


Rhabdomyolysis

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- ▶ Background
 - ▶ Pathophysiology
 - ▶ Treatment
 - ▶ Role of RRT
 - ▶ New developments
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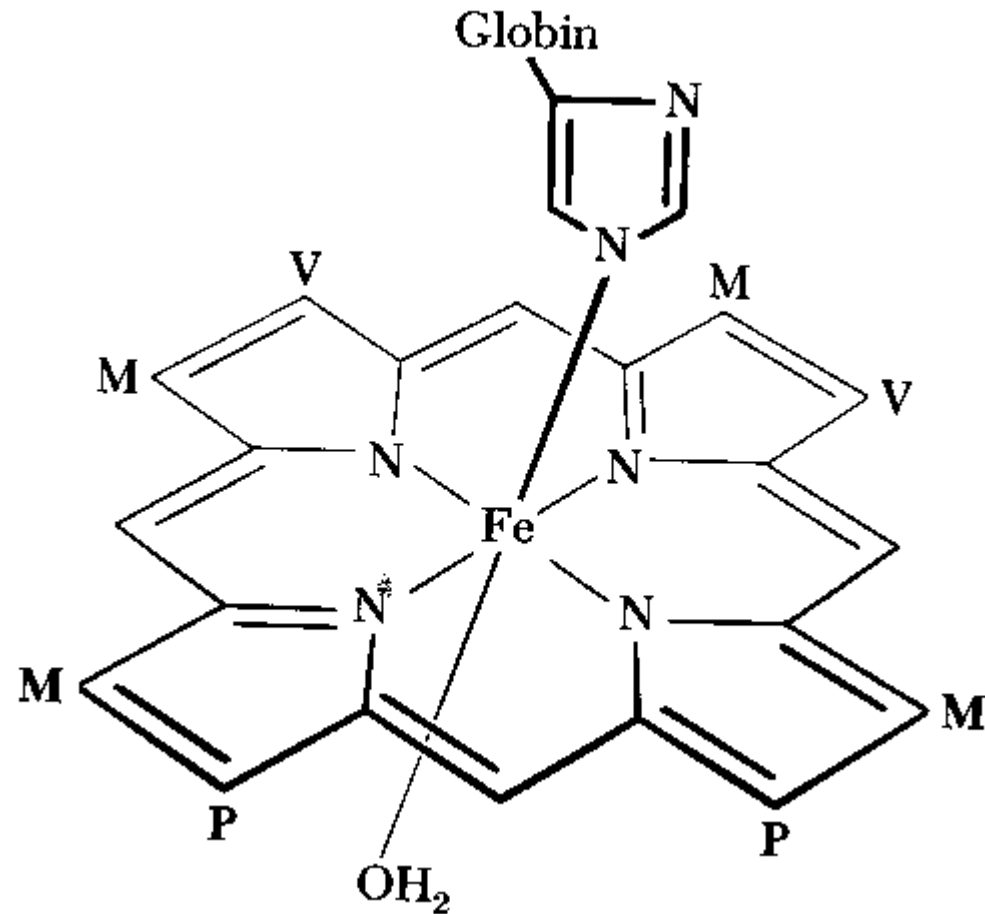
Background

- ▶ Rhabdomyolysis was first described in 1941 in the London Blitz.
- ▶ Characteristics by the leakage of muscle-cell contents, including electrolytes, myoglobin, and other sarcoplasmic proteins (creatine kinase, aldolase, LDH, AST, and ALT) into the circulation.

Epidemiology

- ▶ Acute kidney injury as a complication of rhabdomyolysis represents about 7 to 10% of all cases of acute kidney injury in the United States.
 - ▶ Majority of patients with Rhabdomyolysis will recover.
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Myoglobin- 17.8Kdalton

