CRUSH SYNDROME

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CRUSH Syndrome

Long – term smash tissue syndrome

Long-term crumple syndrome

Compression syndrome

Recirculative syndrome

Traumatic Rhabdomyolysis

Also known as Bywaters Syndrome/ Reperfusion injury

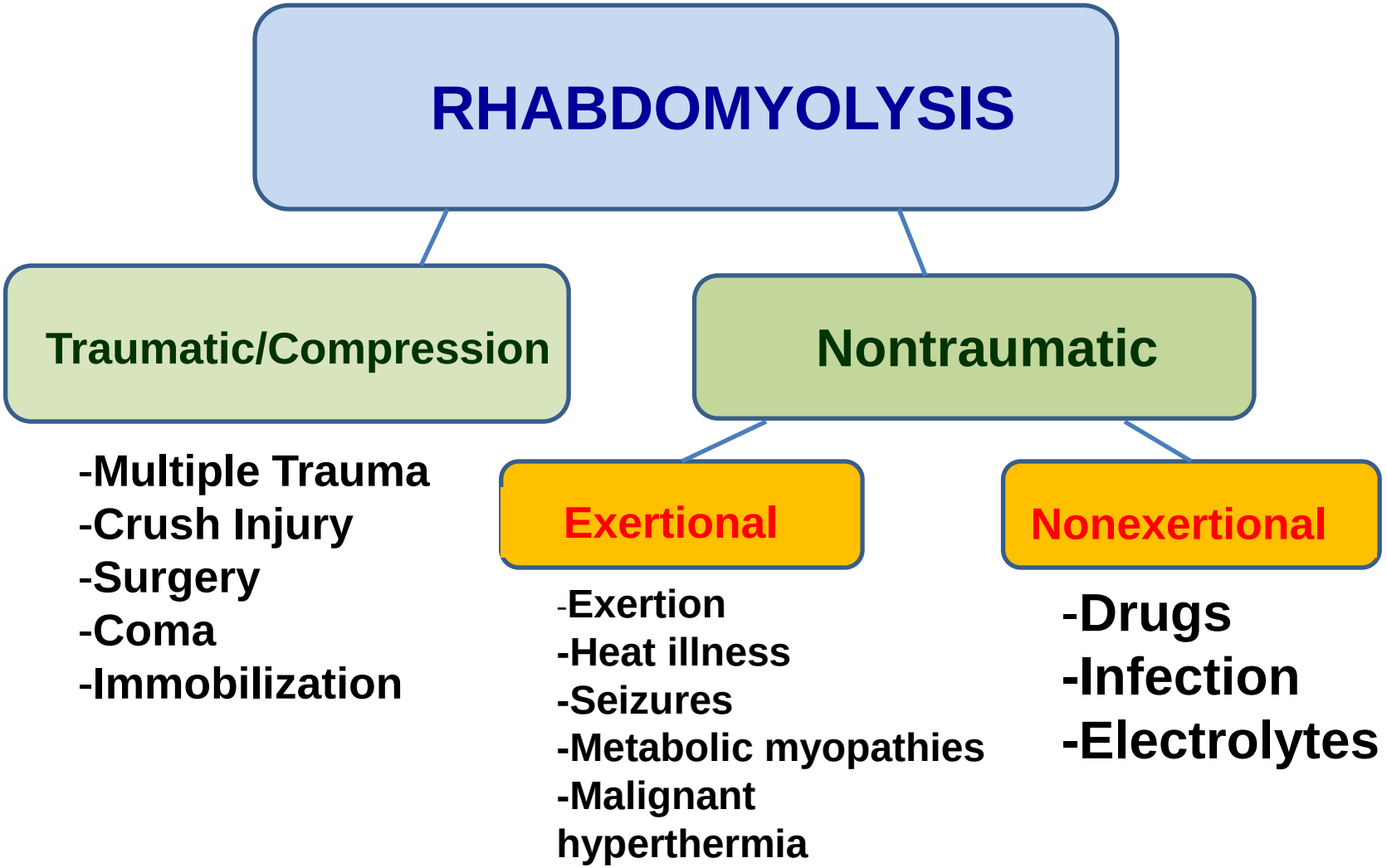
- **Rhabdomyolysis - destruction of striated muscle. Breakdown of muscle fibers, specifically of the sarcolemma of skeletal muscle, resulting in release of myoglobin.**
- **A crush syndrome is the systemic manifestation of muscle cell damage, resulting from pressure or crushing.**

Crush Syndrome

Crush syndrome is the clinical condition caused by compression of muscle with subsequent rhabdomyolysis which can then cause the complications of electrolyte disturbances, fluid sequestration, and myoglobinuria.

Crush syndrome is a ***reperfusion*** injury as a result of traumatic rhabdomyolysis!

Causes (Muscle Breakdown)



Based on 3 criteria

Any injury that has:

