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Mechanism of Acute Renal Failure secondary to Rhabdomyolysis

HIDEOUS INJURIES

Crush injury, pressure sores, freezing injuries, extensive burns, psychopathically excessive exercise, vascular disease causing whole-limb ischaemia, widespread sepsis, inflammatory myopathy, blast injury eg. bomb explosion, alcoholism, and over-use of MDMA in a rave dance-club setting

Widespread cell destruction, on a massive scale, and thus **TORRENTIAL LEAKAGE OF CELLULAR CONTENTS**

MYOGLOBIN

URIC ACID , Lactic acid,

PHOSPHATE

POTASSIUM

Metabolic Acidosis

Excess phosphate combines with serum calcium and leads to **HYPOCALCEMIA**

In combination hyperkalemia and hypocalcemia lead to increased **CARDIAC TOXICITY eg. ARRHYTHMIA**

ACIDURIA

Sodium and water move into the damaged muscle: **MANY LITRES MAY BECOME SEQUESTERED!**

Injury-related haemorrhage (or, drugged +/- drunken dehydration)

Low molecular weight → means it easily excreted, thus **tea coloured urine** and **blood +++ on urinalysis** because the dipstick only tests for heme

MYOGLOBINURIA

HYPOVOLEMIA

HYPOTENSION

Myoglobin in the bloostream scavenges NO, and this causes **reduced vasodilation**

Low urine pH means lower solubility of the heme units

RENAL HYPOPERFUSION
Due to vasoconstriction secondary to RAAS activation

Reduced GFR, thus reduced rate of wash-out

MYOGLOBIN PRECIPITATES INTO TUBULAR CASTS

MAJOR PATHOLOGY HAPPENS HERE:
Now you got iron-rich protein congealing up your tubule. This has numerous unsavoury CONSEQUENCES:

MECHANICAL:
Tubules crammed full of myoglobin casts become dilated with backpressure, and the fragile tubular **brush border is destroyed** by the crude effect of having proteinaceous waste forced through it.

Loss of brush border: Its full of enzymes, eg. carbonic anhydrase, which produces your renal bicarbonate- and so **THE ABILITY TO REGULATE ACID- BASE BALANCE IS LOST** which contributes to the heme-depositing tubule-clogging aciduria

BIOCHEMICAL
Myoglobin is a protein, and the tubule attempts to transport it back into the bloodstream using its normal mechanism of ATP-dependant transport There being so much of it, the ATP reserves of the blood-starved tubule are depleted rather quickly.
ATP depletion means you cant power all those ion pumps, and thus control of electrolyte concentration is lost.

CELLULAR GENETIC:
Iron, of which myoglobin is full, seems to be toxic to the tubule epithelium. By itself its a free radical, and it will generate new free radicals when you reperfuse the kidneys with your well-intentioned litre of IV saline., and oxygen actually gets down there.Superoxide dismutase will cope with this ...for a while. Then, the oxidative stress will burn the DNA and the lipid bi-layers. This is irreversible.

Eventually the macrophages will come and bulldoze down the dead tubules and clean out all the myoglobin.

PROLONGED ATP DEPLETION (i.e. you DONT get the kidneys re-perfused) = CORTICAL NECROSIS = no recovery

OTHERWISE...
Lots of mitosis and a little fibrosis: the kidneys restore their architecture; tubule cells recover their ion pump functins AFTER the tubules are cleared up, and thus there is a period of **massive polyuria** , while the urine concentrating mechansms still havent come back online . this is the so-called **DIURESIS PHASE.**