Rhabdomyolysis

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Outline

- Definition
- Pathophysiology
- Causes
- Presentation and physical exam findings
- Diagnosis and investigations
- Management
- Take home message summary

Rhabdomyolysis

- Syndrome characterized by muscle necrosis and the release of intracellular muscle constituents into the circulation.
- Elevated CK, muscle pain, and myoglobinuria
- Presentation has a wide range of variety.

Pathophysiology

ATP depletion and\or direct muscle injury and rupture of the cell membrane

- Increase intracellular Ca+2
- Na+\k+ ATPase and Ca+2 ATPase pump dysfunction.

- Activation of intracellular proteases
- Mitochondrial dysfunction
- Increased muscle contractility
- Production of free radicals

MUSCLE DEATH

Leading to release of intracellular muscle contituents

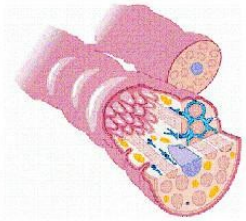
Emboli
Compression
Alcohol
Exercise

ENZYME DEFICIENCIES **HYPOKALEMIA** **HYPOXIA**

ATP depletion

Extracellular Calcium

Na^+-K^+ ATPase
Ca^{++}-Na^+ exchanger
} Dysfunction



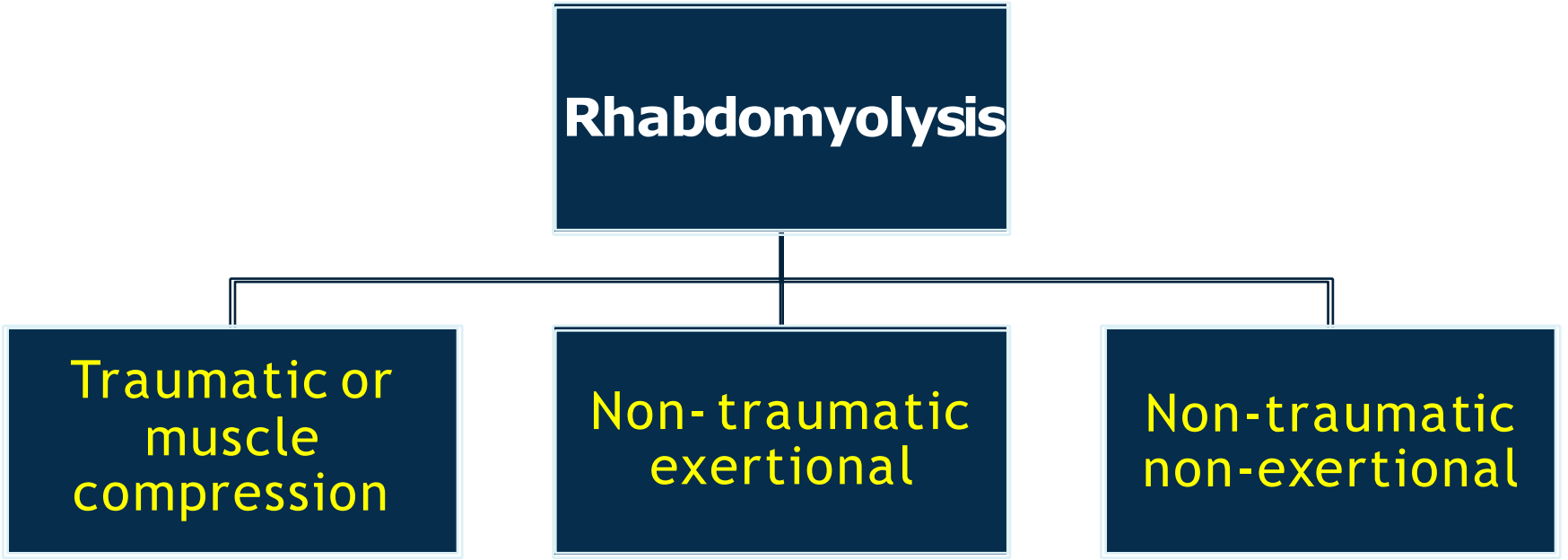
Myofibril

Muscle Destruction
Fiber necrosis

Potassium, Phosphorus Myoglobin CK, Urate

RENAL TUBULAR OBSTRUCTION

Causes


Rhabdomyolysis
Traumatic or muscle compression
Non- traumatic exertional
Non-traumatic non-exertional

1. Traumatic and Muscle Compression

- Multiple trauma
- Crush injuries
- Vascular or orthopedic surgery
- Coma
- Immobilization
- High voltage electrical energy
- Compartment syndrome

2. Non-traumatic Exertional

- Energy supply to muscle is insufficient to meet demands
- Extreme exertion or exertion under conditions in which muscle oxygenation is impaired
- Normal muscle or abnormal

Extreme exertion	Malignant hyperthermia
Heat stroke and environmental heat illness	Neuroleptic syndrome
Sickle cell disease	Mitochondrial myopathies
Seizures	Hyperkinetic movements
Metabolic myopathies	Hypokalemia

3. Non-traumatic non-exertional

Alcohol
Drugs: LSD, heroin, cocaine, amphetamines, methadone, statins, antipsychotics, SSRIs, antihistamines, colchicine
Toxins: carbon monoxide, snake and insects venoms, mushroom toxin
Infections
Electrolyte disturbance
Endocrinopathies
Inflammatory
Miscellaneous

Table 1. Major Categories and Commonly Reported Causes of Rhabdomyolysis.