1. **Involvement of Muscle Mass**
2. **Prolonged Compression**

usually 4-6 hours

3. Compromised local circulation

Epidemiology

- Earthquakes
- Bombings
- Structural Collapse
- Trench Collapse

Structural Collapse

- 10% survive with severe injuries
- 7/10 develop crush syndrome

- 80% dead
- 10% survive with minor injuries

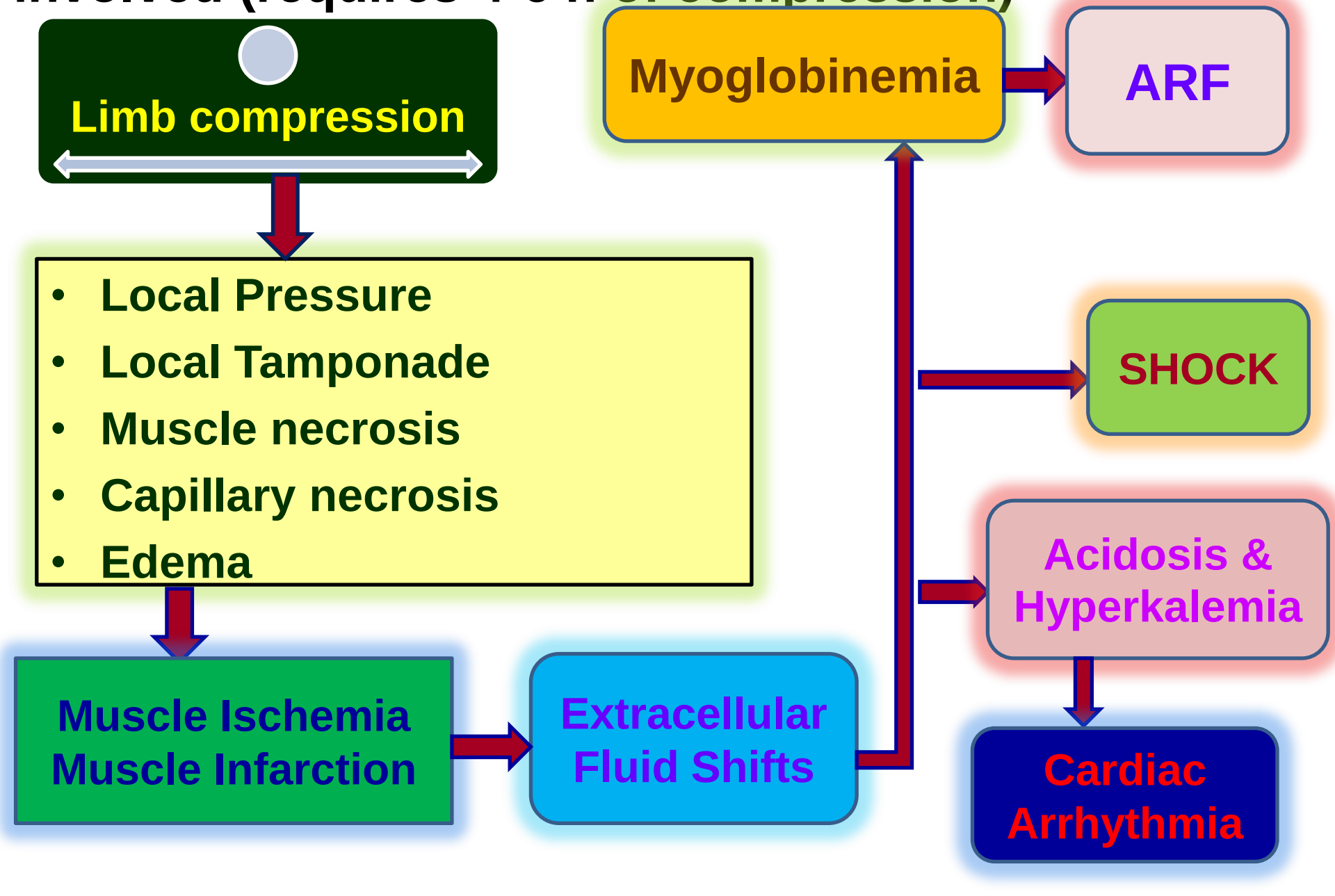
PATHOGENESIS

CRUSHING INJURY

ISCHAEMIC DAMAGE TO MUSCLES

RELEASE OF TOXIC METABOLITES

Severity of syndrome is relative to muscle mass involved (requires 4-6 h of compression)



Mechanisms of muscle cell injury:

Immediate cell disruption

Direct pressure on muscle cells

Vascular Compromise (4 hours)

- **Microvascular pressure**
- **Edema and/or Compartment Syndrome**
- **Bleeding**

Crushed +/- ischemic muscle

Deficiency in ATP

Failure of Na/K ATPase

Sarcolemma Leakage (Influx of Ca)

Lysis of muscle cell membrane

Leaks K, Ca, CK, myoglobin

Hypovolemia

- **Fluid Sequestration**
- **Increased osmoles in EC space**

Pathogenesis

Compressive forces leads to cellular hypoperfusion and hypoxia

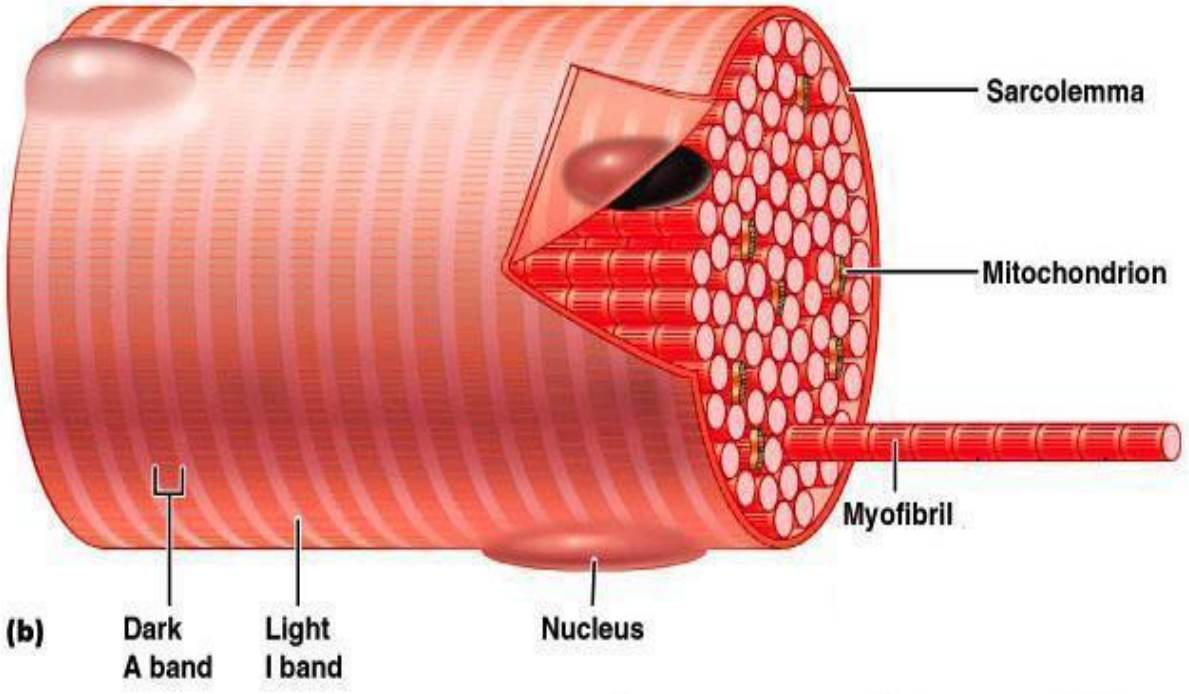
Decrease in ATPase → failure of ATPase pump and sarcolemma leakage

