- receptor
- sense organ

Motor neuron
- axon hillock

Skeletal muscle
- effector

Sensory neuron
- Schwann cell nucleus
- node of Ranvier
The message transmission at the NMJ

The Neuromuscular Junction

1. Action potential
2. Ca²⁺ influx
3. Vesicle of acetylcholine release
4. Acetylcholine receptor activation
5. Open ion channels
6. Sodium influx
7. Potassium efflux

Terminal button
Muscle fibers
Axon terminals
Voltage-gated calcium channel
Action potential propagation in muscle fiber
Neurotransmitter-gated channel
Motor end plate
Development and molecular architecture of the NMJ
Neuromuscular junction proteins and autoimmunity in myasthenia
Pathophysiology of neuromuscular junction in myasthenia

- Antibodies directly block AChR
- Reduction of AChRs due to the cross-linking by divalent antibodies and internalization
- Most important: AChR loss through complement-mediated destruction of the postsynaptic membrane
- Simplification of the postsynaptic folds
What causes myasthenia?

**AchR-specific CD4+ T cells** are found in the blood and in the thymus of patients with MG

CD4+ T cells cause activation of B-lymphocytes to produce antibodies targeting NMJ molecules (AchR, MuSK, ...?)

Activation of autoreactive T-cells may be the result of

- Reduced activity of the regulating/suppressing arm of the immune system
- Genetic predisposition for autoimmunity (MHC/HLA-class II molecules DQ8, DR3, and HLA-class B8, A1)- **molecules that enhance the presentation of antigens to the immune cells**- are found more frequently in patients with MG
Cytokine network and cells involved in the pathogenesis and immunoregulation of MG

IFN-$\gamma$ stimulates expression of MHC class II molecules on the muscle cell membrane, thus facilitating presentation of muscle AChR

IL-18 secreted by APCs favors the differentiation of Th1 cells both directly and indirectly through the action of NK cells

Th1 cytokines stimulate production of IgG subclasses

IL-4 is also a differentiation factor for immunosuppressive Th3 cells

CD1-d–restricted NKT cells can activate Tregs, thereby inhibiting autoimmune processes
Epidemiology of myasthenia

- Annual incidence of 4-11/million
- Prevalence 50-400 per million (at least 100,000 in Europe)
  $\rightarrow$ estimated number for Cyprus: 200-250 patients

Gender differences in age of onset

In Caucasians
Two peak ages of onset with higher incidence in females under age 50 and in males over age 50

In Oriental populations
High frequency of pediatric cases with no clear difference in sex distribution

Zhang, 2007
• Different frequencies in different populations

• There is an increasing incidence of myasthenia (perhaps also due to better diagnosis, or other, unknown biological factors)

Carr et al. BMC Neurology 2010, 10:46
Frequency of MG in each age group: women
Myasthenia in Cyprus

87 patients followed at CING:
→ 49 females (56.3%) and 38 males (43.7%) (M:F ratio 1:1.29)
→ Females: average age at onset 42.5 years (range: 12-75y)
→ Males: average age at onset 47.9 years (range 15-84y)
Clinical features of myasthenia

- Painless voluntary muscle weakness with fatigability
- Typical pattern of weakness in most cases: diplopia, ptosis (asymmetric, fatigues with upgaze), dysarthria (nasal speech), dysphagia, dysphonia, dyspnea (exertional), proximal limb (arms>legs), facial and neck muscle weakness
- Fluctuating, chronic course with remissions and relapses
- Deterioration of fatigability towards the end of the day and with repetitive exercise, improvement with rest

Not typical in myasthenia:
- “generalized fatigue”
- reflex and sensory abnormalities
- elevated serum CK level
- muscle atrophy is rare (but more frequent in MuSK-Ab+ patients) and restricted to single muscles
Immunological associations of myasthenia

- Association with genetic autoimmune factors:
  - HLA B8 and DR3 in early peak,
  - B7 and DR2 in late peak,
  - DR14-DQ5 in +MuSK Ab

- Association with other autoimmune disorders:
  - RA, SLE, pernicious anaemia/B12 deficiency (about 5%), thyroid disease (Graves) in about 10%, asthma (3%)

- Thymoma in about 10-15%

- Lymphoid thymus hyperplasia with proliferation of germinal centres in 50-70%
Edrophonium (Tensilon) Test

- Tensilon (2 mg→8 mg i.v) inhibits acetylcholin-esterase
- Works within 3-45 sec, for a few minutes
- Have atropin available to reverse hemodynamic effects – caution in elderly!