Category	Commonly Reported Cause
Trauma	Crush syndrome
Exertion	Strenuous exercise, seizures, alcohol withdrawal syndrome
Muscle hypoxia	Limb compression by head or torso during prolonged immobilization or loss of consciousness,* major artery occlusion
Genetic defects	Disorders of glycolysis or glycogenolysis, including myophosphorylase (glycogenosis type V), phosphofructokinase (glycogenosis type VII), phosphorylase kinase (glycogenosis type VIII), phosphoglycerate kinase (glycogenosis type IX), phosphoglycerate mutase (glycogenosis type X), lactate dehydrogenase (glycogenosis type XI) Disorders of lipid metabolism, including carnitine palmitoyl transferase II, long-chain acyl-CoA dehydrogenase, short-chain L-3-hydroxyacyl-CoA dehydrogenase, medium-chain acyl-CoA dehydrogenase, very-long-chain acyl-CoA dehydrogenase, medium-chain 3-ketoacyl-CoA, thiolase† Mitochondrial disorders, including succinate dehydrogenase, cytochrome *c* oxidase, coenzyme Q10 Pentose phosphate pathway: glucose-6-phosphate dehydrogenase Purine nucleotide cycle: myoadenylate deaminase
Infections‡	Influenza A and B, coxsackievirus, Epstein–Barr virus, primary human immunodeficiency virus, legionella species *Streptococcus pyogenes*, *Staphylococcus aureus* (pyomyositis), clostridium
Body-temperature changes	Heat stroke, malignant hyperthermia, malignant neuroleptic syndrome, hypothermia
Metabolic and electrolyte disorders	Hypokalemia, hypophosphatemia, hypocalcemia, nonketotic hyperosmotic conditions, diabetic ketoacidosis
Drugs and toxins	Lipid-lowering drugs (fibrates, statins), alcohol, heroin, cocaine
Idiopathic (sometimes recurrent)	

* Rhabdomyolysis from this cause is associated with a crush syndrome–like mechanism.
† CoA denotes coenzyme A.
‡ In most cases, the mechanism is unclear.

Presentation

- A triad of: 1- muscle weakness 2-muscle pain
  3- dark urine (cola-colored urine)
- Muscle pain appears in the proximal muscles mostly.
- Other symptoms include malaise, fever, tachycardia, nausea and vomiting, and abdominal pain, decreased urine output.

P\E

- Muscle tenderness and swelling.
- Muscle weakness.
- Limb induration.
- Skin changes of ischemic tissue injury, such as discoloration or blisters. (Seen in less than 10% of patients).

Dx and Investigations

- Based on the presence of an acute neuromuscular illness or dark urine without other symptoms, plus a marked acute elevation in serum creatine kinase (CK) >5000 international units/L.

- Elevated serum CK (>5000 international units/L).
- Urinalysis, dipstick (positive for "heme") and microscopic (fresh urine specimen to exclude RBCs).

- Other investigations

Complications

- Fluid & electrolyte imbalance
- AKI
- Compartment syndrome
- DIC

Management

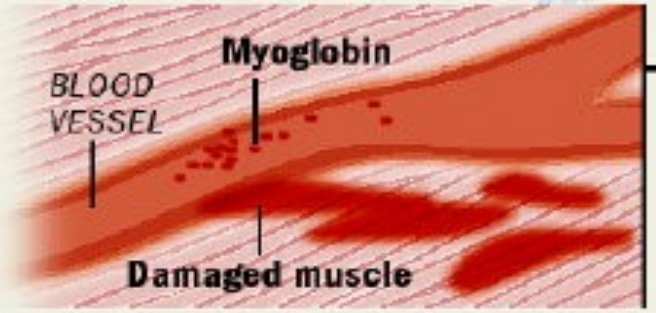
- Correct fluid and electrolyte abnormalities.
- Remove and treat the cause
- Treat compartment syndrome if present

Bad blood

Rhabdomyolysis can be caused by injuries or conditions that damage skeletal muscle. Heat stroke, severe exertion or trauma can increase the risk.

BROKEN DOWN

Muscle-fiber contents known as myoglobin are released into the bloodstream when damaged muscle tissue ruptures.



SIDE EFFECTS

KIDNEY DAMAGE

Myoglobin is filtered out of the body through the kidneys but breaks down into substances that can cause renal injuries.

DARK URINE

Urine of an abnormal color (red or dark brown) can indicate kidney damage.

Source: U.S. National Library of Medicine

THE COLUMBUS DISPATCH

Take Home Message

- Clinical manifestations and complications of
  - rhabdomyolysis result from muscle cell death, with the release of intracellular muscle constituents into the circulation
- Causes:
  - Traumatic or direct injury
  - Non traumatic exertional
  - Non traumatic non exertional
- Most common clinical conditions associated with rhabdomyolysis include trauma, immobilization, sepsis, and vascular and cardiac surgeries

Take Home Message

- Clinical manifestations of rhabdomyolysis include myalgias, weakness, red to brown urine due to myoglobinuria, and elevated serum muscle enzymes (including creatine kinase [CK])
- Based on the presence of an acute neuromuscular illness or dark urine without other symptoms, plus a marked acute elevation in serum creatine kinase (CK) >5000 international units/L.
- Treat the cause and fluid electrolyte correction

References:

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- http://www.ncbi.nlm.nih.gov/pubmed/17338959
- Batch 9's files
- Kumar Medicine

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