

Title: DISSOCIATION OF POTASSIUM AND GLUCOSE UPTAKE RESPONSES TO HYPERINSULINEMIA IN CRITICALLY ILL PATIENTS

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INTRODUCTION: Sepsis and extensive burn injury are clinical states characterized by glucose intolerance. However, it is unclear whether the nature of glucose intolerance in septic patients is similar to that following burn injury. The purpose of this study was to determine if the maximal biological effectiveness of exogenously-administered insulin is altered in septic or burned patients, to quantitate their potassium and glucose uptake responses to hyperinsulinemia, and to examine the relationship between these two insulin-mediated responses.

METHODS: Three septic patients and six non-septic burn patients in the Surgical Intensive Care Units at the University of Texas Medical Branch were studied. To distinguish the response to sepsis or burn injury from the response to bedrest alone (1), six healthy young men confined to strict bedrest for one week served as controls. All subjects provided Institutional Review Board-approved informed consent. Septic patients were studied early after the diagnosis was made, and were hyperdynamic (C.I. 6.12 ± 0.44 , SVRI 910 ± 46) at the time of study. The non-septic burn patients (total surface, $52 \pm 4\%$ with $17 \pm 5\%$ 3rd degree) were studied on postburn day 7. Studies were made following overnight fast with the hyperinsulinemic euglycemic clamp technique (2). Plasma glucose was monitored (Beckman Autoanalyzer, Brea, CA) at 5 min intervals and maintained at 90 ± 3 mg/dl by infusion of aqueous dextrose. Plasma K⁺ was monitored at 30 min intervals and maintained within normal range by infusion of KCl. Indirect calorimetry (Horizon, Anaheim, CA) was performed during the 4-hour basal period (no insulin) and subsequent 4-hour hyperinsulinemic period. Data are expressed as means \pm SE.

RESULTS/DISCUSSION: Fasting plasma glucose in septic or burned patients was elevated 41% and 38%, respectively ($p < 0.01$) compared to bedrested volunteers, who served as controls (Table 1). Combined

TABLE 1 - SUBJECT CHARACTERISTICS

	Bedrest	Sepsis	Burns
Age (Years)	23 \pm 1	37 \pm 2*	34 \pm 5*
Weight (Kg)	66 \pm 6	91 \pm 15	76 \pm 3
REE (Kcal/d)	1484 \pm 34	2927 \pm 198*	2807 \pm 105*
REE (% predicted)	90 \pm 3	155 \pm 10*	156 \pm 5*
Fasting Plasma Glucose (mg/dl)	80 \pm 1	112 \pm 9*	110 \pm 8*

Asterisk (*) = $p < 0.05$ vs. Bedrest

with a basal RQ of less than 0.8, these data indicate a preferential utilization of fat and protein over glucose in the two overnight-fasted patient groups. During this time, plasma insulin was not different from control in either septic or burned patients. Clearance of insulin was increased in both septic and burned patients, with respective circulating levels only 46% and 43% ($p < 0.01$) of control at the same infusion rate. Therefore the data are tabulated according to comparable circulating insulin, rather than infusion rate, in Table 2. Maximal response of glucose utilization in bedrested man (= glucose infusion rate at steady state) was achieved at a plasma insulin of 200-250 uU/ml,

and was stable by 60 min of hyperinsulinemia. In contrast, glucose utilization was depressed 59% ($p < 0.001$) in septic patients, with no improvement over time (up to 5 hr). Burned patients exhibited only a modest 18% ($p < 0.05$) inhibition of glucose uptake, which became stable after 90-120 min of hyperinsulinemia. When plasma insulin was raised to 1060 ± 129 uU/ml in burned patients, glucose uptake became similar to control. The RQ increase in response to hyperinsulinemia shows a conversion to carbohydrate metabolism (RQ = 0.98) in controls, but not in septic (RQ = 0.84) or burned (RQ=0.88) patients. Potassium requirements in all subject groups were increased during hyperinsulinemia. The relatively larger requirements in the septic and burned patients versus controls may represent a depletion of total body potassium stores despite maintenance of near-control plasma K⁺ concentrations. Potassium uptake response to hyperinsulinemia was brisk in all subject groups, within 15 minutes after the start of insulin infusion, and was maximal in both septic and burned patients at a plasma insulin concentration of 314-335 uU/ml.

Parameter	Condition	TABLE 2 - EUGLYCEMIC CLAMP Insulin Infusion Rate		
		0	1	3
[Insulin] Plasma (uU/ml)	Bedrest	9 \pm 1	220 \pm 7	730 \pm 11
	Sepsis	19 \pm 10	335 \pm 31*	—
	Burns	11 \pm 2	314 \pm 14*	1060 \pm 129
Glucose Infusion Rate (mg/kg.min)	Bedrest	—	11.40 \pm 0.93	13.73 \pm 1.10
	Sepsis	—	4.62 \pm 0.32*	—
	Burns	—	9.32 \pm 0.83*	12.22 \pm 0.86
RQ	Bedrest	0.84 \pm 0.02	0.98 \pm 0.01	1.00 \pm 0.03
	Sepsis	0.77 \pm 0.02*	0.84 \pm 0.03*	—
	Burns	0.79 \pm 0.02*	0.88 \pm 0.01*	0.96 \pm 0.02
K ⁺ Infusion Rate (mEq/kg.hr)	Bedrest	0.01 \pm 0.00	0.12 \pm 0.01	0.12 \pm 0.01
	Sepsis	0.07 \pm 0.01	0.24 \pm 0.01*	—
	Burns	0.07 \pm 0.01	0.23 \pm 0.04*	0.26 \pm 0.02
[K] Plasma (mEq/l)	Bedrest	4.2 \pm 0.1	3.9 \pm 0.1	3.9 \pm 0.1
	Sepsis	4.1 \pm 0.4	4.0 \pm 0.3	—
	Burns	3.9 \pm 0.1	3.4 \pm 0.2	4.0 \pm 0.1

Asterisk (*) = $p < 0.05$ vs. Bedrest Cross (+) = $p < 0.02$ vs. Burns

These results show that hyperinsulinemia causes a brisk cellular K⁺ uptake response in both controls and critically ill patients. However, insulin-induced glucose uptake was markedly impaired in septic patients. Even if the exogenous glucose taken up by septic patients were completely oxidized, it would yield only 2422 cal, or 83% of their requirements. This contrasts with the situation following severe but non-septic burn injury, where full oxidation of exogenous glucose would yield 4080 cal, or 145% of their needs. It is concluded that cellular K⁺ uptake in response to insulin is independent of glucose entry, and that a postreceptor defect in insulin responsiveness impairs glucose metabolism in septic patients while K⁺ responsiveness to insulin is preserved.

REFERENCES:

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