TITLE: HEPATIC O_2 REGULATION DURING ENDOTOXEMIA

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Most tissues display O_2 regulatory behavior such that O_2 consumption (VO_2) is independent of O_2 delivery (DO_2) until a critical value of DO_2 (DO_2c) is reached. Below DO_2c, VO_2 becomes O_2 supply dependent. However it is not clear whether O_2 supply dependency represents exhaustion of O_2 regulatory mechanisms, or simply O_2 conformity (i.e. arrest of non-essential metabolism) in individual organs. We measured liver DO_2 and VO_2 using hepatic arterial and portal venous electromagnetic flow probes and O_2 content differences, and estimated liver NADH/NAD as hepatic venous B-hydroxybutyrate to acetoacetate ratio (BAR) (1) in seven pentobarbital-anesthetized mongrel dogs following bolus infusion of E. coli lipopolysaccharide, 5 mg/kg. We assessed hepatic O_2 regulation by progressive hemorrhage in 50 to 100 ml increments, and estimated liver DO_2c by applying dual line regression (2) to pooled data (figure 1). BAR was relatively constant during O_2 supply independency but rose progressively during O_2 supply dependency (figure 2). These data are in agreement with observations in control animals (3). We conclude that liver O_2 supply dependency in endotoxin-treated dogs, as well as in control dogs, represents exhaustion of O_2 regulatory mechanisms, rather than O_2 conformity.

Figure 1

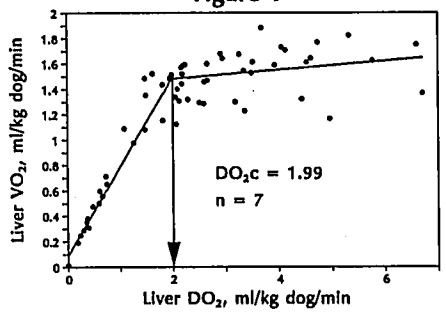
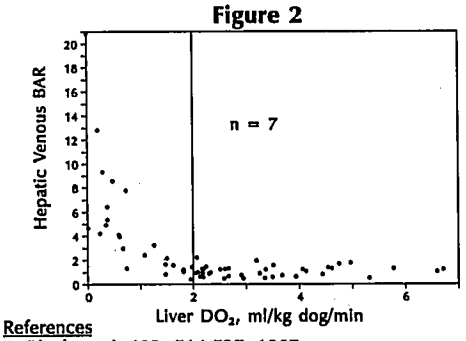


Figure 2



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TITLE: EFFECTS OF FLUID BALANCE AND PROSTAGLANDIN E_1 (PGE_1) ON REIMPLANTATION PULMONARY EDEMA (RPE) IN HEART-LUNG TRANSPLANT RECIPIENTS (HLTR)

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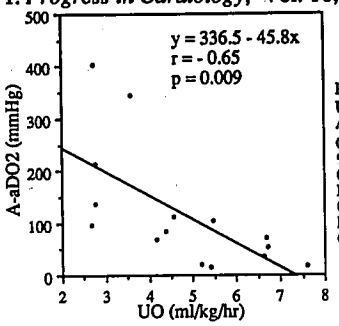
To determine the effects of perioperative fluid management on the RPE[1] of HLTR, we examined fluid balance [percent change from pre-operative body weight, (%Δ BW)], gas exchange, [pHa, PaO_2 (mmHg), $PaCO_2$ (mmHg), HCO_3-(mEq/L), A-aDO_2 (mmHg)], urine output [(UO), (ml/kg/hr)], hemodynamics [CI (l/min/m^2), PVRI (dyne·sec/cm^5·m^2), CVP (mmHg), PAD (mmHg)] and chest x-rays at 24 hours post-implantation (24-HPI) in two groups of HLTR. Two HLTR with graft dysfunction (A-aDO_2 ≥ 390 at 24 hrs) due to pulmonary contusion or protamine-induced pulmonary edema were not included. Group I [n = 6, male/female ratio (M/F) = 2, 34 ± 1 yrs (mean ± SEM), 67 ± 6 kg, primary pulmonary hypertension (PPH) 66%, Eisenmenger complex (EMC) 17%, other 17%] received grafts from locally procured donors [graft ischemia time (GIT) = 99 ± 10 min], while group II (n = 10, M/F = 2, 30 ± 3 yrs, 53 ± 8 kg, PPH 40%, EMC 30%, other 30%) received grafts from distantly procured donors (GIT = 204 ± 14 min) during hypothermic cardiopulmonary bypass [(CPB), (28°C, Hct 25%)]. Donors had PaO_2 ≥ 100 mmHg at FiO_2 ≤ .4 with PIP ≤ 30 cmH_2O at V_T 10-12 ml/kg and were preserved at 4°C with Collins solution. Whereas 80% of group II was treated with PGE_1 (.05 ± .01 μg/kg/min) post-CPB, only 17% of group I received PGE_1 (p = .01, chi-squared). Diuresis was forced in group II but not group I. At 24-HPI, 16 HLTR, 5 extubated (FiO_2 = .35 ± .04) and 11 intubated (FiO_2 = .39 ± .04, IMV 8 ± 2 bpm, V_T 769 ± 42 ml, PEEP 5 ± 1 cmH_2O) from groups I and II had hemodynamics, gas exchange, UO and %Δ BW as shown (Table). RPE was present in all but one HLTR; the radiologic severity of RPE was not different between groups. The A-aDO_2 in group II (58 ± 11 mmHg) was significantly lower than in group I (220 ± 52 mmHg) at 24-HPI (p = .0009, unpaired Student's t-test) despite a longer GIT (p = .0001) and higher PAD (p = .01). While UO at 24-HPI, higher in group II (p = .0001), was a good predictor of A-aDO_2 [(r = -.65, y = 336.5 - 45.8x, p = .009) (Fig.)]; GIT, CPB time and %Δ BW were not. These data demonstrate that RPE, a frequent finding in HLTR 24-HPI, and the concomitant abnormalities of gas exchange may be favorably influenced by a forced diuresis and PGE_1 therapy during and up to 24-HPI in spite of a longer GIT.

References
1. *Progress in Cardiology*, Vol. 16, Chapter 3, pp. 51-80, 1988.



	GROUP I	GROUP II	p value
PGE_1	17%	80%	.01
UO	3 ± 0.2	6 ± 0.4	.0001
A-aDO_2	220 ± 52	58 ± 11	.0009
GIT	99 ± 10	204 ± 14	.0001
%Δ BW	4 ± 2	3 ± 2	NS
CVP	10 ± 1	13 ± 2	NS
PAD	11 ± 1	16 ± 1	.01
CI	4.4 ± 1.3	4.2 ± 0.4	NS
PVRI	66 ± 6	68 ± 10	NS
CPB time	209 ± 15	221 ± 12	NS