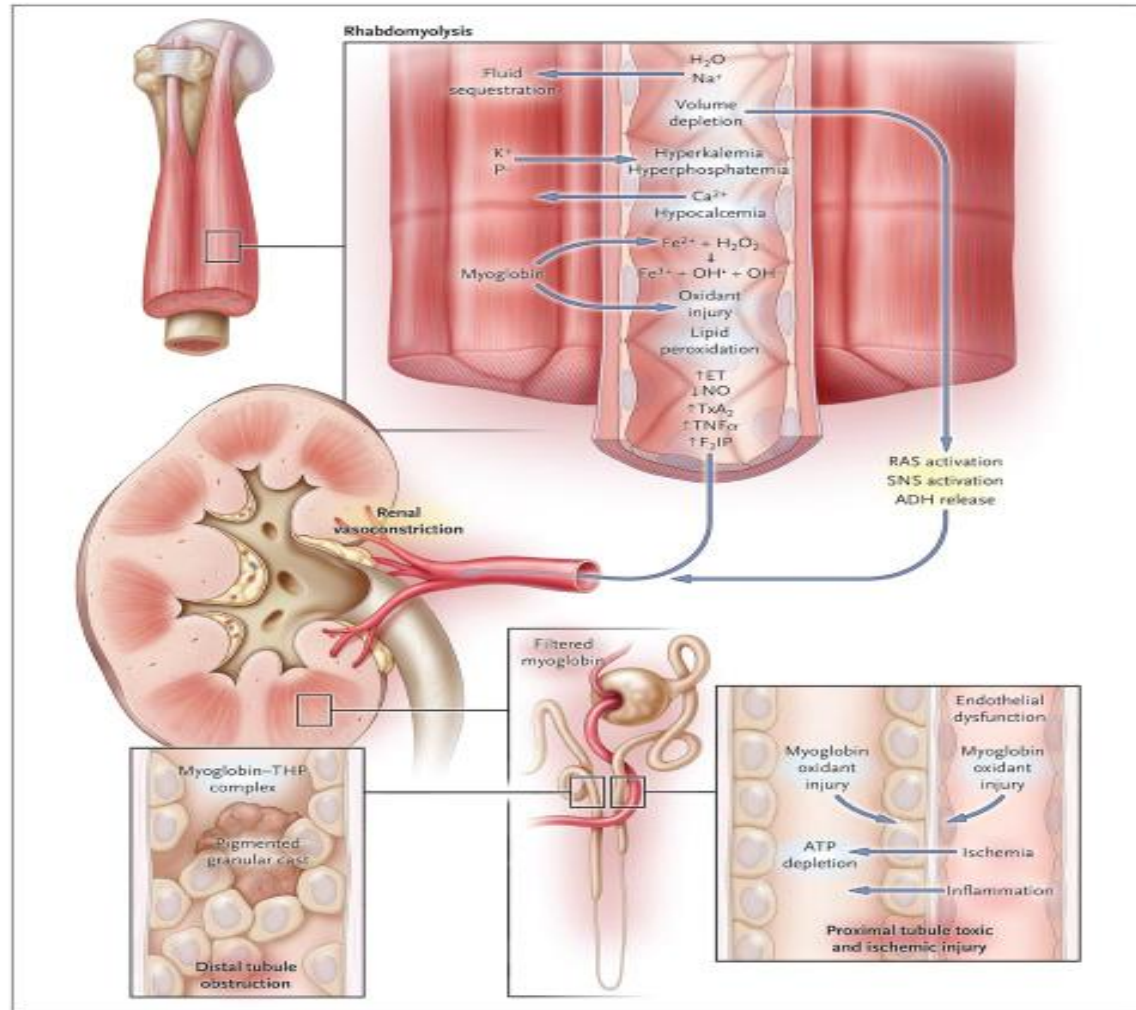


Pathophysiology

- ▶ Intra renal vasoconstriction
- ▶ Direct and ischemic tubular injury– by Fe induced lipid peroxidation and cytotoxicity.*
- ▶ Tubular obstruction

* Demonstrated by in vivo studies on rat prox tubular segment– Univ of washington. *J Clin Invest.* 1992 Mar;89(3):989–95

Pathophysiology



Pathophysiology

Ferrous Fe $2+$
oxidised



MetMb (ferric Fe $3+$)

Redox cycle



Ferryl Mb [Fe=O] $2+$


Initiates Lipid peroxidation- forming Isoprostanes

Pathophysiology


- ▶ Measured urinary excretion of isoprostanes in 8 patients admitted with rhabdomyolysis vs control -7 ckd(non dialysis) + 10 normal
- ▶ Increased in patients with Rhabdo (46pgm/ml creatinine cl) vs 16 pgm/ml in control grp.
P<0.02