Utility of Tensilon test
- Only useful in patients with objective, measurable, findings
- Rarely helpful in the diagnostic evaluation of equivocal cases of MG
- Sensitivity for MG is low (60%) compared to other diagnostic tests
- False positive results in patients with LEMS, ALS, GBS, or even localized, intracranial mass lesions
- In anti-MuSK+ MG often negative and can even increase weakness

→ Rarely used due to the availability of more sensitive methods!
Repetitive nerve stimulation

Low-frequency (3 Hz) RNS:
- Positive if >10% CMAP decrement
- 80% of patients with generalized MG
- up to 50% of cases with purely ocular disease

Often negative in MG with anti-MuSK Abs
- unless facial muscles are tested

A decremental response on RNS can also be found in:
- Other disorders of NMJ (incl. LEMS → increment after exercise or stimulation at 10 Hz)
- ALS (if clinically possible → needle EMG to exclude denervation)
SFEMG in myasthenia gravis

- SF-EMG is positive in 98% of MG patients
- An increased jitter is not specific for MG as it occurs in:
  - other NMJ disorders
  - ALS, muscle and nerve diseases
Diagnosing myasthenia step by step

Meriggioli and Sanders 2009
Differential diagnosis: mainly for seronegative MG

The diagnosis of seronegative MG requires the exclusion of other conditions that can mimic MG (ocular or generalized):

- Lambert-Eaton myasthenic syndrome (limbs, autonomic!)
- Congenital myasthenic syndromes (onset in infancy-childhood, no response to immunotherapy)
- Botulism (rapid-descending, pupils, autonomic)
- Mitochondrial myopathies (gradual, PEO but no diplopia)
- Oculopharyngeal muscular dystrophy
- Dysthyroid opthalmopathy (exophthalmus)
- “Dropped-head” syndrome (PD, myopathy, MND)
- Miller-Fisher syndrome (areflexia, no fluctuation, acute onset)
- CNS mass lesions, stroke-brainstem! (sudden onset, ataxia, sensory)
- ALS, polymyositis (fasciculation, atrophy, UMN signs)
- Blepharospasm
- Hypokalemia, hypophosphatemia
# Myasthenia Gravis Foundation of America (MGFA) clinical classification

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade I</td>
<td>Ocular involvement only</td>
</tr>
<tr>
<td>Grade II</td>
<td>Mild weakness affecting predominantly limb (IIa) or bulbar muscles (IIb)</td>
</tr>
<tr>
<td>Grade III</td>
<td>Moderate (limb IIIa/ bulbar IIIb)</td>
</tr>
<tr>
<td>Grade IV</td>
<td>Severe (limb IVa/ bulbar IVb: may need nasogastric tube)</td>
</tr>
<tr>
<td>Grade V</td>
<td>Respiratory crisis (ventilator, ICU)</td>
</tr>
</tbody>
</table>

Jaretzki, 2000
Initial presentation of myasthenia in Cyprus

→ 34.6% presented with ocular symptoms (ptosis and diplopia-MGFA grade I)
→ 63% of those developed generalized myasthenia
→ 37% remained ocular (at least 3 years) (12.8% of all patients → ocular myasthenia)

→ 10.2% mild limb (IIa) and 38.5% with mild bulbar muscle weakness (IIb)
→ 3.8% moderate limb (IIIa) and 7.7% moderate bulbar muscle weakness (IIIb)
→ 2.6% severe weakness (IV)
→ 2.6% respiratory failure requiring mechanical ventilation (MGFA V)
Predictors of disease severity at presentation

Patients with **ocular** (as opposed to bulbar or limb) symptoms at onset are less likely to develop severe clinical course:

→ Only 10.7% of ocular onset patients developed grade >III, as opposed to 31.3% of patients with grade at onset II or higher (p=0.038)

