1. **DYNAMIC (exercise-induced) myopathies** - symptoms (acute myalgia, stiffness → contractions, intermittent weakness → myoglobinuria) appear during / after exercise:

A) **carbohydrate metabolism disorders** - type V (most common), type VII-XI glycogenoses, Szentgyörgyi disease; see p. 734-738
   - hemolytic anemia accompanies only type VII (mild) and type IX (severe).
B) **lipid metabolism disorders** - carnitine palmitoyl transferase deficiencies see p. 750

C) **purine metabolism disorders** - myoadenylate deaminase deficiency see below
D) **mitochondrial myopathies** - succinate dehydrogenase deficiency

**exercise intolerance in childhood:**

- Exertional induced symptoms (muscle pain, weakness, myoglobinuria) in 2-3rd decade
  - contracts cause intense muscle pain, are electrically silent and not associated with ATP depletion.
  - exercise tolerance can be enhanced by slow induction phase (warm-up) or brief rest periods allowing for start of "second wind" phenomenon (i.e. patient can continue exercise at previous level of activity after brief rest - switching to utilization of fatty acids).

- between attacks, muscle strength, diagnostic test results are normal (may become abnormal with advancing age).

2. **STATIC (stable or slowly progressive) myopathies** - chronic fixed muscular weakness (simulates muscular dystrophy) → exercise intolerance, no myoglobinuria.

A) **carbohydrate metabolism disorders** - type IV-P glycogenoses. see p. 734-738
B) **lipid metabolism disorders** - carnitine deficiencies: see p. 750
   1) primary (muscle / systemic)
   2) secondary (lactate deficiencies, valproic acid)
C) **mitochondrial myopathies** (most)

N.B. type I and VI glycogenoses do not affect muscles!

**DIAGNOSIS**

1. **Forearm (grip) exercise** - information about glycolytic (anaerobic) metabolism by evaluating lactate production in ischemic exercise:

   - rested, rested and fasting patient repetitively squeezes handheld ergometer while BP cuff is maintained above systolic pressure (induced ischemia prevents oxidative phosphorylation).
   - workload 4-7 kg-m at 60 Hz for 1 min (such duration does not induce ischemic pain).
   - sustain 1.5-second contractions separated by 0.5-second rest periods for 1 minute.
   - squeeze to 50% of maximum grip strength until exhaustion (usually ≈ 10 minutes).
   - no increase in [ammonia].
   - [lactate] rises 3-fold within 1 minute; [ammonia] rises 2-10-fold within 2-5 minutes after exercise.

- **lactate** elevation does not occur (or is diminished); muscle develops painful contracture; lipid metabolism disorders → normal profile; myoadenylate deaminase deficiency → [ammonia] elevation does not occur; mitochondrial disorders → excessive [lactate] elevation; poor effort → neither [lactate] nor [ammonia] increase.

2. **Incremental bicycle ergometry** - information about aerobic metabolism.

3. **31P-MR spectroscopy** - information about intracellular energy metabolism (i.e. ATP, inorganic phosphate, phosphocreatine).

**EMG**

A) **DYNAMIC myopathies**:
   - during episode - electrical silence.
   - after episodes of severe myoglobinuria - myopathy and fibrillations.
   - between episodes - normal
B) **STATIC myopathies** - myopathy, excessive irritability (incl. myotonic discharges, particularly in lumbar sacral paraspinal muscles in Pompe disease).

5. **Muscle biopsy**

1) scattered necrotic & regenerating fibers (exp. after rhabdomyolysis episode).
2) specific findings (e.g. vacuolar glycogen or lipid accumulations).
3) specific enzyme deficiency (alternatively skin biopsials, intestinal mucosa, lymphocytes may be examined) → definitive diagnosis!

6. **Serum CK** moderately increased (very increased after attacks* and usually normal between attacks of DYNAMIC myopathies).

7. Genetic analysis for mutations

**MYOADENYLATE DEAMINASE DEFICIENCY**

Myoadenylate deaminase (s, muscle AMP deaminase) provides short-term ATP supply by catalyzing conversion of AMP → IMP through removal of ammonia. see p. 832:

- arrhythmic myalgia ± myoglobinuria (DYNAMIC myopathy)
- asymptomatic (myoadenylate deaminase gene 1p31.21 is mutated in ≈ 2% normal people).
- forearm exercise test - no increase in [ammonia].

Methylmalonyl dehydrogenase (s, muscle AMP deaminase) provides short-term ATP supply by catalyzing conversion of AMP → IMP through removal of ammonia.

CARRIHYDROGENES are essential for anaerobic energy needs (primarily → cytoplasmic GLYCOGEN → glycolysis). see p. 734-738

LIPIDS are essential for aerobic energy needs during sustained exercise (primarily - serum LONG-CHAIN FATTY ACIDS → β-oxidation in mitochondria).

Metabolic Myopathies

Updated: April 19, 2019

**Metabolic Myopathies** - decreased muscle energy supply due to biochemical abnormalities.

**Myoadenylate deaminase (s, muscle AMP deaminase) provides short-term ATP supply by catalyzing conversion of AMP → IMP through removal of ammonia. see p. 832:**

- arrhythmic myalgia ± myoglobinuria (DYNAMIC myopathy)
- asymptomatic (myoadenylate deaminase gene 1p31.21 is mutated in ≈ 2% normal people).
- forearm exercise test - no increase in [ammonia].