Lancet April 10, 1999; vol 353- Kevin Moore et all

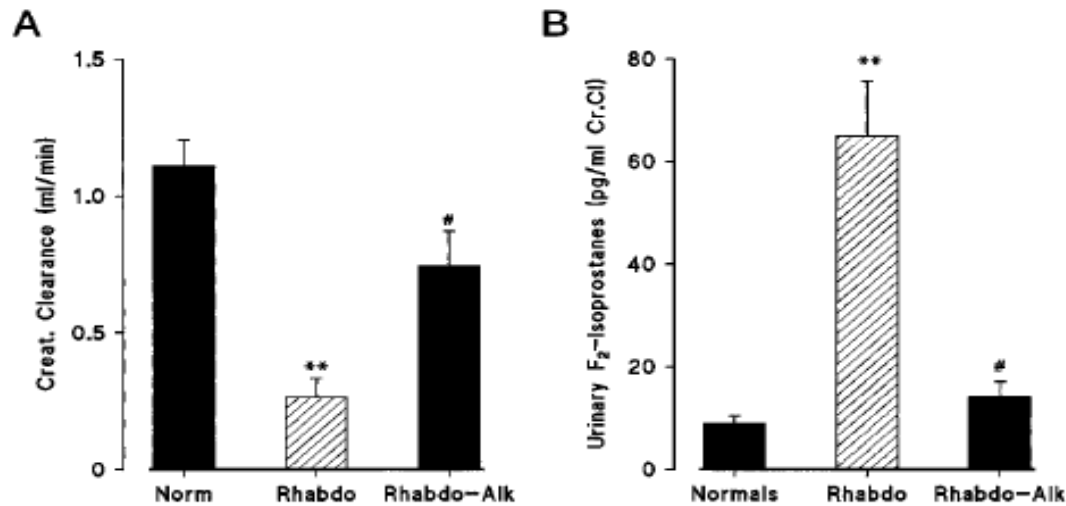
Treatment

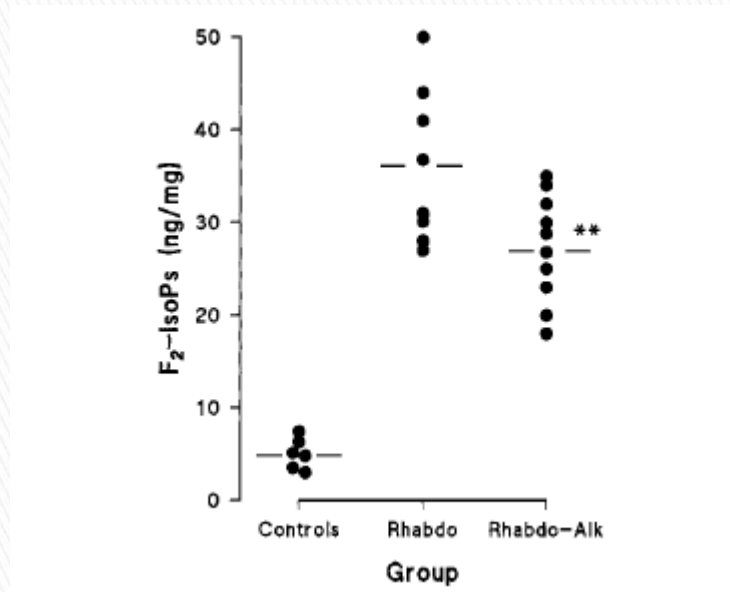
- ▶ Supportive– volume resuscitation normal saline or bicarbonate with target urine output 3ml/kg/hr till urine myoglobin is cleared (negative urine dipstick).
 - ▶ Role of redox cycling of Myoglobin and its inhibition by Alkalinization in the pathogenesis and treatment of rhabdomyolysis induced renal failure.
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Role of bicarbonate

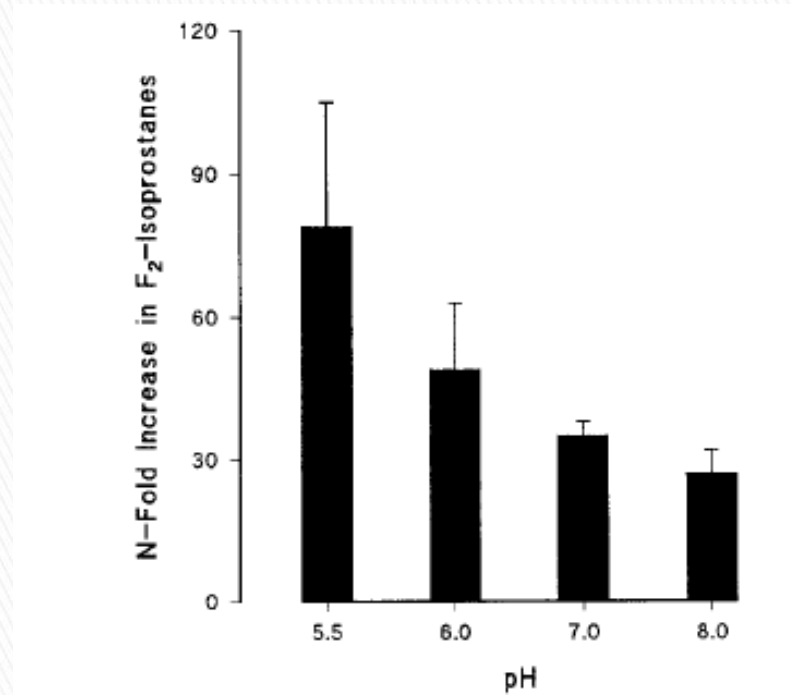
- ▶ Used rat model of rhabdo and measured urinary levels of isoprostanes.
 - ▶ 3 grps– control, rhabdo and rhabdo–alk
 - ▶ Glycerol 10mg/kg 50% solution and potassium bicarbonate used
 - ▶ Urine collected at 0 and 24hr
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Effect of alkalization on renal function and isoprostanes excretion





