Findings on first investigation

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<th></th>
<th>Total</th>
<th>Men</th>
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</table>

EMG IN MYOPATHIES

Björn Falck, M.D., Ph.D.
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University Hospital
Uppsala, Sweden

Myopathies

- Muscle dystrophies
  - Hereditary progressive myopathies
  - Congenital myopathies
    - Heterogeneous group of myopathies with onset in the newborn
  - Distal myopathies
  - Inflammatory myopathies
  - Critical illness myopathy
  - Metabolic myopathies
  - Mitochondrial myopathies
  - Rhabdomyolysis
  - Drug induced myopathies

Site of the abnormality

- Muscle dystrophies
  - Dystrophinopathies
    - Duchenne dystrophy
    - Becker dystrophy
    - X-linked Xp21, mutation of dystrophin gene
  - Facio-Scapulo-humeral dystrophy
  - Limb-girdle dystrophies
    - Recessive and dominantly inhereted
  - Emery-Dreifuss dystrophy
    - Three different mutations
  - Myotonic dystrophy type 1 and 2

Muscle dystrophies

- Congenital myopathies
  - Central core
  - Nemaline myopathy
  - Centronuclear myopathy
  - Etc…
Distal myopathies
- Welander type
- Tibial muscular dystrophy (Udd)
- Mioshi myopathy
  - Dysferlinopathy

Inflammatory myopathies
- Inclusion body myositis (IBM)
- Dermatomyositis
- Polymyositis
  - Quite rare
  - Adults only

Mitochondrial myopathies
- MERFF – myoclonic epilepsy and ragged red fibers
- MELAS - mitochondrial encephalopathy, lactic acidosis and stroke-like episodes
- Kerns-Sayre
- PEO – progressive external ophthaloplegia
- MNGIE –myoneurogastrointestinal encephalopathy

Metabolic myopathies
- Type 2 glycogenosis – Pompe
- Type 5 glycogenosis – McArdle disease

Rhabdomyolysis
- Acute necrosis of muscles
- Triggered by drug or alcohol induced immobility
- A small number may have a hereditary metabolic disorder
- Swelling of muscles, weakness
- Myoglobinuria (urine dark)
- Outcome usually good

Diagnosis of neuromuscular disorders
- History
- Clinical examination
- Clinical chemistry
- Clinical genetics
- ENMG
- Muscle histology
- Imaging
**Specialties involved in diagnosis**

- Adult neurology
- Pediatric neurology
- Internal medicine
- Dermatology
- Rheumatology
- Clinical neurophysiology
- Neuropathology
- Clinical genetics
- Radiology
- Clinical chemistry
- Clinical physiology

**History**

- Weakness
  - Functional deficits
- Fatigue
- Pain
  - Rare in myopathies
  - Polymyositis, dermatomyositis sometimes
  - Dystrophia myotonica type 2
  - *Muscle pain without weakness is not myopathy*
- Age of onset
- Progression
- Family history

**Clinical examination**

- Inspection
  - Atrophy
  - Hypertrophy
  - Skin changes
- Muscle strength
- Tendon reflexes

**Distribution of weakness**

- Limb-girdle
  - Proximal weakness of arms and legs
  - Common in most myopathies
- Distal
  - Quite common, especially in the Nordic countries
  - Scapuloperoneal
  - Forearm flexors – quadriceps (IBM)
  - Oculo-pharyngeal
  - Neck extensors

**Clinical chemistry**

- Creatine kinase (CK)
  - >3-50 above the upper limit of normal
  - Mild abnormalities 2-3 x are not significant
  - Physical exercise elevates CK
  - In neuropathies 2-5 times elevated
- Aldolase, LD, ASAT, ALAT
  - No significant advantage over CK
- Specific metabolic tests
  - Lactate in mitochondrial disorders

**DNA testing in myopathies**

- Nucleotide repeats
  - Myotonic dystrophy type 1
    - DMPK gene trinucleotide repeat
  - Myotonic dystrophy type 2
    - ZNF-9 gene tetrancleotide repeat
  - Oculopharyngeal muscular dystrophy
- Deletions
  - Dystrophin
- Mitochondrial cytopathies
### Role of EMG

- EMG used as a first line test
  - Is there an abnormality?
  - Normal EMG does not rule out myopathy
  - Differentiate between neuropathic and myopathic disorders
- In myopathies EMG is rarely specific
  - Limits diagnostic alternatives
  - IBM - very typical distribution of findings
- Some myopathies are rarely seen in the EMG lab
  - Diagnosis based on clinical findings and DNA testing
  - Myotonic dystrophy type 1
  - Duchenne dystrophy

### Neurophysiological methods

- Neurography
- EMG
- SFEMG
- Decrement

### Classic EMG features in myopathies

- Spontaneous activity
  - Fibrillation potentials indicate active myopathy
  - Complex repetitive discharges non-specific finding
- MUP analysis
  - Low amplitude, short duration
  - High amplitude, normal duration
  - Sometimes polyphasic
  - Increased jiggle
- Early recruitment
  - Motor units are weak and all units are recruited early

