Rhabdomyolysis, Myoglobinuria

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* in acute muscle necrosis (rhabdomyolysis), myoglobin escapes into blood → urine (myoglobinuria).

rhabdomyolysis is synonym for myoglobinuria

* **serum [myoglobin]** has same diagnostic significance as **serum [CK]**.
* modern techniques can detect minute amounts, so that brown urine discoloration may not be evident.

If there is no *hematuria*, positive benzidine test result strongly suggests *myoglobinuria*!

N.B. myoglobinuria itself can induce microhematuria!

* macroscopic myoglobinuria indicates massive rhabdomyolysis (risk of renal failure!).

N.B. renal failure is more likely if *hypotension (hypovolemia)* and *acidosis* coexist.

* clinically important syndromes are associated with *gross pigmenturia*.

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| I.  *Hereditary Myoglobinuria*  |
|   Carnitine palmityl transferase deficiency - most frequent metabolic defect presenting with myoglobinuria! |
|   Glycogenoses type V, VII-XI  |
|   Incompletely characterized syndromes: Excess lactate production (Larsson), some mitochondrial myopathies |
|   Uncharacterized: |
|     Familial; biochemical defect unknown: provoked by diarrhea / infection / exercise |
|     Malignant hyperthermia |
|     Repeated attacks in individual; biochemical defect unknown  |
| II.  *Sporadic Myoglobinuria*  |
|   **Exertion in untrained individuals** (e.g. military recruits) |
|     "Squat-jump" and related syndromes, anterior tibial syndrome |
|     Convulsions, agitated delirium, restraints, prolonged myoclonus or acute dystonia, status asthmaticus, high-voltage electric shock |
|   **Crush syndrome**  |
|   **Ischemia**: arterial occlusion, compression and anterior tibial syndromes, DIC |
|   **Metabolic abnormalities**  |
|     Metabolic muscle depression  |
|       Barbiturate, carbon monoxide, narcotic coma  |
|       Diabetic acidosis  |
|       General anesthesia  |
|       Hypothermia  |
|     Exogenous toxins and drugs  |
|       Haff disease  |
|       Ethanol (binge drink), heroin, Malayan sea-snake bite poison, plasmocid |
|       Glycyrrhizate, carbenoxolone, amphotericin-B, phenylpropanolamine, lovastatin, succinylcholine |
|       Malignant neuroleptic syndrome  |
|     Chronic hypokalemia of any cause  |
|     Heat stroke  |
|     Toxic shock syndrome  |
|   **Progressive muscle disease** ("polymyositis", "alcoholic myopathy")  |

Clinical syndrome

1. Widespread myalgia, muscle swelling and weakness (may persist for weeks!)
2. Renal pain → renal failure (anuria, azotemia, hyperkalemia)
3. Fever

Diagnosis

1. **Serum enzymes**↑ (CK can be > 1000 times normal), **K**↑, **phosphate**↑.
2. **Pigmenturia** (ceases within few days).
3. **EMG** abnormalities (fibrillations and myopathic units) can persist for several months.
4. **Muscle biopsy**:
	* shortly after attack - large numbers of necrotic fibers;
	* later - many regenerating fibers.

Treatment

1. Halt **muscle destruction** – bed rest (up to neuromuscular blockade), treat cause.
2. Promote **diuresis** > 2 ml/kg/h (with mannitol / dialysis)
3. **Urine alkalinization**\* (with sodium bicarbonate).

\*keep urinary pH > 7 - prevents toxic ferrihemate release from myoglobin

1. Control **hyperkalemia**.

Toxic Myopathies

**Inflammatory myopathy**: cimetidine, D-penicillamine, procainamide, L-tryptophan, L-dopa

**Non-inflammatory necrotizing or vacuolar myopathy**: cholesterol-lowering agents, amiodarone, chloroquine, colchicine, emetine, ε-aminocaproic acid, labetalol, cyclosporine and tacrolimus, isotretinoin, vincristine, alcohol.

**Rhabdomyolysis and myoglobinuria**: cholesterol-lowering drugs, alcohol (due to prolonged obtundation, seizures, hypokalemia, and hypophosphatemia), heroin, amphetamine, phencyclidine, cocaine, ε-aminocaproic acid, pentazocine, toluene.

**Myofibrillar myopathy**: emetine.

**Myosin loss myopathy**: glucocorticoids (see [p. 2740 >>](http://www.neurosurgeryresident.net/USMLE%202%5CEndocrine%20system%2C%20metabolism%20%282701-2800%29%5C2740.%20Adrenocortical%20Disorders.pdf)), non-depolarizing neuromuscular blockers.

**Mitochondrial myopathy**: zidovudine.

**Myotonia**: cholesterol-lowering drugs, propranolol, clofibrate, penicillamine, chloroquine, cyclosporine, anthracene-9-carboxycyclic acid, 2,4-d-chlorophenoxyacetic acid.

**Malignant hyperthermia** → see [p. 3910 >>](http://WWW.NEUROSURGERYRESIDENT.NET/USMLE%202/Intensive%20Care%20%283901-3950%29/3910_%283%29.%20Malignant%20Hyperthermia.pdf)

**Focal muscle damage** - injection of narcotic analgesics (esp. pentazocine, meperidine, and heroin).

Bibliography for ch. “Neuromuscular, Muscular Disorders” → follow this [link >>](http://www.neurosurgeryresident.net/Mus.%20Muscular%2C%20Neuromuscular%20disorders%5CMus.%20Bibliography.pdf)

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