Levels of IsoP in renal lipids



Effect of pH on Metmb induced IsoP in LDL

Role of RRT


- ▶ Prognostic value, kinetics and effect of cvvhdf on myoglobin & CK in ICU patients with rhabdomyolysis.– prospective and retrospective cohort
- ▶ 47 patients with rhabdomyolysis and Myoglobin > 5000mcg
- ▶ No significant difference in ck and myoglobin measured in patients with AKI who received cvvhdf versus those who did not.

What's new.

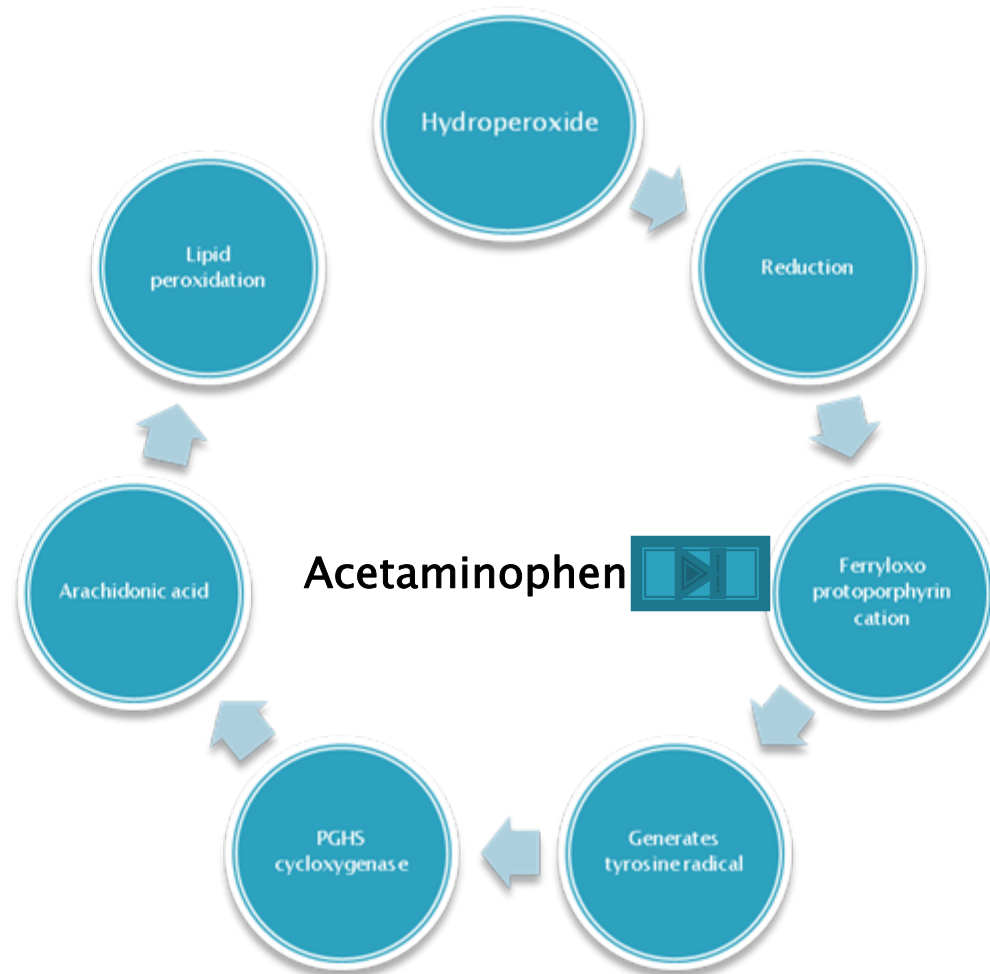
- ▶ Role of acetaminophen in oxidative stress -- demonstrate in vitro that acetaminophen inhibits hemoprotein-induced lipid peroxidation by reducing ferryl heme to its ferric state and quenching globin radicals