Lysed cells release inflammatory mediators

Platelet aggregation

Vasoconstriction

↑vascular permeability

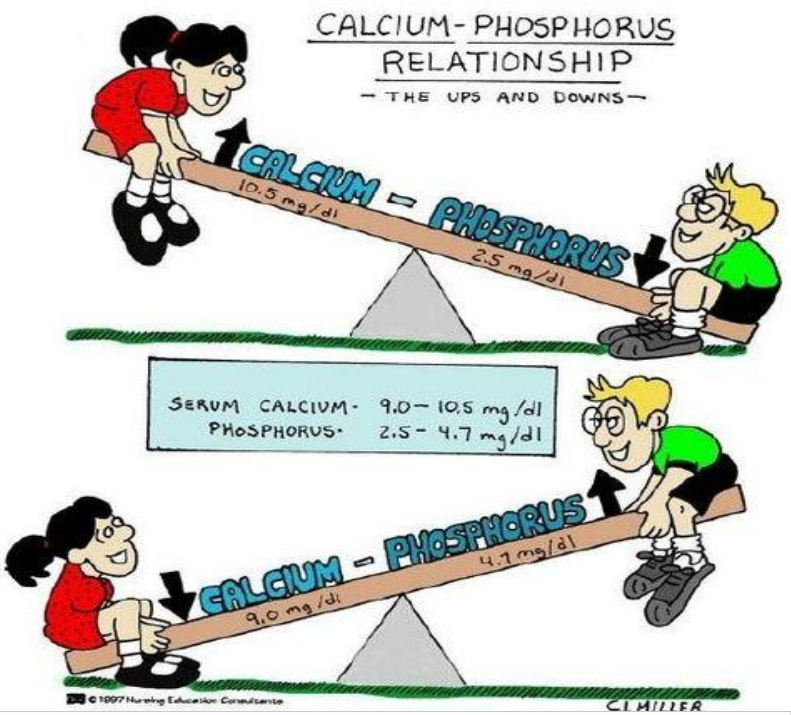


- ❖ Not usually directly due to ischemia.
- ❖ Main cause is **stretch of the muscle sarcolemma**.
- Sarcolemma permeability increases.
- Influx of sodium, water, and extracellular calcium into the sarcoplasm
- ❑ Results in cellular swelling, increased intracellular calcium, disrupted cellular function and respiration, decreased ATP production, and subsequent myocytic death.

Muscle swelling can then cause early or even days delayed compartment syndrome.

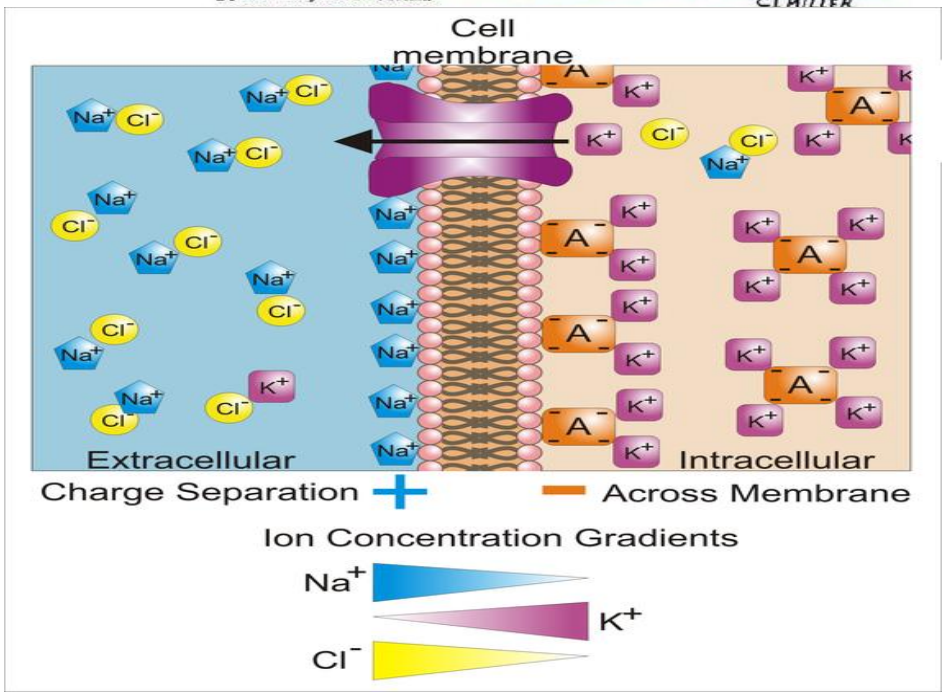
Lysed cells release

- Potassium
- Phospate
- Creatine kinase
- Myoglobin



Electrolyte disturbances

- Hyperkalaemia
- Hypocalcaemia
- Hyperphosphatemia
- Hyperuricaemia
- Metabolic acidosis



Revascularization

- Fluids trapped in damaged tissue
- Oedema of affected limb
- Haemoconcentration and shock
- Myoglobin, potassium, phosphate enter venous circulation

Products of Muscle Breakdown

- ✓ **Amino acids and other organic acids**
  - – Acidosis
  - – Aciduria
  - – Dysrhythmias
- ✓ **Creatine phosphokinase**
  - – laboratory marker for crush injury
- ✓ **Free radicals, superoxides, peroxides**
  - – further tissue damage

Products of Muscle Breakdown

- **Histamines:**
  - Vasodilation
  - Bronchoconstriction
- **Lactic acid**
  - acidosis
  - Dysrhythmias
- **Leukotrienes**
  - lung injury
  - hepatic injury.
- **Lysozymes**
  - cell-digesting enzymes that cause further cellular injury
- **Myoglobin**
  - precipitates in kidney tubules, especially in the setting of acidosis with low urine pH; leads to renal failure
- **Nitric oxide**
  - causes vasodilation which worsens hemodynamic shock

Products of Muscle Breakdown

- **Phosphate**
  - hyperphosphatemia causes precipitation of serum calcium
  - Hypocalcemic dysrhythmias
- **Potassium**
  - Dysrhythmias
  - Worsened when associated with acidosis and hypocalcemia.
- **Prostaglandins**
  - Vasodilatation
  - lung injury
- **Purines (uric acid)**
  - Nephrotoxic
- **Thromboplastin**
  - disseminated intravascular coagulation (DIC)

