

## **Hypoxia is Not the Sole Cause of Lactate Production During Shock**

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### **Introduction:**

Traditionally, elevated blood lactate following hemorrhage is interpreted as tissue hypoperfusion, hypoxia and anaerobic glycolysis. The severity and duration of the increase in blood lactate correlate with death. Recent *in vitro* studies indicate that epinephrine stimulates lactate production in well-oxygenated skeletal muscle by increasing activity of the Na<sup>+</sup>-K<sup>+</sup> ATPase, which derives a significant amount of ATP from glycolysis.

### **Rationale:**

Using *in vivo* microdialysis, we tested whether inhibiting the Na<sup>+</sup>-K<sup>+</sup> pump with ouabain could reduce muscle lactate production during local exposure, *via* the microdialysis probe, to epinephrine or during hemorrhage in rats.

### **Methods:**

Microdialysis catheters were placed in the muscle of both thighs of pentobarbital anesthetized male SD rats (275-350g) and perfused (1 µl/min) with Krebs-phosphate buffer (pH 7.4) containing ethanol (5 mM) to permit assessment of changes in local blood flow. To inhibit the Na<sup>+</sup>-K<sup>+</sup> ATPase, ouabain (2-3 mM) was added to the perfusate of one leg. In one series of studies, epinephrine (10<sup>-5</sup> M) was added to the perfusate. In another series, rats were hemorrhaged to a MAP of 45 mm Hg for 30 min, followed by resuscitation with shed blood and 0.9% NaCl. Dialysate fractions were analyzed for lactate and ethanol fluorometrically.

### **Results:**

Lactate rose during epinephrine exposure or during hemorrhage and resuscitation. Treatment with ouabain reduced dialysate lactate concentration significantly in both series of studies. Local blood flow was reduced by either epinephrine exposure or hemorrhage, but returned toward baseline afterwards. Ouabain had no apparent effect on local blood flow.

### **Conclusions:**

Increased Na<sup>+</sup>-K<sup>+</sup> ATPase activity during epinephrine treatment or hemorrhage contributes to muscle lactate production. Hypoxia is not necessarily the sole cause of hyperlactatemia during and after hemorrhagic shock.