

TITLE: LIDOCAINE HCl INCREASES GLUCOSE UPTAKE IN CULTURED MOUSE FIBROBLASTS
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INTRODUCTION: Injection of local anesthetics into diabetic male Sprague-Dawley rats has been demonstrated to decrease serum blood glucose levels. This study was designed to delineate a mechanism for this change in blood glucose level by evaluating the effect of lidocaine HCl on glucose uptake.

METHODS: Embryonic Swiss mouse fibroblasts (3T3-C2 cells) were cultured in Dulbecco's modified Eagle's medium (DMEM) containing 10% calf serum, and grown to confluence at 37°C, 95% CO₂ in monolayer culture. Four days after attaining confluence, the cells were incubated with 0.5 mM lidocaine HCl over an eight-hour time course. At the appropriate times, the cells were washed with glucose-free Krebs-Ringer phosphate buffer containing 1% bovine serum albumin. Basal and insulin-stimulated (100nM) glucose uptake were assessed by incubating the monolayers with [1,2-³H] 2-deoxy-D-glucose, 0.2 mM, 2.5 µCi/µmol, for 20 minutes. Uptake of radiolabel was a linear function of time for at least 90 minutes. Following washing the monolayers were solubilized and counted in a liquid scintillation counter. The resultant counts were analyzed by the method of internal

standards. Significance of data was detected using ANOVA ($p < 0.05$).
RESULTS: As indicated in Figure 1, lidocaine induced a progressive and transient increase in both basal and insulin-stimulated glucose uptake.
DISCUSSION: It is established that serum blood glucose levels are regulated by gluconeogenesis, glycogenolysis and peripheral glucose uptake. Our data suggest that local anesthetic effects on serum blood glucose may induce an increase in peripheral glucose uptake.

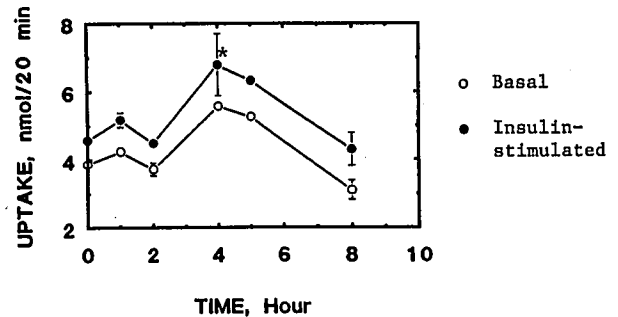


Figure 1
Mean glucose uptake ± S.D. * $p < 0.05$ vs. control

REFERENCE: 1. Krauss-Friedmann, N. and Juliano, R., *Biochimica et Biophysica Acta*, 1984, p.p. 195-98.

TITLE: PLACENTAL METABOLISM DURING HYPOXIA
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INTRODUCTION: The dually perfused isolated cotyledon of human placenta was used to study placental glucose utilization and lactate production during hypoxia. Previous authors have validated this model for this purpose.

METHODS: Placentas were obtained from 8 full term healthy parturients undergoing elective cesarean section. Cannulation and perfusion of the fetal side was done immediately. The placenta was then placed in the perfusion chamber and opened perfusion started with Earl's balanced salt solution at 37°C at flow rates of 990ml/hr and 350ml/hr for the maternal (M) and fetal (F) sides respectively. All placentas had a normal antipyrine clearance. For the first 30 min, normoxic perfusion (PO₂ = 98 mm Hg) continued followed by 30 min of hypoxic perfusion (inflow PO₂ = 20 mm Hg), which was in turn followed by normoxic perfusion at constant inflow PCO₂ of 35 mm Hg. The perfusate samples were collected for glucose, lactate, pyruvate, pH, PCO₂, PO₂ from the M outflow, and F umbilical vein outflow. Glucose utilization was taken as the difference between inflow and outflow concentrations. Results were expressed as mean ± 1 SE and analyzed with t-test.

RESULTS: During hypoxia, lactate levels increased in both the M and F outflows (F > M, $P < 0.01$, Fig 1). Increased glucose utilization occurred in the M and F perfusates (F > M, $p < 0.05$, Fig 2). The F outflow pH decreased from 7.35 ± 0.01 to 7.29 ± 0.02 ($p < 0.05$) and PCO₂ increased from 45 ± 3 to 49 ± 4 mm Hg ($p < 0.05$). Upon restoration of normoxia, both lactate levels and

glucose utilization returned to baseline.
DISCUSSION: Data show that during periods of maternal hypoxia the human placenta produces and releases lactate preferentially into the fetal circulation. Thus, placenta may contribute to increased fetal lactate levels seen in human fetuses during maternal hypoxia. The augmented glucose utilization perhaps signifies placental anaerobic glycolysis in an attempt to supply energy substrates to the baby.

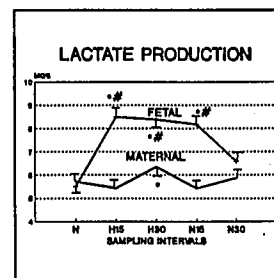


Figure 1

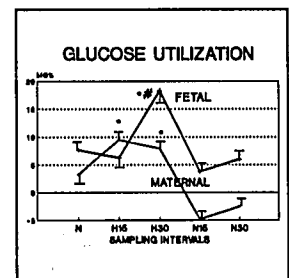


Figure 2

Legend: N - Normoxia; H15- Hypoxia 15 min; H30- Hypoxia 30 min. N15 and N 30 at 15 and 30 min after restoration of normoxia. * - significantly different from the respective baseline; # different from the maternal side.

REFERENCE: 1. Schneider H, Dancis J: In Vitro Perfusion of Human Placental Tissue. New York, S. Karger, 1985.