Metabolic Disorders from Crush Syndrome

- Hypovolemia (fluid sequestration in damaged muscle)
- Hyperkalemia
- Hypocalcemia (due to calcium deposition in muscle)
- Hyperphosphatemia
- Metabolic acidosis
- Myoglobinemia / myoglobinuria

Systemic Sequelae of Crush Injury

- Result from death of muscle cells and leak of intracellular metabolites into the systemic circulation ("reperfusion injury“).
- Superoxide anions (free radicals) then cause further membrane injury.
- May not manifest until just after entrapped part of body is extricated

Cell Death

- Platelet Aggregation
- Vasoconstriction
- Hemorrhage
- Increased Vascular Permeability
- Edema
- Hypoxia

Mechanisms of Acute Renal Failure (ARF) in Crush syndrome

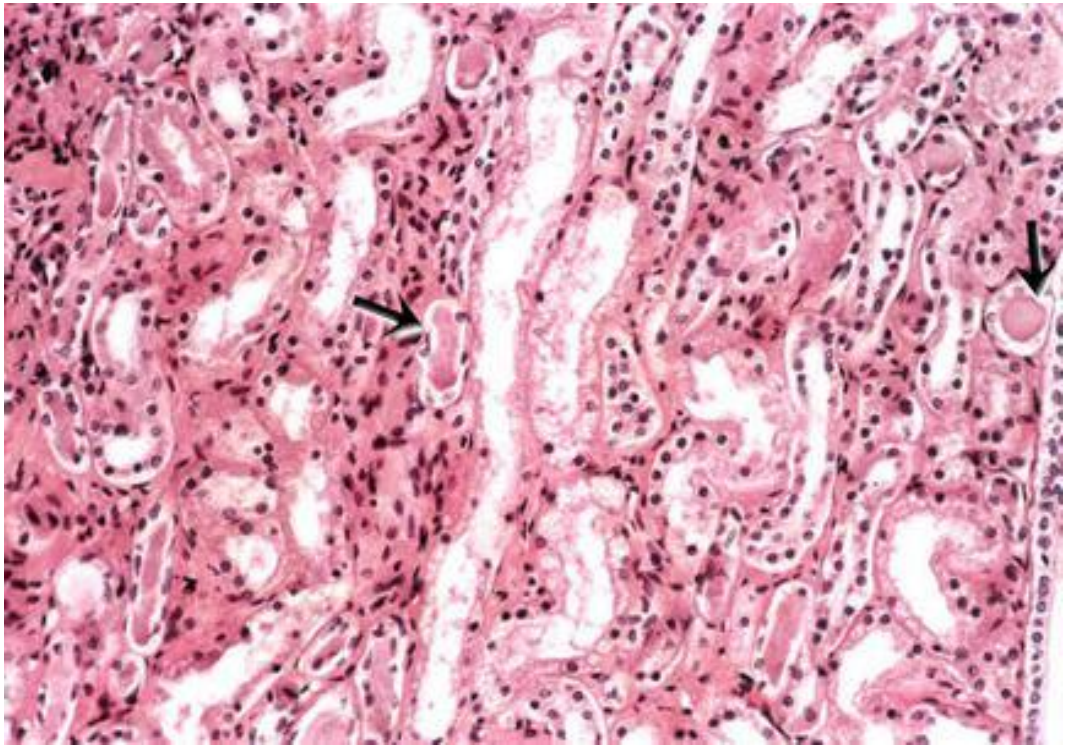
Renal vasoconstriction with diminished renal perfusion

Cast formation leads to tubular obstruction

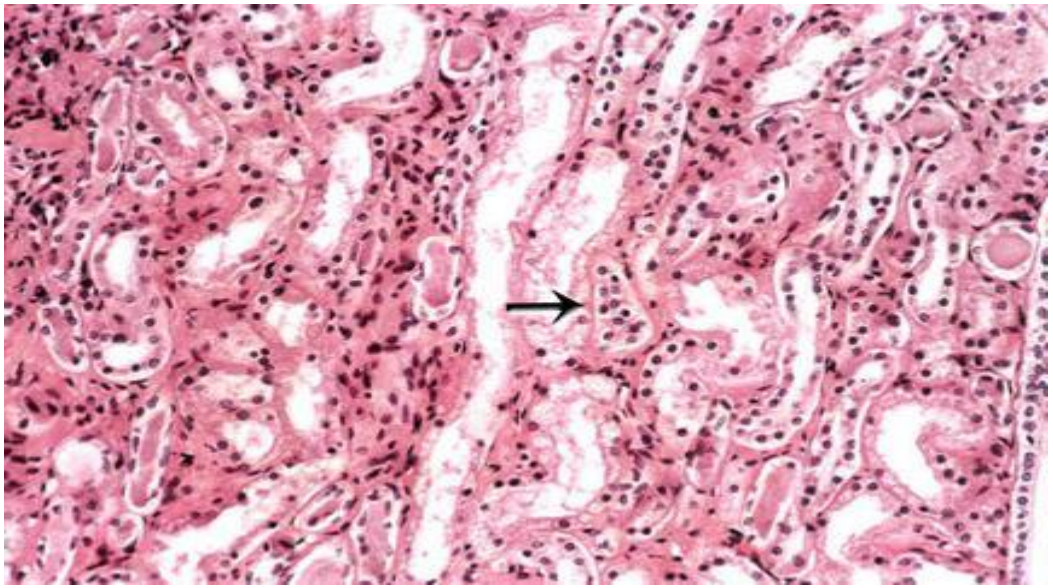
Renal hypoperfusion + Renal Tubular Necrosis = Renal Failure

Direct Myoglobin nephrotoxicity
Haem - produced free radicals

Tubular epithelial cell cast



Acute tubular necrosis. Intratubular cast formation.



Formation of granular casts, a feature of acute tubular necrosis

Renal Toxicity of Myoglobin

- Crush syndrome studies showed **acid urine** is required for myoglobin to cause renal injury.
- At pH < 5.6, myoglobin dissociates into its 2 components :
  - Globin (shown nontoxic if infused)
  - Ferrihemate (probably the toxic component)
  - Myoglobin can precipitate (particularly with hypovolemia and acidosis) and directly obstruct renal tubular flow.
  - Myoglobin is also directly toxic to the renal tubular cells.