PNAS February 9, 2010 vol. 107 no. 6 2699-2704

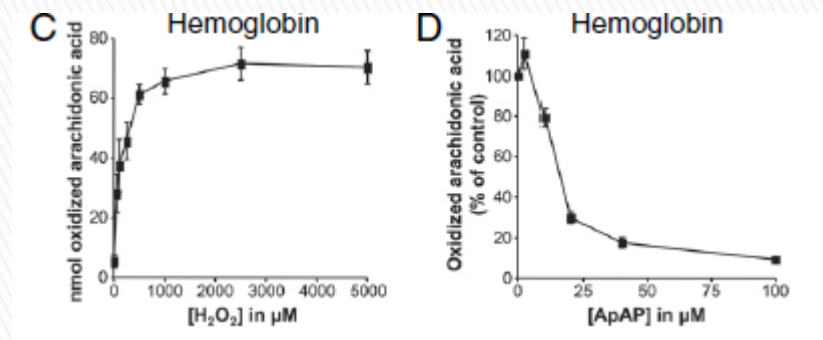
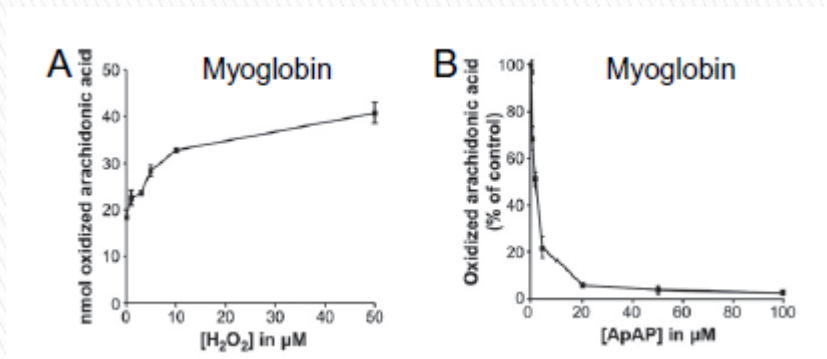


- ▶ Used horse myoglobin and human hemoglobin
 - ▶ Induction of rhabdo using 50% glycerol
 - ▶ All pre treatment analysis was at 20hr and 2hrs and post treatment was at 2 hrs and 22hrs.
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hypothesis



