Myasthenia gravis Myopathy

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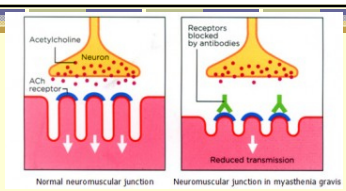
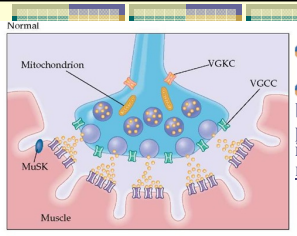
Myasthenia gravis and myasthenic syndromes



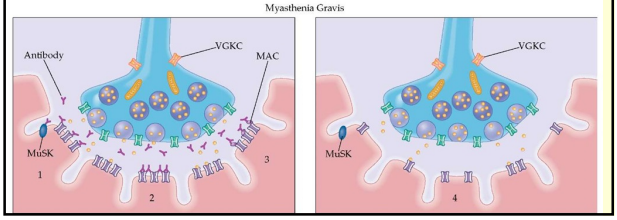
- MG, definition: autoimmune disease with circulating antibodies against Ach-R (Acetylcholine Receptor), or other antigens of postsynaptic membrane (titin, MUsK-enzyme,...)
- Clinical symptoms: progredient muscle weakness during daily activities, with evening acces, repair after rest time
- Onset: small muscles – eye (diplopia), pharynx (dysphagia), soft palate (rhinolalia), general ...

MG- epidemiology

- **Incidence**: 14,8 / mil. inhabitants
- Prevalence: 191 /mil. inhab. /Slovakia 2007/
- **Disease onset**: mostly: 30. year (F), 60.-70. year (M)
- Sex rate F:M= 1,7:1
- No hereditary cases, familial increased susceptibility for autoimmune disease (HLA)



- Acquired autoimmune disease
- **Ab+Ach-Receptor => functional block and destruction=> decrease postsynaptic actional potential => insuficient muscle contraction => muscle weakness**



MG- manifestation

- Clinical symptoms: progredient muscle weakness during daily activities, with evening acces, repair after rest time
- Onset: small muscles – eye (diplopia), pharynx (dysphagia), soft palate (rhinolalia), general ...
- Thymus abnormalities - ¾ of MG patients
- **85% - hyperplasia**
  15% - thymoma (benign / malign)

MG- disease course

- **Subjective**: abnormal muscle fatigue, weakness - paresis, recovery after resting
- **Objective**:
- repetitive muscle activity provocates weakness- ptosis, diplopia, rhinolalia, dysphagia, dysarthria, dysphonia
- weak of jawing, mimic paresis
- neck dicrease
- short breathing
- tendon reflexes- presented or slight decrease

MGFA (Foundation of America)- Clinical symptoms scaling
(Osserman´s classification)

- I. Ocular form MG
- II. Ocular + slight generalised MG (limbs /bulbar)
- III: Moderate weakness of ocular + extraocular muscles (limbs, respiratory, bulbar muscles)
- IV: Severe weakness of ocular + extraocular muscles
- V: Respiratory failure, suported ventilation

MG- diagnosis

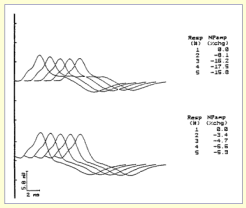
1. **History and clinical picture**
2. **EMG**
3. **Laboratory tests**: serum antibodies anti-Ach-R (75% positivity)
4. **Clinical tests**: Simpson´s test- vertical gaze
   Seeman´s test- dysarthria
   Gorelick´s test
   pharmacol. Tensilon test: iv. amp. inhib. AchE
5. **X-rays chest, mediastinal CT, MRI**

Static and dynamic (repetitive) tests

- Demasking of latent MG or enhancing of present muscle weakness
- **Simpson´s test** – slight ptosis – patient is looking upward 1 minute- more severe ptosis
- **Gorelick´s sign** – bilateral asymetrical ptosis: patient is looking up, finger elevation of eyelid opposite side, on contralateral side wa can see total decrease
- (pathognomic for MG)

MG- EMG

- EMG - repetitive stimulation, low freq.stimulation - 3Hz
  Abnormality: **gradual decrement of response amplitude**
- min.15%, max. in the 2.- 4. response, normalization of EMG after Tensilone inj.