### Usefulness of EMG findings

- Never pathognomonic
- Discriminate between myopathy and neuropathy
- Distribution of findings between muscles helpful
- Combination of all information often gives the diagnosis

### Why should MUP analysis be used?

- Documentation
- Systematic approach to problems gives more detailed information
- Less biased than qualitative analysis
- Follow-up studies

---

**Björn Falck**
MUSCLE BIOPSY

Indications
- Differential diagnosis of myopathies
  - Is there a myopathy?
  - What type of myopathy?
- Diagnosis not possible using DNA analysis
  - Most Duchenne patients do not have biopsy
  - Myotonic dystrophy not required
- When clinical picture is clear biopsy is not necessary
  - Inclusion body myositis
  - Dermatomyositis

Types of biopsy
- Open biopsy
  - Large incision 4-5 cm
  - Significant discomfort
  - Easy to secure quality of biopsy material
- Needle biopsy
  - Bergström needle
  - Difficult to get good quality of material in atrophic muscles

Semi-open biopsy
- Introduced by KG Henriksson in 1970s in Linköping
- Local anesthesia
- 1 cm incision
- Alligator forceps
- 3-4 pieces with a diameter of 3-4 mm
- Well tolerated
- Can be repeated

Semi-open biopsy
- Done in association to EMG
- Muscles easily biopsied
  - M.vastus lateralis
  - M.deltoides
  - M.tibialis anterior
  - M.gastrocnemius
  - Paravertebral muscles
  - M.infraspinatus
  - M.biceps femoris

Tools

MUP analysis

Incision

Take biopsy from the muscle

Result

Beware!

- M. tibialis anterior
  - Deep peroneal nerve may be at risk!
  - Never take biopsy in the posterior direction (downwards)
  - Start laterally and move towards the tibial bone
- Very small babies
  - Can be done in 3-6 month old babies

Histology

- Ordinary hemotoxylin-eosin staining
- Enzymehistochemistry
- Immunohistochemistry
- Electronmicroscopy

Dermatomyositis - HE

Penfascicular atrophy and necrosis
MUP analysis

**PM – NADH**
Ring fibers, targetoid fibers, fiber size variation

**IBM - COX negative fibers**
Ragged-red fibers are cytochrome oxidase negative but succinate dehydrogenase positive (blue) in COX-SDH staining

**M.vastus lateralis - Dystrophin**

**DM - electron microscopy**
Undulating tubules

**Example of histology in myopathy**

**Pathophysiology of myopathies**
- Fiber necrosis
- Fiber atrophy
- Fiber splitting
- Hypertrophy
- Regeneration of muscle fibers from satellite cells
- Reinnervation of degenerated fibers
- Increase of connective tissue
MUP analysis

**Myopathy**

**Distal myopathy – m.ext.dig**

**Facio-scapulo-humeral dystrophy, tib ant**

**Facio-scapulo-humeral dystrophy, tib ant**

**Myotonia congenita – Thomsen, Vastus lat**
Myotonia congenita – Thomsen, vastus lateralis

Duchenne dystrophy – m.vast.lat.

Alpha sarcoglycanopathy

Björn Falck
Myotonic dystrophy - m.deltoides

DM2 - m.deltoides

Dermatomyositis

DM
- Idiopathic inflammatory myopathy with characteristic cutaneous manifestations
- Occurs in all ages
  - Children 4-15 years, even infants
- Incidence of PM+DM in Finland around 1/100000 (Oka et al 1988)

Heliotrope rash in DM
### Skin changes over the hands

- Malaise, mild fever
- Skin rash often precedes weakness
- Proximal muscle weakness
- Weeks or months
- Myalgia and muscle tenderness
  - Children > adults
- Dysphagia in 25%
- Rarely severe weakness of respiratory muscles

### DM – muscle weakness

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### DM – associated manifestations

- Cardiac
  - Overt symptoms uncommon
  - ECG abnormalities common
- Pulmonary
  - Interstitial lung disease (ILD) in 10%
- Joints
  - Arthralgia without arthritis
  - Arthritis of small joints
  - Contractures
- Vascuilitis

### DM - association with malignancy

- The rates of reported malignancies 6-60%
- Carefully designed controlled prospective studies have not been done

### DM - association with malignancy (Sigurgeirsson et al, NEJM 1992;326:363-67)

<table>
<thead>
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<th>DM - association with malignancy</th>
<th>DM - temporal relation with malignancy</th>
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| Risk for cancer in DM
  - 2.4 (1.6-3.6, 95% CI) in men
  - 3.4 (2.44-4.7, 95% CI) for women.
- The cancer mortality in DM
  - 3.8 (2.9-4.8 95% CI) times higher than the general population.
- Particularly ovarian carcinoma has been implicated, but any type of malignancy may be related with DM.