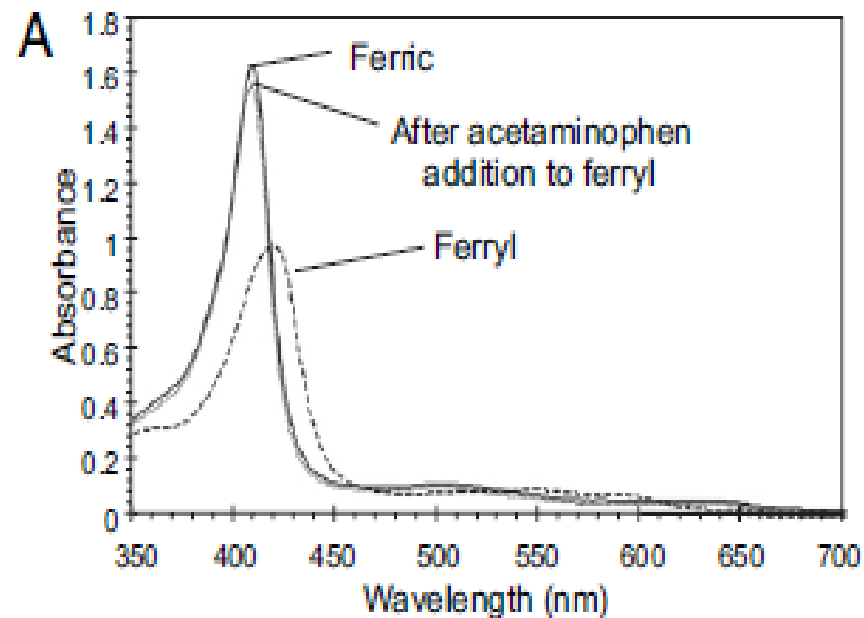
Inhibition by ApaP of Mb & Hb



Myoglobin

Hemoglobin

Decrease in Ferryl on adding ApaP



Gross appearance of Kidney

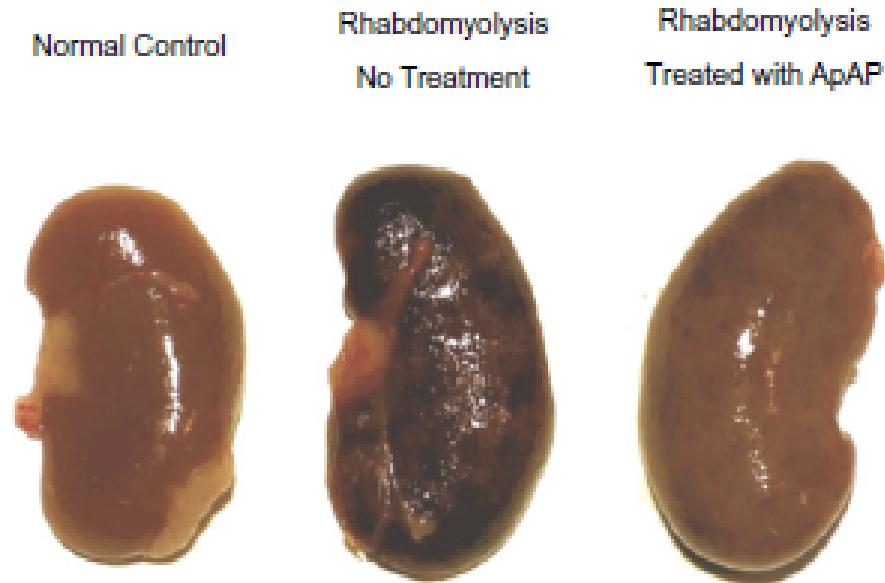
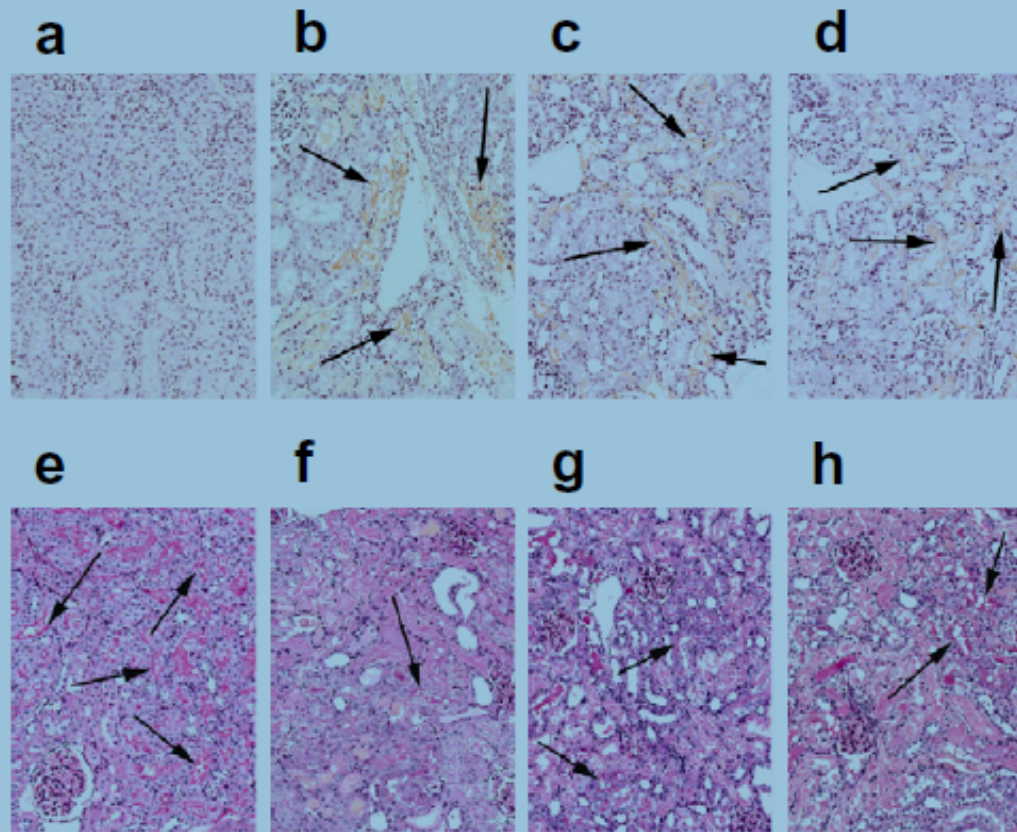