MG- therapy

Currently - no deaths, previously - 30% mortality

1. **Pharmacological**: IS + symptomatic th
2. **Surgical** – thymectomy

Pharmacological therapy:

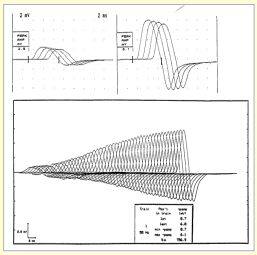
- Immunosupression: **Prednison, Azathioprine,Cyclosporine A**
- Plasma exchange or IVIG
- inhib.ChE **(Pyridostigmine, Mestinon)**

LEMS, Lambert- Eaton myasthenic syndrom

- is a rare autoimmune disorder
- muscle weakness of the limb
- Antibodies against presynaptic voltage-gated calcium channels, and likely other nerve terminal proteins
- Prevalence: 3.4 cases/million
- Around 60% of LEMS -have an underlying malignancy, small cell lung cance -paraneoplastic syndrome
- KP: fatigue, weakness of proximal mm., inferior extremities, spared eye and bulbar mm.
- autonomic difficulties: dry mouth, low lacrimation, orthostatic collapses, impotentia

LEMS

High frequency repetitive EMG (30 Hz) => gradual increase of AP amplitude



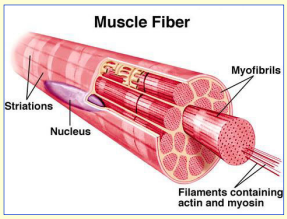
Therapy:

steroids, Azathioprine, plasma exchange

Transient neonatal myasthenia

- 10-15 % of myasthenic patients
- transplacentar Ab penetration
- transient clinical symptoms - 2-5 weeks
- spontaneous elimination of Ab from child organism
- Th: CHE inhibitors, steroids

Myopathy



Myopathy

A- **congenital**, hereditary
B- **acquired**

Classification:

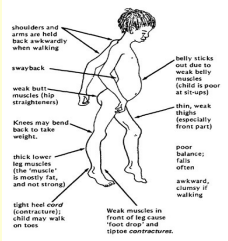
1. **Progressive muscular dystrophies**
2. **Congenital myopathy (structural lesions)**
3. **Myotonia / myopathies of ionic channels**
4. **Myotonic dystrophy**
5. **Myopathies caused by toxic substances**
6. **Familial periodic palsy**
7. **Endocrine myopathies**
8. **Metabolic myopathies (mitochondrial)**
9. **Inflammatory myopathy- myositis,dermatomyositis**

Myopathy

- **Muscular symmetric weakness!**
  Limb girdle muscles, duck gait, hyperlordosis, body „climbing", pseudohypertrophy, muscle atrophy, cramps, myalgia
- **Laboratory tests:**
  high CK, LDH, aldolase, myoglobin
- **Muscle biopsy:**
  Muscular degeneration, necrosis
- **EMG- pattern of myopathy**

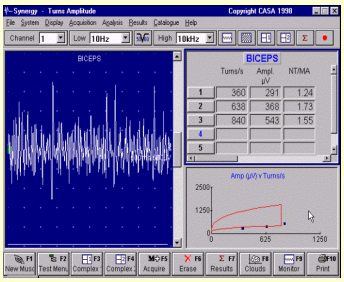
Myopathy

- Tendon jerks - decreased or absent
- Progressive muscle atrophy
- CSF- normal
- MRI mm.spectroscopy (31P) - shows energetic metabolism abnormalities
- CT or MRI – abnormal muscle density - early subclinical abnormalities
- Molecular genetics - gene analysis, abnormal gene identification (PCR)