→ Most (77.7%) of the patients with ocular onset who generalized developed only mild grade (II) of severity, compared to 35.3% of patients with grade at onset II or higher that reached only II (p=0.002)

→ **Sex (M/F)** was not predictive of a more severe course (25.6% of women and 25% of men developed max. scores > III)

→ **Age at onset** over 50 yrs more frequently associated with development of grade > III (in 35.5%), as opposed to patients with onset <50yrs (20%)- but not statistically significant
Myasthenia severity at different time points (MGFA grade)

Onset:
- I: 34.6%
- II: 2.6%
- III: a: 3.8%, b: 7.7%
- IV: 2.6%
- V: 2.6%

Maximum:
- I: 34.6%
- II: a: 10.2%, b: 38.5%
- III: a: 6.4%, b: 20.5%
- IV: a: 2.5%, b: 8.9%
- V: 13.9%

Last visit:
- I: 1.3%
- II: 25.3%
- III: 39.2%
- IV: 34.2%
- V: 0%
Additional investigations in the initial evaluation of patients with myasthenia gravis

- **CT-scan/MRI of the mediastinum** → rule out thymoma
- Thyroid function tests and thyroid auto-Abs
- Vitamin B12 level, routine blood studies
- Assess disorders that may interfere with long-term immunosuppressive therapy (osteoporosis, diabetes, hypertension, tuberculosis, peptic ulcer)
- Baseline dexta bone density scan
- Baseline ophthalmological examination
Thymus hyperplasia

Thymoma

T2-MRI

CT

FDT-PET

-Differentiates hyperplasia from thymoma/Ca when CT unclear
-Useful after thymectomy to detect recurrence
-Inferior to CT for ectopic thymus

(El-Bawab 2007)
By standard immunoassay anti-AChR Abs are detected in:
- 85-90% of patients with generalized disease
- 50% of cases with purely ocular symptoms

- Seronegative MG (SNMG) patients (negative AchR and MuSK Ab testing) are similar to AchR-Ab+ patients in clinical features and thymic pathology
Antibody status in 76 Cypriot patients with generalized myasthenia

- AchR-Ab but not yet tested for MuSK: 17.1%
- AchR-Ab: 40.8%
- Double seronegative: 27.6%
- MuSK-Ab: 14.5%
Binding to rapsyn –clustered recombinant AchR detected in 66% of seronegative MG patients

AChR clustering enhances detection of AChR antibodies in SNMG samples

Detection of antibodies to unclustered AChRs on the transfected HEK cell surface

(Leite et al., Brain 2008)
Anti-MuSK positive MG

- Decreasing frequency with increasing latitude north of equator
- Mainly bulbar weakness, possible focal weakness (laryngeal, pharyngeal, respiratory, neck)-no ocular!
- Diurnal fluctuations uncommon
- EMG test on limb muscles are frequently negative
- Poor response to mestinon or tensilon
- Thymus histology is generally “normal-for-age” (rare cases with thymoma → imaging still necessary!)
- Thymectomy does not appear to improve disease outcome
- Good response to immunosuppression
- But less likely to go in remission

Vincent, 2008
Muscle atrophy in anti-MuSK positive myasthenia

Central tongue wasting (central furrowing) with some lateral thinning giving a ‘triple furrowed’ tongue in a MuSK antibody positive patient.

(Farrugia at al, Brain 2006)
Patients with anti-MuSK antibodies in Cyprus

- 6 F, 5M (ages 12-60 years)- frequency is similar to other Mediterranean countries
- All with predominantly bulbar and respiratory weakness
- None with ocular MG
- Severity does not differ significantly compared to non-MuSK generalized MG patients (severe/MGFA IV-V in 30% vs. 28.9%; moderate in 30% vs. 33.4%; and mild MG n 40% vs. 42.6%)
- However, less likely (0%) to go in remission (either drug free or pharmacological) as opposed to 39.1% of non-MuSK patients (p=0.019)
Features of late onset myasthenia in Cyprus