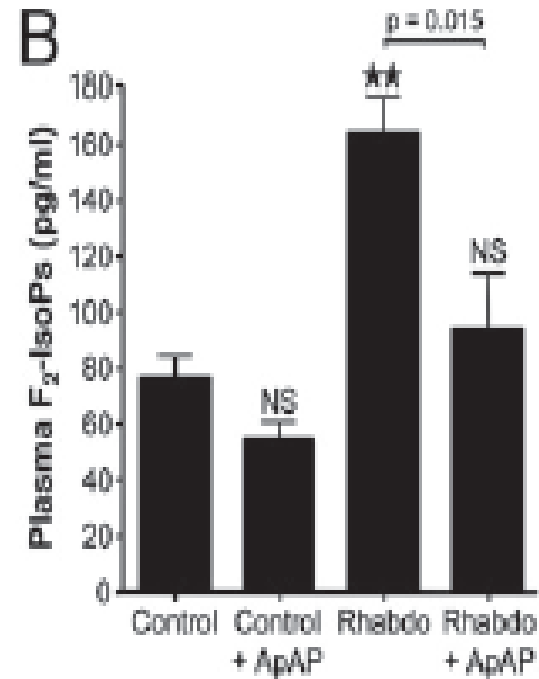
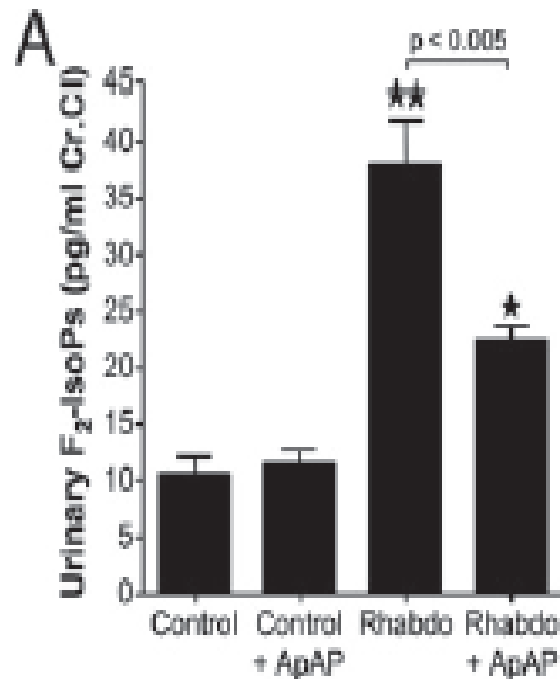
Fig. 4. Visual examination of a representative kidney from a normal rat (*Left*), a rat with rhabdomyolysis (*Center*), and a rat with rhabdomyolysis treated with ApAP (*Right*).



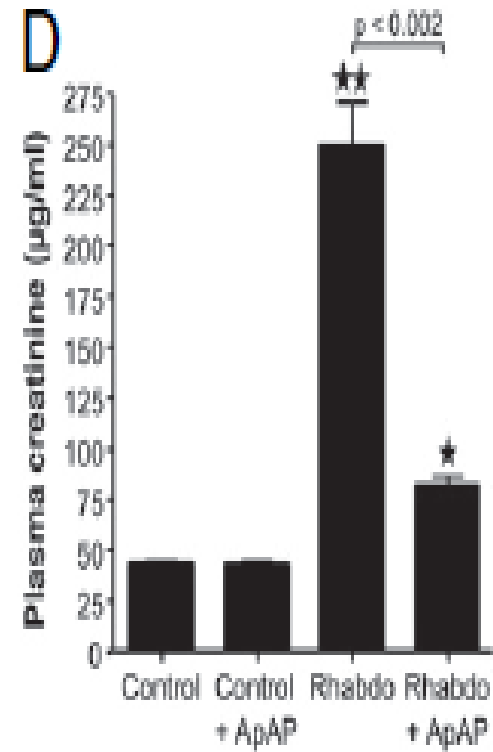
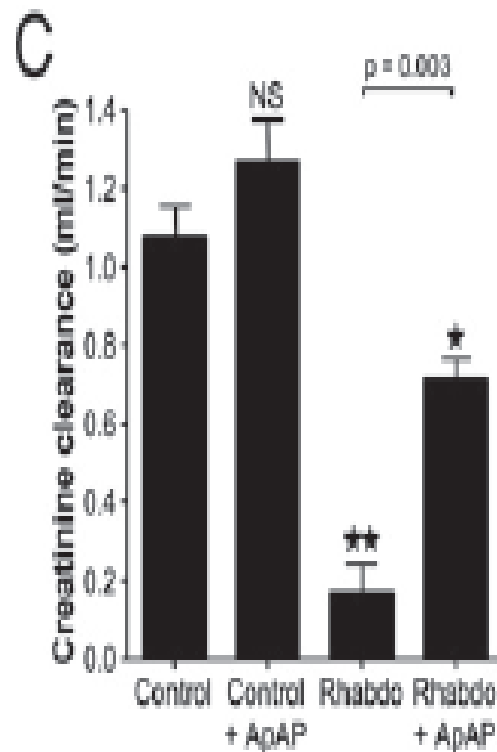
Myoglobin and H/E staining