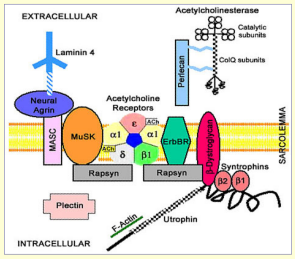
Myopathy- EMG

Native needle EMG: decreased and shortened action potentials



Progressive muscular dystrophy

- **Dystrophinopathy**
- **Dystroglycanopathy**
- **Sarcoglycanopathy**
- **Lamininopathy**
- **Rapsynopathy**
- **Syntrophinopathy**
- **Utrophynopathy, ...**



Progressive muscular dystrophy

- **Duchenne muscular dystrophy-dystrophinopathy**

Gene abnormality of dystrophin protein (muscle, brain, heart)

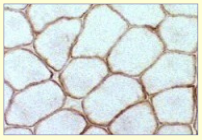
- **Gene mutation Xp21- abnormal muscle metabolism**
- **Klinical symmptoms: boys, disease onset between 2.-5.y.,**
  - **Hyperlordosis, duck gait**
  - **Climbing, unable to run**
  - **Freq. falls, allar scapules, PHT of legs, scoliosis**
  - **Immobility at least 13.yrs, death about 30.yrs**
  - **1/3 mental retardation**
  - **½ cardiomyopathy – letal complications**

Duchenne muscular dystrophy- dystrophinopathy

Diagnosis= onset age, clin.symptoms + labs + EMG + biopsy

Blood- extreme high CK, myoglobine

Biopsy - dystrophin absence, degenerative changes, atrophy, regenerative changes



Becker muscular dystrophy- dystrophinopathy

- 5x decreased incidence than Duchenne m.d.
- more benign
- inability of gait- about 30. yrs
- surviving about 40.- 50.yrs
- mental retardation, scoliosis, CMP - not present
- biopsy - dystrophin is present (small %)
- individual disease course - different prognosis

Duchenne MD (DMD)

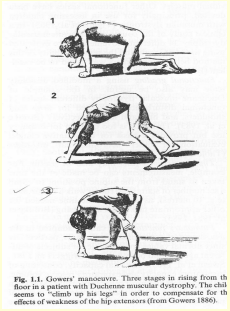


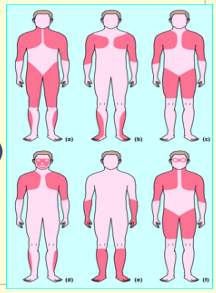
Fig. 1.1. Gowers' manoeuvre. Three stages in rising from th floor in a patient with Duchenne muscular dystrophy. The chil seems to "climb up his legs" in order to compensate for th effects of weakness of the hip extensors (from Gowers 1886).

Muscular dystrophy

- EDMD- Emery- Dreifus MD- X-chrom. linked, protein emerin, onset 6.-12.y., benign slow progression of musc. weakness, CMP-limit of surviving (AV block)
- Facio-scapulo-humeral dystrophy- 20.y., facies myopathica, benign course
- Limb- girdle muscular dystrophy-benign forms, 20.-40.y., deficit of sarcoglycan adhaline
- Distal muscular dystrophy
- Ocular muscular dystrophy
- Oculo- pharyngeal muscular dystrophy

Other progressive muscular dystrophies

1. DMD (A)
2. BMD (A)
3. Emery- Dreifuss MD (B)
4. Limb girdle MD ©
5. Facioscapulohumeral MD (D
6. Distal MD (E)
7. Oculophfaryngeal myopathy (F)
8. Ocular myopathy



Muscular dystrophy

- **Treatment:**

1. Causal: unknown
2. Preventive: genetic analysis
3. Symptomatic

- Fyziotherapy, contracture prevention
- deformities operations, ptosis oper.- lifting
- prosthesis aid, wheel chair
- ATP, B vitamins, carnitine, coenzyme Q, laevadosine, steroids- individually benefit effect

