319 CHRONIC HYPOXEMIA IN THE NEWBORN LAMB

David F. Teitel, Daniel Sidi, Dan Bernstein, Michael A. Heymann, Abraham M. Rudolph.
Cardiovascular Research Institute, University of California, San Francisco, Department of Pediatrics, San Francisco.

The adaptive mechanisms by which oxygen delivery is maintained during chronic hypoxemia, and the costs of such adaptations, are not well defined. In the newborn lamb, we have induced chronic hypoxemia by placing an inflatable balloon around the pulmonary artery after performing an atrial septostomy. Three days after surgery, the balloon was gradually inflated in 11 lambs to create a right-to-left atrial shunt such that arterial oxygen saturation was between 60 and 75%. Twice weekly studies were performed on these lambs and weekly studies on 12 normoxemic lambs. Growth decreased sharply (47 ± 123 vs 221 ± 82 g/day) at the onset of hypoxemia and remained low, although oxygen consumption followed the normal gradual decline. Systemic blood flow decreased at balloon inflation but quickly returned to normal. Mixed venous and coronary sinus saturations were low, but could decrease further with shivering. Systemic oxygen delivery returned to normal as hemoglobin concentration rose (from 9.4 ± 1.5 to 12.5 ± 2.2 g/dl). P50 did not change. Four of the 11 hypoxemic lambs died during the 2 week study period. These data show that systemic oxygen delivery is maintained primarily by rising hemoglobin in the chronically hypoxemic newborn. There is a signal to decrease growth apparently to maintain some reserve. The limited reserve is shown by a high mortality rate despite normal oxygen delivery at rest.

● 320 AMNIOTIC FLUID (AF) ERYTHROPOIETIN (EP) IN HIGH-RISK PREGNANCIES.

Kari A. Teramo, John A. Widness, Gisela K. Clemons, Riita Saarinen, Petri Voutilainen, and Robert Schwartz. Dept. of Ob/Gyn, Univ. of Helsinki, Finland; Dept. of Pediatrics, Brown Univ., Providence; and Lawrence Berkeley Laboratory, Univ. of California, Berkeley.

An increase in Ep synthesis is initiated by hypoxemia in adult and fetal animals. Elevated Ep levels have been found in umbilical plasma (Umb) in high-risk pregnancies. Since Ep is excreted into AF, we measured AF Ep in high-risk pregnancies during the last trimester as well as at delivery by cesarean section, and compared AF Ep with Umb Ep values. Ep was analyzed by RIA in 37 insulin-treated diabetics, 39 hypertensives including 31 pre-eclamptics, 7 with other complicating diseases, and 16 controls. Umb and AF Ep levels obtained simultaneously at sections were:

Ep (mU/ml)		Controls (12)	Diabetics (18)	Hypertensives (24)
Umb	Median	25.2	40.9	57.0
	Range	5.7 - 54.2	16.3 - 197	18.7 - 2800
AF	Median	12.3	15.2	20.7
	Range	5.7 - 19.1	5.3 - 417	7.0 - 1512

The correlation between ln-transformed AF and Umb Ep was highly significant in diabetics ($r = 0.80$, $p < 0.001$) and hypertensives ($r = 0.74$, $p < 0.001$) as well as in the total group ($N = 61$; $r = 0.77$, $p < 0.001$). In contrast, there was less significant correlation ($r = 0.39$, $p < 0.05$) between AF obtained at induction and Umb obtained after 148 - 1184 minutes of labor (30 patients). In serial AF samples, 21 of 39 hypertensives and 9 of 37 diabetics had AF Ep values above control range. We conclude that in the absence of labor, AF Ep reflects fetal plasma Ep. We speculate that AF Ep may be an antepartum indicator of fetal hypoxemia.

= 321 Dihydrotestosterone Antagonizes Glucocorticoid-dependent Surfactant Synthesis in Explant Culture.

J.S. Torday, Dept. of Pediatrics, Harvard Medical School, Boston, MA

Male fetuses produce less pulmonary surfactant than female fetuses during the active phase of lung maturation characterized by increased synthesis of saturated phosphatidylcholine (SPC). A previous study has shown that Dihydrotestosterone (DHT) can inhibit SPC production by the fetal rabbit lung in vivo (Nielsen et al JCI 69; 611, 1982). The present study was designed to test whether DHT antagonizes glucocorticoid-stimulated surfactant synthesis by fetal rabbit lung explants, a system in which active SPC synthesis is glucocorticoid-dependent. Day 19 fetal lung explants were cultured in Waymouth's medium plus 10% charcoal-stripped fetal calf serum(FCS-) and 10^{-7}M DHT , 10^{-7}M cortisol or 10^{-7}M DHT+10^{-7}M cortisol for 9 days (=day 28 in utero). Explants maintained in FCS- showed no increase in ^{3}H-choline incorporation into ^{3}H-SPC; cortisol caused a 4-fold increase in SPC synthesis; DHT had no effect on baseline SPC synthesis - however DHT-treated explants did not respond to a cortisol challenge. Furthermore, sex-specific explants showed no difference in either baseline or cortisol-challenged SPC synthesis. These data support the hypothesis that the sex difference in pulmonary surfactant production is due to androgen antagonism of cortisol-stimulated surfactant phospholipid synthesis. There is extensive evidence that this increase in SPC synthesis is due to glucocorticoid stimulation, and that the delay in male surfactant production is due to androgen inhibition. This study was supported by NIH grant #28315.

● 322 Formal Demonstration of Glucocorticoid-Dependent Fetal Lung SPC Synthesis.

