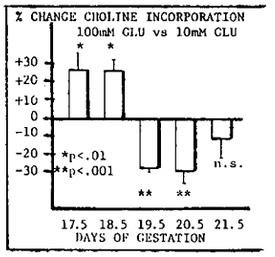
●242 HUMAN FETAL AND MATERNAL PLASMA AMINO ACID LEVELS IN NORMAL AND INTRAUTERINE GROWTH RETARDED (IUGR) GESTATIONS. William A. Gahl, Kypros H. Nicolaides, Isa Bernardini, Robert Bradley, Mark I. Evans. Section on Human Biochem. Gen., NICHD, Bethesda, MD, Harris B-C, OB, King's Coll., London, Reproductive Genetics, OB-Gyn., Wayne State Univ., Detroit, MI.

Human fetal blood was obtained by cordocentesis from 38 second & third trimester high-risk fetuses. For 31 of these gestations, simultaneously-obtained maternal blood was also available. 14 of the 38 (11 of the 31) gestations resulted in IUGR infants. All samples were assayed for plasma amino acids (AAs), i.e., thr, ser, pro, gly, ala, cit, val, met, ileu, leu, tyr, phe, orn, lys, his, and arg. For both fetal and maternal samples, plasma AAs of the IUGR group did not differ from normal. Fetal plasma levels were significantly higher than maternal levels for at least 6 AAs: thr, val, met, tyr, phe, and lys; these are apparently concentrated in the fetal circulation by the placenta. For 20 normal fetal/maternal plasma pairings, the mean ratio of fetal to maternal AA levels ranged from 1.2 to 2.4 for the 6 AAs. Of 11 IUGR fetal/maternal ratios, 8 fell within the normal range, but 3 were between 0.99 and 1.02; these IUGR gestations exhibited impaired ability to concentrate these 6 AAs in the fetal circulation. These findings 1.) Establish for the first time standard levels for fetal plasma AAs in utero; 2.) Require confirmation and correlation with gestational age as more results accrue; and 3.) Suggest that a portion of IUGR gestations exhibit a defect in the ability to concentrate nutrients within the fetus. These data provide a basis for future diagnostic and, perhaps, therapeutic investigations into gestations at risk for IUGR.

●243 DIFFERENTIAL EFFECTS OF HIGH GLUCOSE ON FETAL LUNG MATURATION IN VITRO AS A FUNCTION OF GESTATIONAL AGE. Ira H. Gewolb (Spon. A. Fleischman), Dept. of Peds., Albert Einstein College of Medicine, Bronx, NY.

Hyperglycemia has been implicated as a cause of delayed fetal lung maturation in the diabetic pregnancy. Previous work has shown that high glucose levels inhibit biochemical and morphologic maturation of fetal lung in vitro. The aim of the present study was to examine the effect of high glucose on fetal lung development at different times during gestation.

Fetal rat lung explants (17.5-21.5 days) were grown for 48 hr in media containing 10, 50, or 100mM glucose, pulsed with H^3-choline, and the rate of incorporation into phosphatidylcholine assayed.



Significantly decreased rates of choline incorporation were seen with 19.5 and 20.5 day lungs grown in 100mM glucose, compared to those grown in 10mM glucose (27% and 29% inhibition, respectively; p<.001). Earlier in gestation (17.5 and 18.5 days) 100mM glucose resulted in significant increases in choline incorporation rate (26% acceleration; p<.01)(Fig). Explants grown in 50 mM glucose had effects similar to, but of lesser magnitude than, those grown in 100mM glucose. Equiosmolar mannitol controls did not have equivalent inhibitory or acceleratory effect.

These results suggest that high glucose exerts differing effects on fetal lung development at different times during gestation. The critical period for inhibition appears limited to a time late in gestation, consistent with our previous in vivo data.

244 HIGH GLUCOSE CONCENTRATIONS CAUSE DELAYED FETAL LUNG MATURATION AS MEASURED BY FLUORESCENCE ANISOTROPY AND INTENSITY. Ira H. Gewolb, Joan Deutsch, and Ralph L. Cavalieri (Spon. A. Fleischman) Depts. of Peds. & Ob-Gyn, Albert Einstein College of Medicine, Bronx, NY.

Previous studies have shown that fetal rat lung cultured in high glucose media exhibits decreased rate of choline incorporation into phosphatidylcholine, indicating delayed lung maturation. We have also demonstrated that by measuring fluorescence of a surfactant-associated probe both the quantity (intensity) and fluidity (anisotropy) of surfactant produced by this explant system and secreted into the culture media can be assessed. The present study was designed to explore the effects of differing glucose levels on fluorescence intensity and anisotropy.