Clinical Signs and Symptoms

- Range from asymptomatic to acute renal failure and DIC
- Triad : muscle pain, weakness, dark urine !!!
- Musculoskeletal signs: pain (incl. joint pain), weakness, swelling
- General manifestations:
  - Malaise
  - Fever
  - Tachycardia
  - Nausea
  - Vomiting
  - Seizures

There are three periods of long-term smash tissue syndrome

- **Early** – shock manifestation (till day 3rd after trauma);
- **Intermediate** - acute renal failure;
- **Late** (convalescence) – 2nd week – 1-2 months after crushing injury.

After shock an intermediate or light period can be observed. The patient's condition is getting better. There is no pain, normalization of a pulse and blood pressure. Body temperature is 37,6 - 38,5 C. An oliguria appears. It can be also in a hard form, leading to death.

This period is followed by next stage of crush syndrome (till 4 – 5 days after trauma) when signs and symptoms of ARF (insufficiency) become exhibited: hyperazotemia, hyperkalemia, metabolic acidosis. Diuresis diminished distinctly till critical level (30-20 ml/h). Also there are anemia, hyponatremia (Na), hypocalcaemia. Albumin content decreased. ARF can be observed also at those cases, when there is no shock.

Generalized and long-term process of microcirculation damage causes fat globules and micro thrombus formation in the micro vessel gap. After resuming the hemodynamics, a large quantity of these globules were spread by blood flow in different organs and tissues causing an obstruction of microcirculatory system and disorganization of different organs and tissues (brain, lungs, liver, kidneys, etc.) So, long-term smash tissue syndrome is many-sided, intricate for diagnosis.

Pathological changes due to direct cell destruction appear immediately, but during ischemic injuries of muscle, they appear some hours later. Because the medium-term of ischemic death of striated muscles is near 6 hours, so the cause of early necrosis (first hours) is ***mechanical factor***, but later it is ***hypoxya***. Because of direct tissue destruction, intracellular substances get into blood. During the compressive- and ischemic muscle injuries, ischemic toxins penetrate into blood flowing (metabolites of anaerobic glycolysis). In both cases, direct and ischemic injuries, destroying the blood circulation and breathing appear.

Complications

Early

- Hypovolaemia
- Hyperkalaemia
- Hypocalcaemia
- Cardiac arrhythmias
- Cardiac arrest
- Compartment syndrome

Late (12-72 hrs)

- Acute renal failure
- DIC
- ARDS
- Sepsis

Laboratory Findings

- **Creatine Kinase** (**CK**)

Serum reference values:

male: 38-174/200 IU/L or 2.86 SI units (mkat/L);

female: 26-140 IU/L or 2.42 SI units (mkat/L)

Rises within **2 to 12** hours following the onset of muscle injury and reaches its max within **24 to 72** hours. A decline is usually seen within **3-5** days of cessation of muscle injury.

- **Hyperkalemia**
- **Hyperphosphatemia**
- **Hypocalcemia**
- **Hyperuricemia (uric acid)**
- **Myoglobinuria**

Other muscle markers

- Measuring **myoglobin** level in **serum or urine**
- Appears in urine when plasma concentration exceeds 1.5 mg/dl
- Urine becomes **dark red –brown** colour > 100mg/dl
- Myoglobin has short $T_{1/2}$ (2-3 hours)
- Serum levels return to normal after 6-8 hours

ECG as early as possible to look for signs of hyperkalemia

Other clinical syndromes with similar effects as Crush Syndrome

- Tumor lysis syndrome
- Heat stroke
- Exertional rhabdomyolysis
- High voltage (> 1000 volts) electrical injury

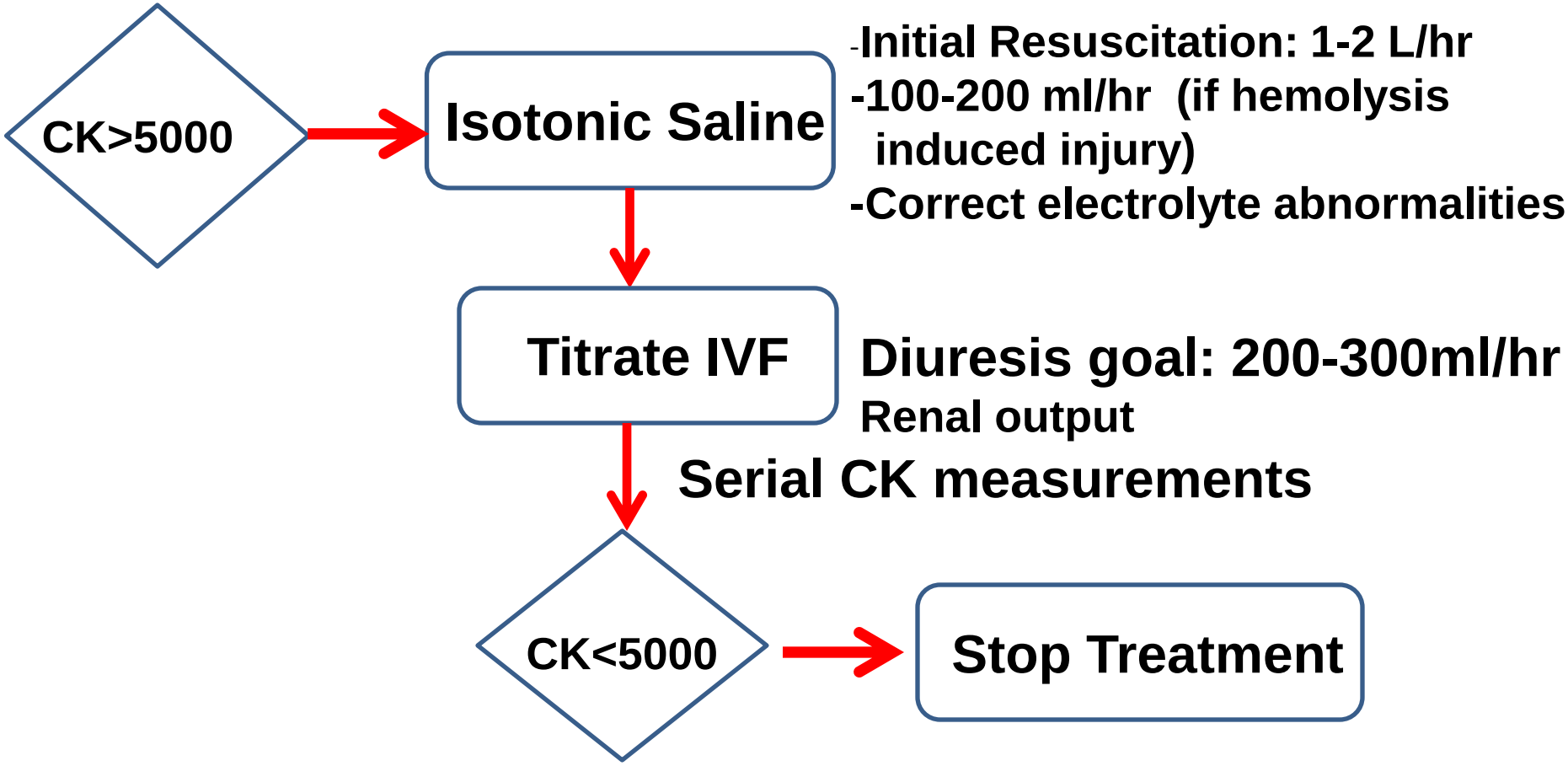
Other Injuries in the Crush Syndrome Patient