### Risk for cancer in DM

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- The cancer mortality in DM
  - 3.8 (2.9-4.8 95% CI) times higher than the general population.
- Particularly ovarian carcinoma has been implicated, but any type of malignancy may be related with DM.
### DM-treatment
- Prednisone
- Azathioprine, cyclophosphamide, methotrexate, cyclosporin
- IV IgG in adults
- Plasmapheresis
- Physiotherapy to prevent contractures in children
- Calcinosis (topical steroids, colchicine, may require surgery)

### Course and prognosis
- In adults DM is usually chronic
- Considerable mortality even today, especially in patients with cancer
- In most children remission, withdrawal of medication can be anticipated

### Dermatomyositis - pathogenesis
- B-cell mediated immunopathology against endothelial cells of small blood vessels
- Complement activation by antibody
- Reduced number of capillaries, microinfarcts and ischemia
- Antinuclear antibodies in 25-60%
- Factors initiating vascular damage not known

### Childhood DM - pathogenesis
- 85% have the HLA-DQA1*0501 allele
- Maternal chimerism
- Prognosis is usually good
- Calcinosis of skin may be a problem

### Polymyositis (PM)
- Muscle weakness proximal>distal
- Weeks to months
- Dysphagia
- No skin changes
- Myalgia in 20-30%, rarely chief complaint
- Ventilatory failure is uncommon

### Polymyositis - clinical features
**Polymyositis epidemiology**
- Most patients > 20 years
- Rarely in children
  - In connection with connective tissue disorders

**Polymyositis syndromes**
- Idiopathic
- Graft versus host
- Collagen vascular disease
- Anti t-RNA antibodies (JO-1 antibodies)
- Signal recognition particle antibody
- MAS-antibody
- Drug induced (D-penicillamine)
- Malignancy (necrotic)

**PM – associated manifestations**
- Cardiac
  - Overt symptoms are not common
  - ECG abnormalities are common
- Pulmonary
  - Interstitial lung disease (ILD) in 10% (anti-Jo-1 antibodies)
- Joints
  - Arthralgia without arthritis frequent
- Vasculitis

**PM - association with malignancies**
(Sigurgeirsson et al, NEJM 1992;326:363-67)
- Risk for malignancy in PM
  - 1.8 (1.1-2.7, 95% CI)
- The mortality from cancer in PM
  - 0.9 (0.6-1.4, 95% CI)
- Rates due to cancer search in patients with polymyositis.

**PM – temporal relation to cancer**
(Sigurgeirsson et al, NEJM 1992;326:363-67)

![Bar chart showing temporal relation between polymyositis diagnosis and cancer diagnosis.](chart.png)

**PM - pathogenesis**
- CD8+T-cell mediated immunopathology against muscle fibers
- CD8+T-cells and macrophages surround non-necrotic muscle fibers, invade and destroy them
- Association with HLA-DR3, HLA-B8 and HLA-DRw52
Acute polymyositis - m. deltoideus

M. deltoideus

EMG in polymyositis

- Acute stage
  - Fibrillation potentials
  - Short, small potentials

- Remission
  - Less fibrillation potentials
  - Amplitude variable
  - Duration short or normal

Inclusion body myositis (IBM)
IBM - epidemiology

- Onset mostly > 50 years
- Men > women
- Prevalence 9/1 000 000
- Prevalence in the population > 50 years 35/1 000 000

IBM - weakness

- Evolves slowly
- Distinctive pattern
  - Quadriceps femoris
  - Finger and wrist flexors
  - Weakness often asymmetric
- Dysphagia in 30%
- Facial muscle weakness rare
- Extraocular muscles spared
- Tendon reflexes initially normal, patellar reflex lost

Distribution of weakness in IBM

IBM - treatment

- No treatment sustained effect
- Transient effect with steroids and IV IgG
- Some offer a six month trial with prednisone
- Steroids decrease inflammatory response but do not halt the progression of vacuoles

IBM - associated manifestations

- Peripheral nerves
  - Mild generalized polyneuropathy on ENMG
  - No subjective symptoms
- Autoimmune disorders
  - SLE, Sjögren’s sd, scleroderma, sarcoidosis in 15%
  - Diabetes mellitus?

IBM – course and prognosis

- Slowly progressive disorder
- Muscle strength decreases 10% per year
- Progression leads to significant disability
- Almost normal life expectancy
IBM - pathogenesis

- Virus
  - Myxovirus was initially implicated
- Immune mediated
  - T-cells similar PM
- Mitochondrial disorder
  - COX-negative fibers
- Abnormal aging
  - "Alzheimer characteristic proteins" (ubiquitin, beta-amyloid protein, apolipoprotein, prion protein) in the rimmed vacuoles
  - Apolipoprotein E 4 frequency increased in IMB
- Genetic factors (HLA-DR3 in 90%, DR52, B8)

Classical findings in myopathy

- Fibrillation potentials
  - Suggest muscle fibre damage
  - Correlate with CK
- Unstable MUPs
- MUPs
  - Short and small in amplitude
  - May be polyphasic
  - Large amplitude and normal duration
- Findings depend on disorder and stage of the disorder

The role of EMG today

- If clinical picture is clear in suspected genetic neuromuscular disorders – confirmation with DNA tests (myotonic dystrophy)
- If there are affected family members DNA test is preferable
- If the clinical picture is not clear EMG is helpful in narrowing the diagnostic alternatives
- EMG and MRI are helpful for choosing the right muscle for biopsy

The end