

Title: THE EFFECTS OF SEVERE ALKALOSIS AND HYPOXEMIA ON CEREBRAL METABOLISM IN THE NEWBORN LAMB

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**Introduction.** Pulmonary hypertension is a common, often life threatening problem in neonates and young children after cardiac surgery. Hyperventilation to a  $\text{PaCO}_2$  of approximately 20 mmHg reduces the pulmonary artery pressure (PAP) and improves the  $\text{PaO}_2$  in many instances. However, this degree of alkalosis reduces cerebral blood flow (CBF) and shifts the infant's already left shifted oxygen dissociation curve further to the left and thus, may compromise blood flow, oxygenation and metabolism of the brain. To determine what effect hyperventilation may have, we examined the effects of severe alkalosis and of hypoxemia on CBF and cerebral metabolism in the newborn lamb.

**Methods.** Seven 1-5 day old lambs were anesthetized with 70% nitrous oxide and local anesthesia and paralyzed with Pavulon. The trachea was intubated and ventilation was controlled to maintain normal blood gases. Catheters were inserted into the femoral artery and the sagittal sinus. In four animals a catheter was also inserted to obtain cerebral spinal fluid. Cerebral blood flow was measured with radioactive xenon. A two lead electroencephalogram (EEG) was measured throughout the study. The animal's condition was allowed to stabilize for one hour. The arterial and sagittal sinus pressures, blood gases, pH, arterial and sagittal sinus glucose and lactate levels, CSF lactate levels and cerebral blood flow were measured at the following times: (1) after one hour of stabilization (control); (2) after one and (3) two hours of hyperventilation ( $\text{PaCO}_2$  20 mmHg) and hyperoxia; (4) after one hour of hypocarbia and hypoxemia ( $\text{PaO}_2$  30 mmHg); (5) after one hour of normocarbia and hypoxemia ( $\text{PaO}_2$  30 mmHg); and (6) after one hour of return to normocarbia and hyperoxia. The data were analyzed by analysis of variance.

**Results.** The cerebral perfusion pressures and EEG remained constant throughout the study. Cerebral blood flow was reduced 40% after both one and two hours of hypocapnea and hyperoxia. Hypoxemia increased CBF 23% above control (212% above hypocapnic levels) despite continued hyperventilation and completely overrode the alkalotic cerebral vasoconstriction. The cerebral metabolic rates for oxygen ( $\text{CMRO}_2$ ) and glucose (CMR-glu) remained constant throughout the study. However, the CSF lactate levels fell below arterial and the a-v differences for lactate became negative, i.e., lactate was taken up by the brain, especially during the two periods of hypoxemia and during recovery. The cerebral metabolic rate for lactate increased.

**Discussion.** These newborn lambs maintain their  $\text{CMRO}_2$  and CMR glu constant despite severe alkalosis and/or hypoxemia. In addition, lactate was taken up

by the brain during alkalosis and during hypoxemia, presumably to be used as a metabolic fuel. The adult is also able to use lactate for cerebral metabolism,<sup>2</sup> but to a lesser degree than shown here in the normoxic puppy.<sup>3</sup> Lactate metabolism appears to provide an additional source of metabolic fuel during periods of reduced cerebral blood flow and reduced oxygenation. These data suggest that the newborn lamb is able to regulate and maintain his  $\text{CMRO}_2$  and CMR-glu at control levels despite severe alkalosis and/or hypoxemia and that he may be meeting additional cerebral metabolic needs by metabolizing lactate.

#### References.

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TABLE 1.

	$\text{PaO}_2$ (SEM)	$\text{PaCO}_2$ (SEM)	$\text{P}_v\text{O}_2$ (SEM)	A-Vd <sub>2</sub> Content (SEM)	Hb (SEM)
Control	169 18	41 2	36 3	5 0.5	9 0.6
LCO <sub>2</sub> 1 Hr	207 7	23* 2	21* 2	7 0.4	9 0.4
LCO <sub>2</sub> 2 Hr	193 8	22* 2	22* 2	6 0.6	9 0.4
LCO <sub>2</sub> LO <sub>2</sub>	29* 1	24* 2	18* 1	4* 0.6	8 0.3
NCO <sub>2</sub> LO <sub>2</sub>	30* 5	39 1	20* 3	3* 0.3	8 0.5
NCO <sub>2</sub> HO <sub>2</sub>	139 3	39 2	24* 3	6 0.6	8 0.5

TABLE 2.

	CBF (SEM)	$\text{CMRO}_2$ (SEM)	CMR glucose (SEM)	CMR lactate (SEM)
Control	71 10	3.2 0.4	13 7	2.4 2
LCO <sub>2</sub> 1 Hr	42* 4	3.1 0.4	14 4	0.4 1
LCO <sub>2</sub> 2 Hr	39* 4	2.6 0.3	14 6	-1.6* 2
LCO <sub>2</sub> LO <sub>2</sub>	85* 13	3.3 0.6	16 14	-13.4* 7
NCO <sub>2</sub> LO <sub>2</sub>	80 13	2.3 0.3	0.2 3	-4.4* 4
NCO <sub>2</sub> HO <sub>2</sub>	53 2	3.1 0.4	6 2	-0.4* 0.4

\* Significantly different from control ( $P < 0.05$ )

H = High L = Low N = Normal