- High incidence of associated injuries
- Extremity fractures and lacerations are most common
- With crush injury to trunk, can have internal abdominal injuries in addition to abdominal wall muscle compression injury
- May have "traumatic asphyxia" if chest compressed
- Dust inhalation common in concrete building collapse
- Fires common with earthquakes, so may have burns, smoke inhalation, and CO poisoning
- Hypothermia or hyperthermia

First aid at the crush-syndrome

1. Remove the compressing factor
2. Apply a proximal tourniquet to prevent a spread of toxins to the organism
3. Prescribe the narcotic analgetics to prevent the formation of pain shock
4. Intensive therapy during crush syndrome should be started in the earliest phase, because the characteristic changes are formed during 5-6 hours after trauma.

TREATMENT
Algorithm



Nowadays in system of pre-hospital measures during crush syndrome special accent is put on early base infusion into the organism. But there must be excluded solutions containing potassium (Ringer’s, Hartmann’s solutions).

Bicarbonate

Bicarbonate: Forced alkaline diuresis

- May reduce renal heme toxicity;
- May also decrease the release of **free iron from myoglobin**, the formation of **vasoconstricting F_2-isoprostanes**, and the risk for **tubular precipitation of uric acid**. Alkalinization increases the solubility of myoglobin and promotes its excretion;
- Bicarbonate is used to raise the urine pH to **6.5** thereby **increasing solubility of heme pigments**;
- Add 50 ml 8.5% sodium bicarbonate to each liter;
- No clear clinical evidence that an alkaline diuresis is more effective than a saline diuresis in preventing acute kidney insufficiency.

Mannitol: Forced diuresis

- May minimize intratubular heme pigment deposition and cast formation;
- May scavenge free radicals in muscle thus limiting necrosis;
- Positive inotropic effect on the heart;
- May help eliminate myoglobin from the kidney and prevent renal failure;
- May be useful to initiate diuresis;
- Most important may help decompression of compartment syndrome by mobilizing fluid from damaged muscle (thereby preventing need for fasciotomy).

Mannitol

Prerenal effects:

- Intravascular volume expansion
- Increased cardiac output and contractility
- Possibly reduction in intracompartment pressure in compartment syndrome

Renal effects:

- Increases glomerular filtration rate
- Increases intratubular pressure and flow
- Dilatation of renal vasculature
- Osmotic diuresis

Contraindications to Mannitol

- Established anuric renal failure;
- Severe congestive heart failure;
- These patients may require pressors such as dopamine in order to tolerate the fluid load required for treatment, or may need early dialysis

Mannitol Dosage for Crush Syndrome

- Mannitol 20 % solution 0.25 grams per kg IV over 10 to 30 minutes;
- Diuresis should start in 15 to 30 minutes;
- If urine output thereafter drops again, hypovolemia should be assumed, and only after aggressive rehydration a second dose of mannitol should be given;
- Maximum dose : 2 g/kg/d (or 200 grams per day)

Hyperkalemia in Crush Syndrome

- Can occur soon after extrication
- Can be quickly fatal
- May occur before manifestations of renal failure
- May occur without obvious signs of compartment syndrome
- May require emergent prehospital treatment

Treatment of hyperkalemia at hospital:

- IV infusion of **hypertonic** (40%) solution of **glucose** (50 ml) with **insulin**
- 10% solution of **Calcium chloride or Ca gluconate** (30 ml for 20 min – cardiac membrane stabilizing effect, hyper/K – hypo/Ca
- nebulized **albuterol** (2.5 mg in 3 cc) - potassium-lowering effect for hyperkalemia in renal failure (beta 2-adrenergic stimulation on potassium metabolism)
- If the level of potassium in blood plasma is more than 7 mmol/L an emergent **hemodialysis** may be needed. Special attention should be paid to diuresis control.

If the response on diuresis stimulation is absent, you should not prescribe **Furosemide** (**Lasix**) or **Mannitol** one more time, because there is already tubular necrosis in kidneys. Haemoabsorption, and Haemodialysis are needed.

Large attention is paid to simple and safe method of detoxication – haemo - and lymphosorption. During sorptions the content of potassium, magnesium, phosphorus and some toxic substances decrease.

Haemoabsorption and Haemodialysis

- Moderate and severe forms - an indication for haemoabsorption
- Development of acute renal insufficiency – haemodialysis.
- During treatment of patients with severe form of crush syndrome it is necessary to provide both procedures, absorption and dialysis.
- Absorption helps to eliminate encephalopathy, improves general condition, but it hardly changes level of urea and kreatinine in blood.
- Haemodialysis effectively eliminates hyperazotemia and hyperhydration.
- Dangerous hyperkalemia and hyperhydration are absolute indications for “artificial kidney” usage – **remove urea and potassium**.

