**LECTURE SYLLABUS**

**(General medicine)**

**Pathophysiology of the muscle**

**Skeletal muscle**

Type I fibers = slow, red

Type II fibers = fast, white

**Muscle contraction**

Myosin, actin, troponin



Myoglobin – oxygen reserve

**Muscle function control**

Central motoneuron → peripheral motoneuron = α-motoneuron (motor nuclei of the cranial nerves, ventral muscle horns) → neuromuscular plate (cholinergic synapse, nicotinic receptor) → muscle fiber

Muscle spindle

Motor unit = group of muscle fibers innervated by one peripheral motoneuron

Fibers in the motor unit are activated simultaneously.

**Importance of muscle innervation:**

* Contraction control
* Muscle tone control
* Trophic effect

Denervation hypersensitivity → fibrillations

The role of calcium in muscle contraction

- neuromuscular irritability

- induction of muscle contaction

**Ryanodine receptor**

– calcium channel - Ca2+ flow from the sarcoplasmic reticulum into the sarcoplasm

– gating by increase of Ca2+ level in the sarcoplasm or voltage-gated

**Tetanic cramps** – due to ↓ extracellular Ca2+ level (alkalosis, primary hypoparathyroidisms)

**Rigor mortis** – ATP depletion → inability to release actin - myosin interaction, disappears after 15-25 h due to autolysis of muscle proteins

**Muscle energetics and fatigue**

ADP + creatine phosphate → ATP + creatine (creatine kinase in the mitochondria)

Muscle activity

→ intracellular acidosis, reduction of glycogen, accumulation of P, synaptic fatigue (lack of neurotransmitter in synaptic terminals) → **fatigue, muscle pain**

**Electromyography**

= registration of electric potentials from the skeletal muscles

= electrophysiological method of examination of peripheral nerves (peripheral motoneuron, primary sensitive neuron, pre- and postganglionic autonomic neurons), neuromuscular transmission and skeletal muscles

Diagnosis of subclinical lesions, differential diagnosis

**Diseases and disorders of skeletal muscles**

Manifestations:

* Disorders of movements (- as well as +):

 Fibrillations and fasciculations

* Changes of muscle tone
* Changes of muscle volume
* Muscle pain = myalgia
* Release of substances form the muscle
* Hyperthermia

**Disorders of function of skeletal muscles**

* movements of the extremities
* postural motorics
* oculomotor, eyelids
* articulation
* swallowing
* voluntary control of sphincters
* **breathing!!!** – ventilation disorders → type II (global) respiratory insufficiency

**Myopathic syndrome**

= muscle weakness, ↓ muscle tone, trophic changes

- muscle proteins in the serum

**Myotonic syndromes**

= ↑ muscle tone, persisting muscle contraction and delayed relaxation

- at voluntary contraction (action myotonia) or as a response to mechanic irritation (mechanic myotonia)

Myotonia congenita

Dystrophic myotonia

**Muscle atrophy**

= regressive change of the muscle, reduction of muscle mass

Mostly simple atrophy = reduction of muscle fibers size

Numeric atrophy only in severe cases = reduction of muscle fiber number

Causes of atrophy

* Inactivity (long lasting immobilization, palsy)
* Ageing
* Innervation disorders (peripheral motoneuron affection)
* Muscle dystrophy
* Myopathy
* Corticosteroids (Cushing‘s syndrome)
* Ischemia
* Catabolic states, cachexia

**Muscle hypertrophy**

= increase of muscle mass by enlargement of muscle fibers

Myostatin – produced by muscle cells, inhibition of muscle growth

**Causes**

* Long lasting adaptation to activity (exercise)
* Effect of anabolics (androgens)
* Lack of myostatin – due to a mutation (semidominant)

Pseudohypertrophy = accumulation of connective fibrous or fat in the muscle

**Muscle hypertrophy** = enlargement of fiber diameter

Inborn lack of myostatin leads to extreme hypertrophy of the muscles.

Causes:

* Long lasting adaptation to activity (exercise)
* Effect of anabolics (androgens)
* Deficit or absence of myostatin – due to a mutation (semidominant) → extreme muscle hypertrophy

**Pseudohypertrophy** – accumulation of connective fibrous or fat in the muscle

**Abnormal muscle contractions**

Cramps

Spasms

Contractures

 - physiological

 - pathological

**Myopathies**

= muscle disease with primary affection of the muscle

→ myopathic syndrome

Endocrine myopathies (hyperthyroidism, hypothyroidism, steroid myopathy, acromegaly)

Metabolic myopathies (glykogenoses, lipidoses)

Toxic myopathies

Mitochondrial myopathies

**Muscular dystrophias**

=progressive degenerations of muscle fibers

**Duchenne muscular dystrophy**

Mutation of the gene for dystrophin (nonsense, frameshift mutation)

Recessive X-linked heredity → boys

Complete missing of dystrophin



**Becker muscular dystrophia**

Mutation of the dystrophin encoding gene (missense mutation)

Recessive X-linked heredity → boys

Moderate, but high variability of phenotype severity

**Myositis**

= muscle inflammation

**Rhabdomyolysis**

= muscle fiber destruction

→ release of myocyte content (myoglobin, K+…) into the extracellular space → blood

→ acute renal failure, hyperkaliemia, DIC

Causes:

* Enzymopathies disturbing muscle metabolism
* Mitochondrial disorders
* Malignant hyperthermia, hyperthermia in general
* Muscle diseases (myopathies)
* Direct muscle injury – **crush syndrome**, burns, frostbite, el. current
* Muscle ischemia
* Extreme muscle activity (including cramps)
* Hypokalemia, hypophosphatemia
* Myositis, infections (legionella, influenza)
* Diabetic coma
* Toxins – alcohol, snake toxins, CO, cocaine, medicaments (statins, fibrates)

Consequences: Acute renal failure, hyperkaliemia, DIC

**Compartment syndrome**

= consequence of increased pressure in a limited space

**Causes:** edema, bleeding, tight bandage, injury, inflammation, vein obstruction, ischemia, burns…



**Malignant hyperthermia**

= rapid, paroxysmal, life threatening increase of body temperature induced by depolarizing myorelaxants and some anesthetics

Cause: mutation of ryanodine receptor encoding gene, autosomal dominant

**Neuromuscular transmission disorders**

**Muscle tone disorders**