- **Increasing frequency** (same trend also in other countries)
- 35 patients (40%) with onset >50 yrs in our clinic
- Male predominance (F:M=1:1.5)
- ? More likely to develop severe grades >III (34.5%) as opposed to 16% in EOMG (p>0.05)
- Overall good response to treatment and prognosis (currently 58.6% asymptomatic and 20% with only ocular symptoms)

- In general 13-20% of all patients with MG are over 60 yrs → clinicians should be careful about the diagnosis as some have been misdiagnosed as brainstem strokes

Mean annual incidence in Denmark

Somnier, 2005
Basic principles of myasthenia treatment

■ Individualized
  ■ Choice of medications and their dose should not and cannot be the same in all patients- each may have different circumstances
  ■ MG treatment is not static- it may need changes of medications and doses during the course of the illness

■ The choice of medications and their dose depends on the type and severity of MG, and the profile of the patient (life style, family planning, age, co-morbidities, other medications)

■ In most patients a combination of medications will be needed at some point

■ The side effects and the efficacy of the same medication may differ from patient to patient!

■ Close follow-up and good collaboration between patient and doctor is essential for success!
Current Treatment of Myasthenia

Cholinesterase Inhibitors (Pyridostigmine)
• Symptomatic therapy: Increases ACh availability → only a minority will respond as monotherapy!

Thymectomy
• In patients with thymic hyperplasia removes the possible site of auto-sensitization against AChR and a relevant site of antibody production
• In patients with thymoma/Ca removes a potentially invasive tumor

Immunosuppressive therapy
• Inhibits lymphocyte proliferation and antibody production

Short-term, rapid onset therapies
• Plasma-exchange (PE): Removes serum antibodies and cytokines
• IVIG (2 g/kg in 2-5 days): Interfere with T-cell activation, Ab production and activity
→ Useful in myasthenic crisis (PE may have a more rapid effect), patients refractory to immunosupression, or when quick response needed
Thymectomy in MG patients without thymoma

- Thymectomized patients appear to have a better prognosis in terms of drug-free remission rate (2.1 higher than in unthymectomized cases) (Gronseth, 2001)
- Most experts consider thymectomy to be a therapeutic option in anti-AChR-positive, generalised MG with onset < 50 years, in experienced centers
- Generally not recommended in late onset, ocular, or MuSK-Ab+ cases, and questionable in seronegative
- Benefit of thymectomy not definitely proven:
  - Lack of randomized studies and standardized outcome measures
  - Presence of confounding factors (disease duration before surgery, associated treatment, different surgical procedures)
- A multicenter randomized trial (MGTX study) to establish the effect of thymectomy in non-thymomatous patients is currently underway
Myasthenia gravis associated with thymoma or thymic carcinoma

- The disease is generally severe with acute onset and rapid progression
- Thymectomy does not improve MG clinical course (a deterioration in the first months after surgery is frequently observed)
- Most patients need long-term immunosuppression and
- are less likely to go into remission
Corticosteroids

• Commonly used as initial treatment: almost all our patients (>90%) treated with corticosteroids at some point (prednisone, prednisolone, deflazacort)

• Should be considered in all patients with disabling symptoms not responding adequately to mestinon
  – Prednisone 20-60 mg/d with gradual shift to alternate day treatment, progressive dose tapering after improvement
  – 20% of patients (bulbar) may show “early deterioration”
  – Relatively rapid onset of benefit (weeks-months)

• If high doses needed long-term and depending on side effect profile, a steroid sparing immunosuppressing medication should be added

→ Monitor side effects, use minimum necessary!
Immunosuppressant steroid-sparing medications

**Azathioprine:** most commonly used (max dose 2-3mg/Kg), has a long latency (6-18 months) before onset and maximum benefit
  - Other immunosuppressants work more rapidly, but still with latency no less than 2-3 months
  - Monitor (and explain) possible allergy/liver reaction! (5-10%)
  - Caution in thiopurine methyltransferase (TPMT) deficiency!
  - well tolerated in most our patients over long term (including 2 uncomplicated pregnancies- at lowest possible dose)