Additional Treatment for Crush Injury

- oxygen supplementation (even if the patient is not hypoxemic, **O_2** may help ischemic muscle)
- pain medication
- tetanus immunization
- **Acetazolamide** (a carbonic anhydrase inhibitor: 250 mg **PO**)**.** May help excretion of bicarbonate in the urine.
- **Furosemide** may initiate diuresis but not favored since it makes acid urine

- **Hyperbaric oxygen** – At high pressure, physically dissolved levels of oxygen increases in the plasma, tissue viability is enhanced, some vasoconstriction occurs and so fluid outflow from the vascular compartments decrease thus reducing tissue edema. It directly assists wound healing by fibroblast proliferation. Finally it can reduce anaerobic bacterial growth in necrosed muscle. The usual dose is about **2.5** atmospheres for about **one and half hours twice a day for a week.**
- **Plasmapheresis** in complex treatment - high effectiveness of liquidation of DIC-syndrome, and detoxication of the organism.

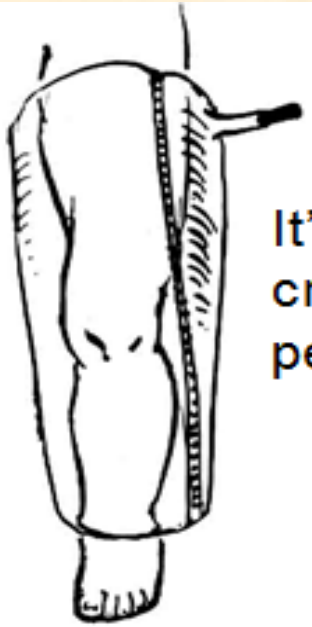
Free radical scavengers and antioxidants

- The magnitude of muscle necrosis caused by ischemia-reperfusion injury has been reduced in experimental models by the administration of free-radical scavengers.
- Many of these agents have been used in the early treatment of crush syndrome to minimize the amount of nephrotoxic material released from the muscle.
- **Pentoxyphylline** is a **xanthine derivative** used to improve microvascular blood flow. In addition, pentoxyphylline acts to decrease neutrophil adhesion and cytokine release.
- **Vitamin E** , **vitamin C**, **lazaroids** (**21-aminosteroids**) and minerals such as **zinc**, **manganese** and **selenium** all have antioxidant activity and may have a role in the treatment of the patient with rhabdomyolysis.

Treatment of infections

- Multiple broad spectrum non nephrotoxic antibiotics may be needed.
- Combined antibiotic therapy (combination of two antibiotics)

Fx need fixation and conservative amputations may have to be performed either as emergencies or as an elective measure.



Usage of pneumatic splint during crush-syndrome.

It's necessary to distinguish in the crush syndrome a compression period.

Prognosis Related to Crush Syndrome

- Major risk factors for renal failure :
  - 2 or more limbs crushed
  - Insufficient early IV fluid
  - Delayed in presentation to hospital
- Children at lesser risk may need dialysis
- 50 % or more may have severe long term limb disability if fasciotomy done
- Patients often need long term physical therapy

Delayed Causes of Death

- ARF
- ARDS
- Sepsis
- Ischemic Organ Injury
- DIC
- Electrolyte Disturbances

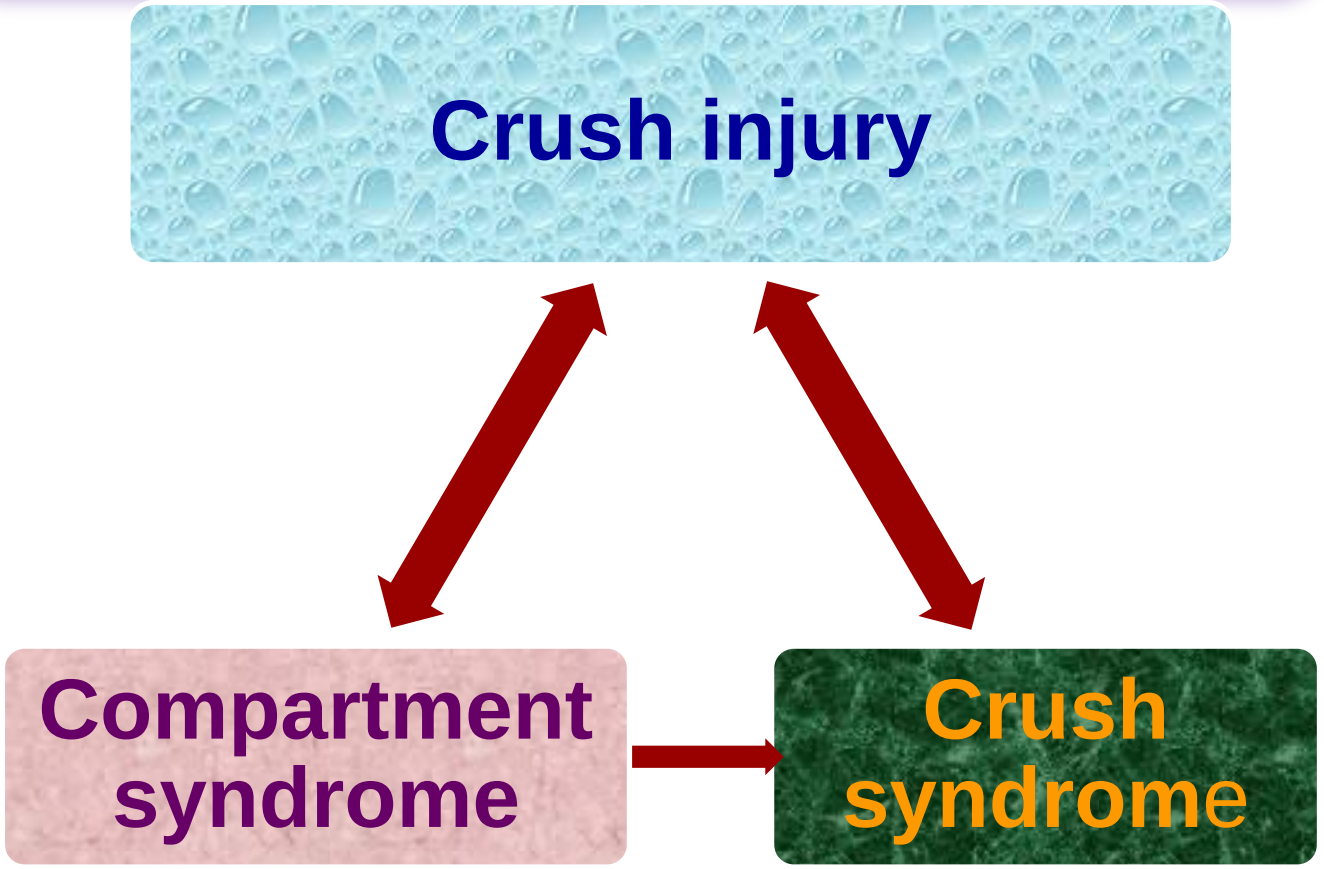
Crush Syndrome
Lecture Summary

- Start IV fluids prior to extrication if possible
- Assess quickly for hyperkalemia and associated injuries
- If extrication > 6 hours after injury, do not perform fasciotomy for compartment syndrome
- Perform careful monitoring after admission to hospital