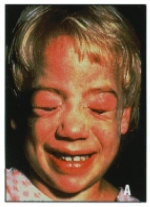
Myositis- inflammatory myopathy

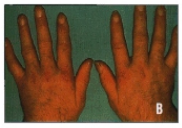
- A – infectious
  - viral- Coxackie B, ECHO, influenza
  - bacterial - staph., tbc, borreliosis
  - parasitic- trichinelosis, cysticercosis, toxoplasmosis
  - mycotic
- B - autoimmune
  - Polymyosistis - PM
  - Dermatomyositis - DM
  - Inclusion body myositis - IBM

Dermatomyositis / DM

- Children, young adults
- Skin changes: red, extensor areas, facial „buterfly“ erythema, violet “periorbital edema, “heliotropic rush“, pulmonary and cardial complications
- DM and PM are often associated with collagen diseases (scleroderma, polyarteritis nodosa, RA, Sjogren sy) – „overlap sy“

Dermatomyosistis





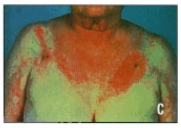


Fig 1A-C.-- Features of dermatomyositis(A) are discoloration of the upper eyelids, periobital edema, malar rash, and dry, shiny, erythematous skin on the forehead. Gottron's papules of the hands(B) show erythematous and slightly scaly lesions on the metacarpophalageal joints. Dermatomyositis of the chest(C) shows an erythmatous eruption in a mantle distribution over light-exposed areas. Reprinted from the Clinical Slide Collection on the Rheumatic Diseases, copyright 1991, 1995. Used by permission of the American College of Rheumatology.

Polymyositis / PM

- Older persons, paraneoplastic syndrome (10%)
- severe disease course, high letality
- proximal mm. weakness
- myopatic syndrome (dysphagia, dysphonia)
- myalgia
- atrophy, contractures, immobility, ...

PM, DM, IBM

- **Labs:** high CK, LDH, myoglobin, CIK, C3, Ig, ANF
- **EMG**: myopathic pattern
- **Biopsy:** immune complexes (IgG, IgM, C3) deposits in vessel vall of muscles resultating to muscle infarctions and muscle fibre necrosis, atrophy
- **Therapy:** steroids, CPA, Cyclosporine, MTX, Azathioprine, PE

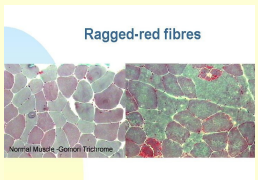
- **IBM-** chronic progressive course, old patients, paraneo sy, slow atrophy, dysphagia, inclusion bodies (Alzheimer of muscle), therapeutic resistance(steroids)

Metabolic myopathies

- **Glycogenosis** - **multisystemic disease (muscles, liver, kidney, myocard)**
  - ✓ **Pompe´s disease - hypotonia, CMP, hepatomegalia, infantile and adult forms,**
  - ✓ **Mc Ardle ś disease**
- **Carnitine myopathy – „floppy infant sy“, proximal weakness, CMP**
  Th. Carnitine substitution

Mitochondrial myopathy

- **Kern- Sayre syndrom**
- **MELAS- mitoch. encephalomyelopathy lactate acidosis stroke**
- **MERRF- mitoch. encephalopathy ragged red fibre myopathy**
- **Alpers´s disease**
- **NARP**
- **LHON**



Toxic myopathy

- **Acute myopathy: vincristine, narcosis**
- **Chronic myopathy: steroids, lithium, digoxin, Ca-blockers, beta-blockers, D-penicilamine, Zidovudin (anti-HIV)**
- **Myositis: AE-hydantoinates, procainamide, L-Dopa, PNC**
- **Rhybdomyolysis, fibrosis: heroin, amfetamine, methadon, isoniazid, barbiturates, ...**
- **Local muscle atrophy or myopathy: steroid inj., opiates, chlorpromazin, diazepam,...**

Endocrine myopathy

- **Thyroid hyperfunction:** myopathy, myalgia, atrophy, orbitopathy, diplopia
- **Thyroid hypofunction:** myalgia, cramps, myoedema, myopathy, weakness
- **Steroid myopathy**: girdle atrophy, myalgia, PM
- **Hyperparathyreosis**
- **Acromegalia**
- **Diabetes mellitus**