**Cyclosporin:** start 3-5 mg/kg; maintenance: 2-3 mg/kg
  → Frequent side effects in most patients (muscle pain and cramps, hirsutism, hypertension, nephrotoxicity)
**Tacrolimus:** 3-4mg; maintenance: 1-2 mg, may be less nephrotoxic- but also has side effects

**Cyclophosphamide:** in refractory MG at high pulse dose 500mg/m2- generally more toxic
Mycophenolate treatment in myasthenia

- **Mycophenolate** mofetil (CellCept) or sodium (Myfortic): 2-3 g/d

- Start **CellCept** (250-500mg/d) or **Myfortic** (360mg/d) and double dose every 2 weeks. Monitor CBC every 2-3 weeks initially and increase up to 2-2.5 g CellCept (or 4-5 tabs Myfortic) daily as tolerated (keep lymphocyte count >1000 µL)

- 27 patients in our clinic with generalized, moderate-severe MG so far treated with mycophenolate (CellCept or Myfortic)

- Rarely (1 patient) persistent diarrhea when started

- 2 patients stopped CellCept after 2 years because of gastric ulcer, and restarted Myfortic several months later without problems

- 26 patients currently taking mycophenolate for a period ranging from 1-8 years and doses ranging from 750mg to 2500mg/d (equivalent of CellCept)
Outcome after mycophenolate treatment

- MGFA grade when starting mycophenolate was $2.88 \pm 0.87$ (range 2-5)
- MGFA grade after taking mycophenolate for at least 1 year (range 1-8 years) was $1.21 \pm 0.81$ (range 0-3)

→ Significant improvement: $p$ (2-tail) = 0.0001, Wilcoxon signed-rank test

![MGFA grade before and after MMF treatment](chart.png)
Steroid sparing effect of mycophenolate

• Prednisone daily dose when starting mycophenolate was 27.9±18.6mg (range 5-60 mg/day)

• Daily dose after taking mycophenolate for at least 1 year (range 1-8 years) was 9.3 ±2.7 (range 0-35 mg/day)

→ Significant reduction of prednisone dose: p (2-tail)=0.0002, Wilcoxon signed-rank test

![Graph showing prednisone dose before and after mycophenolate treatment](image)
Mycophenolate: conclusions from CING experience

• Mycophenolate appears to be safe for patients with myasthenia gravis and compares favourably with other standard medications regarding side effect profile

• Effective for refractory patients: reduces exacerbations, IVIG/PE dependency, and allows significant reduction of steroids

• Mycophenolate should be considered also as the first choice of immunosuppression for moderate-severe MG, or patients refractory to steroid treatment, or patients requiring fast immunosuppression (as opposed to AZT) as these patients appear to benefit most from this medication

• Contraindicated in pregnancy (or planning of it)
Always remember contraindicated medications that can exacerbate myasthenia!

- **ANTI-ARRHYTHMICS** (Procainamide, quinidine)
- **ANTIBIOTICS**
  - Aminoglycosides (Gentamicin, Amikacin, Tobramycin, Streptomycin, Kanamycin)
  - Quinolones (Ciprofloxacin, Norfloxacin, Ofloxacine)
  - Telithromycin
- **BETA-BLOCKERS**
  - Phenytoin
  - Chlorpromazine and related drugs (antipsychotics), Lithium
- **MUSCLE RELAXANTS**

(Cyprus MG Association card for patients includes detailed list)
New symptomatic therapies

- The antisense oligonucleotide (EN 101, Monarsen) preferentially blocks the expression of the Ach-Esterase-R variant which is over-expressed in MG (as opposed to pyridostigmine which non-selectively block AChE-S and AChE-R at the neuro-muscular junction)
- Oral administration of Monarsen was found effective in an open-label study (Argov, 2007)
- U.S. Food and Drug Administration has granted Orphan Drug Designation status for Monarsen - pending approval in Europe

Kaminski, 2007
New immunosuppressive therapies

Monoclonal antibodies (mAbs)

Humanized and chimeric mAbs are designed to interact with specific antigens

**Rituximab** is directed against CD20, expressed on pre-B and B cells

- In uncontrolled reports, it proved effective in both AChR-MG and MuSK-MG.
- Therapeutic effect in autoimmune diseases associated with **B cell depletion** without significant changes in Ab levels (Kessel, 2008; Liossis, 2008)