Major Mass Casualty Events with Reports of Crush Syndrome

- Earthquakes :
  - Tangshan, China 1976
  - Armenia 1988
  - Iran 1990 and 2003
  - Northridge, California 1994
  - Kobe, Japan 1995 ("Hanshin-Awaji")
  - Turkey 1992 (Izmir, "Marmara" 1999)
- Terrorist bombings :
  - Israel
  - Lebanon
  - Saudi Arabia

Compartment syndrome



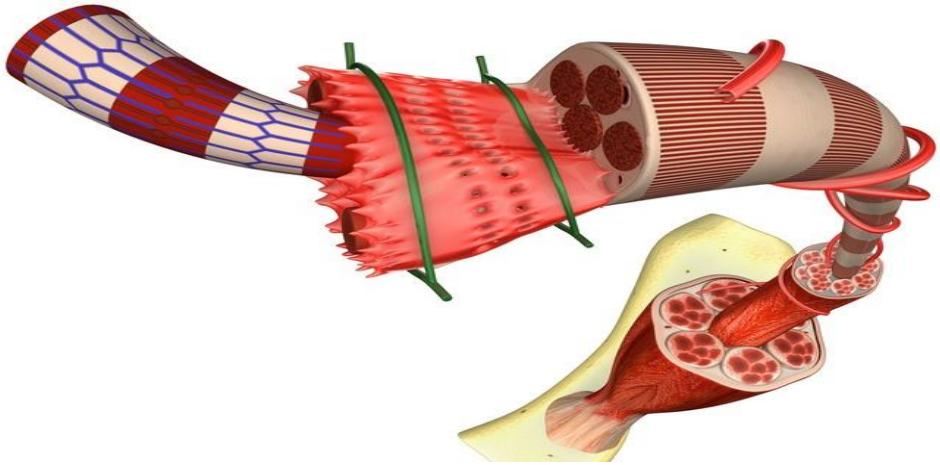
A crushing injury can cause either Compartment Syndrome (CS) or Crush Syndrome

Compartment syndrome

- Defined as an “increased pressure within a confined space that leads to micro-vascular compromise and ultimately to cell death as a result of oxygen starvation”
- Acute compartment syndrome can have severe consequences, including paralysis, loss of limb or loss of life

Pathophysiology

Muscle groups - including the nerves and blood vessels that flow through them- are covered by a tough membrane (strong webs of connective tissue) called fascia that does not readily expand -this area is called a **compartment**.



Compartment syndrome occurs when excessive pressure builds up inside an enclosed muscle space in the body. Compartment syndrome usually results from bleeding or swelling after an injury. The dangerously high pressure in compartment syndrome impedes the flow of blood to and from the affected tissues.

Epidemiology

Acute CS is the most common type of Compartment syndrome.

- Trauma - Fractures, hematoma, animal/insect bites, crush injury, surgery to blood vessels of an arm or leg
- Edema related - frostbite, burns, overuse injuries
- Coagulopathies - genetic, iatrogenic or acquired; a blood clot in a blood vessel in an arm or leg
- Other external compression - overly tight bandaging, prolonged compression of a limb during a period of unconsciousness, extremely vigorous exercise (extension under pressure). Taking anabolic steroids can also contribute to developing compartment syndrome.

Abdominal compartment syndrome almost always develops after a severe injury, surgery, or during critical illness. Some conditions associated with abdominal compartment syndrome include:

- Trauma, especially when it results in shock
- Abdominal surgery, particularly liver transplant
- Burns
- Sepsis (an infection causing inflammation throughout the body)
- Severe ascites or abdominal bleeding
- Pelvic fracture

As the pressure in the abdominal compartment rises, blood flow to and from the abdominal organs is reduced. The liver, bowels, kidneys, and other organs may be injured or permanently damaged.

Compartment Syndrome: Signs and Symptoms
Presents as the Five "Ps"

- **Pain** - is most common and consistent sign; described as diffuse and intense, exacerbated with movement, touch, pressure, stretch;
- **Paresthesias** (or anesthesia) - loss of feeling below CS area and radiating farther away;
- **Passive Stretch** - severe pain when muscles in affected compartment are stretched
- **Pressure** - palpable tenseness in affected compartment (very tight to feel, sometimes warm), not recommended palpation for diagnosis
- **Pulselessness** - least reliable and often late stages; CS affects microvasculature, typically, major vessels not affected

CS is TYPICALLY a localized injury!

Treatment

Pre-hospital Treatment (BLS)

- Oxygen; high flow
- Do NOT ice; ice increases vasoconstriction
- Do NOT elevate; keep in position where found or position of comfort
- Splint for comfort and protection only when necessary (i.e. long transport)
- Transport to appropriate medical facility

Pre-hospital Treatment (ALS)

- Same as BLS
- Keep venous infusion line open (infusion of IV fluids)
- Pain relief - **Fentanyl** is preferred because it provides same pain control as Magnesium sulphate without vasodialation
- USAR/Military Protoco l- **field fasciotomy** may be performed;

Fasciotomy to relieve compartment syndrome

Compartment Syndrome: Sequelae after initial injury

- Tissue damage - irreversible tissue death within 4-12 hours depending on tissue type and compartmental pressure;
- Amputation - sometimes tissue is irreversibly damaged and only measure to prevent gangrene and death is amputation
- Renal failure and/or death- can occur due to chemical imbalance, infectious or cardiac complications

CS is an independent injury, typically no migration to Crush syndrome. This is a crush injury but completely different than Crush syndrome.