a- control, b-rats with rhabdo c- rhabdo pretreatment with ApaP
d-rhabdo post treatment with ApaP

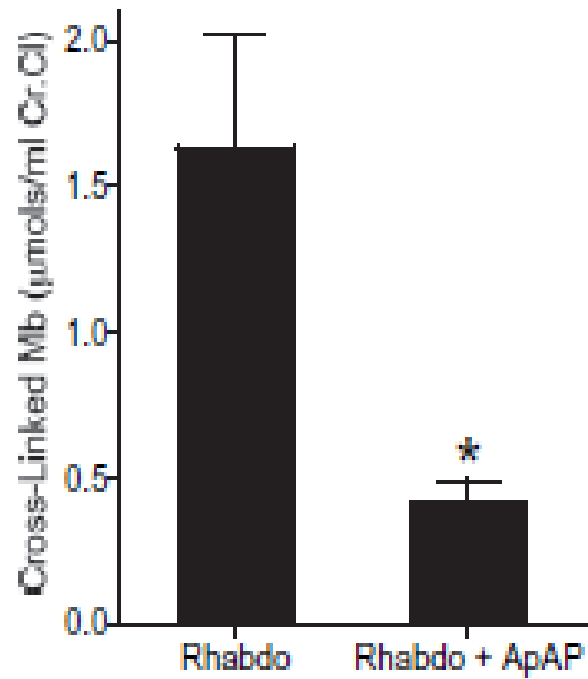
Effect of ApaP on oxidative injury



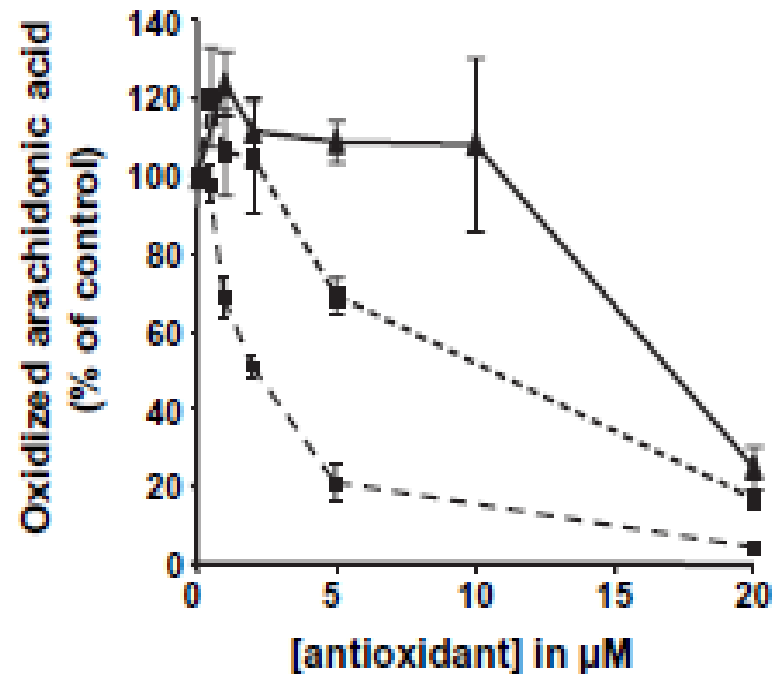
Effect of ApaP on Kidney function in rats




Cross linked Mb



Inhibition of oxidized arachidonic acid by ApaP, Trolox & ascorbic acid



Conclusions

- ▶ ApaP reduces Ferryl Mb to Ferric Mb
 - ▶ ApaP prevents formation of heme– protein cross links
 - ▶ Pretreatment reduces Rhabdoinduced renal failure
 - ▶ Post treatment with ApaP improves renal fn
 - ▶ ApaP used in the study is comparable to doses used clinically.
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Thank You

A decorative graphic at the bottom of the slide consisting of several overlapping, wavy shapes. The primary color is a vibrant blue, with a lighter blue gradient on top and a solid black section on the right side.