Anti-cytokine treatments

TNF-α inhibitors have been used in single cases (**Infliximab** (Kakouliku, 2007) and in a small prospective trial (**Etanercept**) (Rowin, 2008)- **worsening in some patients!!!**

- Therapeutic effect was counterbalanced by **frequent side effects**

C5 Inhibition (**Eculizumab**) is a possible treatment for acute phases of anti-AChR positive MG

- **Under investigation**: anti-IL-6 antibodies (block EAMG)
The future of myasthenia treatment: targeting the pathological antibodies and their production without general immunosuppression

Emerging Antigen-specific treatments for MG

- Selective recognition and elimination of nicotinic acetylcholine receptor-reactive B cells by a recombinant fusion protein AChR-Fc in myasthenia gravis in vitro (Chang et al., J Neuroimmunol 2010)

- In vivo adsorption of autoantibodies in myasthenia gravis using Nanodisc-incorporated acetylcholine receptor (Sheng et al., Exp Neurol 2010)

- AchR-transferrin fusion protein (traps and destroys AchR antibodies) (Keefe et al., Autoimmunity 2010)

- Specific immunotherapy of experimental myasthenia gravis with human muscle AChR constructs: diverting autoantibody production away from pathologically relevant specificities directed at epitopes on the extracellular surface of muscle AChRs toward pathologically irrelevant epitopes on the cytoplasmic domain (Luo et al., Ann Neurol 2010)
Incorporation of ACh-R into the Nanodisc structure

→ Intravenous administration of ND–AChR reduces circulating levels of anti-AChR antibodies in EAMG

(Sheng et al., 2010)
Importance of care provision for patients with myasthenia in a specialized center


Factors leading to unsatisfactory outcome (UO) in MG:
41 patients with autoimmune MG were followed prospectively
- UO in 54% related to **under-treatment** (41%), **poor treatment compliance** (23%), **infections** (23%), and **adverse drug effects** (13%)
- When care was provided by neuromuscular (NM) specialists, patients had significantly better follow-up scores (P = 0.01)
- At final assessment UO rates were 7% and significantly better in patients treated by NM specialists, compared to other physicians where UO rates reached 27%
- Nearly two-thirds of the UOs could have been prevented by appropriate **therapeutic adjustments** and improved compliance
- The differential UO rates at follow-up, their dependency on the degree to which the management was specialized and their correlation with final outcomes suggest that **specialized MG care improves outcomes**
Long term socioeconomic impact of myasthenia

2007 survey of CING social services offered to 60 patients with myasthenia

Patients received social services consultation for:

- Social security and other state financial help: 26 patients-43.3%
- Retirement on disability or early retirement: 15 patients-25%
- Home assistance (household or 24-hour care): 13 patients-21.6%
- Disable's car: 12 patients
- Disable’s ID: 5 patients
- Family and partnership problems: 4 patients
- Assistance finding a job: 3 patients
64% of the patients (n=36) reported problems with their daily living situation including:

- Tension and irritability
- Depression Isolation
- Fatigue
- Arm weakness
- Difficulty driving
- Difficulty with Activities of Daily living
- Dizziness, loss of balance, cramps
- Weight gain due to steroids
- Osteoporosis
- GI problems, ulcer

Psycho-social problems

Myasthenia symptoms

Treatment side effects
Conclusions

- Myasthenia in Cyprus presents a higher proportion of patients without detectable auto-antibodies
- There is a need for further research focusing on the auto-immune and genetic mechanisms in myasthenia:
  - MG genome-wide association study/ Myasthenia genetics consortium
  - Epidemiological study-EuroMyasthenia consortium
- Most patients can improve with combination of treatments currently available, but short-term and long-term side effects of medications remain a major problem → there is a need to improve therapeutic options with better tolerated and specific medications
- Myasthenia is a chronic and often unpredictable condition: patients require regular specialized medical care, social and psychological support services
ACKNOWLEDGEMENTS

Ασθενείς και Σύνδεσμος Ασθενών με Μυασθένεια/Cyprus MG Association

THANK YOU