J.S. Torday, Dept. of Pediatrics, Harvard Medical School, Boston, MA

Fetal lung explants develop the capacity to actively synthesize saturated phosphatidylcholine (SPC) in the presence of culture medium fortified with serum. The following criteria were set up to test whether this process is glucocorticoid(GC)-dependent: 1) GC must promote active SPC synthesis; 2) antiGC must inhibit active SPC synthesis; 3) in the absence of GC active SPC synthesis will not occur, but activity can be restored by adding GC. Day 19 fetal rabbit lung explants were cultured under the following conditions: Waymouth's medium and 10% fetal calf serum(FCS) or 10% stripped FCS(FCS-) plus cortisol(GC) or cortexolone (antiGC) for 9 days. SPC synthesis was quantified by measuring the rate of ^{3}H-choline incorporated into ^{3}H-SPC.

Treatment	day-1	day-6	day-9
a) FCS	1200±225	1800±208	2500±288
b) FCS+cortisol(10^{-7}M)	1150±128	2380±250	4308±310
c) FCS+cortexolone(10^{-5}M)	1350±160	1480±190	1380±127
d) FCS-	1160±190	1180±178	1240±186
e) FCS- +cortisol(10^{-7}M)	1180±187	1920±208	4380±297

*data = mean±SD SPC(cpm/mg protein)

Therefore 1)both serumGC(a) and cortisol(b) support active SPC synthesis; 2)serum GC is inhibited by antiGC(c);3)in the absence of GC(d) active SPC synthesis does not occur, but can be stimulated by cortisol(e). Therefore the fetal lung is dependent on GC for development of active SPC production. This study supported by NIH Grant #HL28315.

323 CELL Na+ METABOLISM IN HUMAN UMBILICAL VASCULAR SMOOTH MUSCLE AND ITS POSSIBLE SIGNIFICANCE.

T.N. Tulenko and S. Imaizumi (Spon. by R.A.Polin) Depts.of Physiology-Biochem, Pediatrics & Ob/Gyn., Medical College of Pa., Phila., Pa.

In excitable cells, cellular Na+ levels are kept low by Na-pump activity of the cell membrane. Since Na-pump activity affects vascular tone, we measured cell NA+ levels and Na-pump activity in umbilical (UA) and chorionic plate arteries (CPA) from term vaginal deliveries and compared them to "normal" adult arteries using rabbit carotid arteries (RCA). Contiguous arterial segments (2.5mg) were obtained from the various sites and used for cell Na+ measures using a LiCl wash followed by flame photometry. Na-pump activity was measured using an ouabain sensitive ^{86}Rb uptake procedure.

	Cell Na+ (n moles/kg d.w.)	Resting Na+ pump (n moles/mg/10 min)	Maximal Na+ pump (n moles/mg/10min)
UA	74.5 ± 7.1	17.9 ± 2.0	15.7 ± 1.9
CPA	36.2 ± 2.1	8.7 ± 2.1	14.0 ± 1.9
RCA	14.0 ± 2.1	1.1 ± 0.2	11.1 ± 1.0

These results indicate that human UA & CPA contain high (CPA) to extraordinarily high (UA) cell Na+ levels compared to RCA and that resting Na-pump activity is maximally turned on in UA and elevated in CPA versus RCA. Rings of arteries isolated in-vitro and contracted with serotonin in K+-free media completely relax when the NA-pump is activated with KCl. Taken together these results suggest a cellular basis for maintenance of placental vascular vasodilation.

† 324 CAN INTRAUTERINE WEIGHT GAIN AND BODY COMPOSITION BE SIMULATED IN THE FORMULA FED VERY LOW BIRTHWEIGHT (VLBW) INFANT?

J. Van Aerde, P. Sauer, T. Heim, J. Smith, P. Swyer, Dept. Paed. & Med. Eng; Univ. Toronto; Res. Inst; The Hospital for Sick Children, Toronto Canada.

Until now no formula has been able to simulate both intra-uterine weight gain and body composition. In order to evaluate a long-chain-triglyceride formula at an energy intake recommended by the Am. Acad. Ped. Nutr. Committee, we compared 12 very-low-birthweight (VLBW) infants with the fetus of the same postconceptional age. Twenty-three studies, combining open-circuit indirect calorimetry, macronutrient balance and anthropometry were performed in 12 growing VLBW infants ($\bar{x}$±S.E.: B.W. 986±36 g; Gest age 27.8±0.4 wks; study wt. 1307±51 g; age 38±3 d).

RESULTS: ($\bar{x}$±S.E.)	Energy (Kcal/kg.d)	CHO (g/kg.d)	Fat (g/kg.d)	Protein (g/kg.d)
Intake	120.9±1.50	12.41±0.16	6.21±0.08	2.59±0.03
Losses	15.1±1.38	0.083±0.005	1.31±0.13	0.377±0.03
Oxidation	56.9±1.05	10.67±0.45	1.40±0.16	0.380±0.02
Storage	48.9±1.80	1.79±0.32	3.50±0.17	1.83±0.04

Weight gain 15.7±0.85 g/kg.d and length gain 1.04±0.09 cm/wk were equal to intra-uterine growth rates (weight 13.9 g/kg.d; length 1.24 cm/wk). The accretion rate of protein was comparable to that of the fetus, fat accretion was 1.4 times higher.

CONCLUSIONS: (1) At a global energy intake of 120 Kcal/kg.d, the intra-uterine weight and length gain could be simulated but body composition not. (2) The higher fat deposition occurred at the expense of water space indicating that caloric intake and/or composition of feeds may have to be modified to attain the intra-uterine accretion for macronutrients.