19.5 day fetal rat lung explants were grown for 48 hr in media containing 10, 50, or 100mM glucose. Tissue homogenates and culture media were purified on Sephacryl columns, a fluorescent probe added to the surfactant fraction, and fluorescence intensity and anisotropy measured.

ANISOTROPY AFTER 48 HR IN CULTURE			
	10mM Glu	50mM Glu	100mM Glu
TISSUE	.220±.006	.230±.015	.230±.007**
MEDIA	.196±.009	.203±.008*	.224±.004**

*p< .05 **p< .01 vs 10mM;paired T-test

Fluorescence intensity was significantly lower in tissue cultured in 100mM glucose (74 ± 6% relative to 10mM values; p <.005). Significantly higher anisotropy (lower fluidity) was found in tissue grown in 100mM glucose; higher anisotropy was also noted in high glucose media samples (100mM>50mM>10mM) (Table).

Thus, glucose inhibits maturation of surfactant as measured by fluorescence in vitro. These results suggest that the delayed fetal lung development in diabetic gestation may be characterized by defects in fluidity as well as quantity of surfactant produced.

†245 CHRONIC MATERNAL THIRD TRIMESTER HYPOXIA ON METHIONINE ENKEPHALIN LEVELS IN PRETERM RABBIT BRAINSTEM. J. Gingras, W. Long, Duke U. Med Ctr, Dept. of Peds, Durham NC, Burroughs Wellcome, RTP, NC (sponsored by JE Brazy)

Acute hypoxia alters the content of the neuropeptide methionine enkephalin (ME) within specific brainstem regions involved in respiratory control. This alteration is both age and region specific (Ped Res 20:655-657, 1986). Since ME is implicated in abnormalities of respiratory control, particularly in the newborn, we examined the effect of chronic hypoxia on ME levels within specific brainstem regions of prenatal animals. 6 pregnant animals were placed in environmental chambers at gestational day E-10. Between days E-14 and E-28, 3 pregnant animals breathed 21% O_2 (control) and 3 pregnant animals breathed 14% O_2. On E-28 (term = E30-31) the fetuses were delivered by hysterotomy and immediately sacrificed. The brains were removed and sectioned into the colliculi, pons and medulla, and ME measured by RIA. The results are reported as ng ME/mg protein ± SEM and are tabulated below:

	Control n=9	Hypoxia n=9	p Values C vs H
medulla	$.177^{.016}$	$.205^{.021}$	.09
pons	$.084^{.005}$	$.105^{.009}$	.028
colliculi	$.068^{.001}$	$.064^{.005}$	.94

These data show: 1) In both control and hypoxia exposed fetuses ME is greatest in the medulla, lesser in the pons and lowest in the colliculi and 2) ME is increased within the pons (a regulator of respiratory frequency) of prenatally hypoxia-exposed animals. This tendency (but not significance) is also seen in the medulla of hypoxia-exposed animals. These results offer additional support for a role of ME in abnormalities of respiratory control under basal conditions and a role in the increased susceptibility of the hypoxic preterm infant.

246 POSTNATAL EFFECTS OF INUTERO HYPOXIA ON THE CONCENTRATION OF METHIONINE ENKEPHALIN WITHIN RABBIT BRAINSTEM REGIONS. J. Gingras, W. Long, Duke U Med Ctr, Dept of Peds, Durham NC and Burroughs Wellcome, RTP, NC. (Spon. by JE Brazy)

The neuropeptide methionine-enkephalin (ME) is involved in respiratory control particularly in the newborn. Its basal concentration and alterations with acute hypoxia are both region and age specific (Brain Res, 336:73-80, 1985; Ped Res 20:655-57, 1986). Additionally, prenatal exposure to toxins produce long term sequelae. We examined the effect of inutero hypoxia on ME in postnatal animals aged 3,7,21 days. 12 pregnant rabbits were housed in environmental chambers at gestational age E-10. Between E-14-E-28, 6 animals breathed 21% O_2 (control, C) and 6 breathed 14% (hypoxia, H). The animals were kindled and young reared in RA until sacrifice. The brains were removed and sectioned into superior, inferior colliculi, pons and medulla. n=6/condition/age. * = p<.05.

	3 d.o.		7d.o		21d.o	
Brain Region	Control	Hypoxia	Control	Hypoxia	Control	Hypoxia
medulla	$5.84^{.68}$	$6.58^{.65}$	$5.36^{.75}$	$5.75^{.24}$	$8.91^{.83}$	$5.02^{.41}$*
pons	$4.10^{.36}$	$4.20^{.46}$	$4.70^{.39}$	$3.93^{.35}$	$6.12^{.13}$	$4.67^{.28}$*
inf. colliculi	$1.45^{.20}$	$1.34^{.33}$	$2.54^{.27}$	$2.78^{.49}$	$3.82^{.23}$	$4.96^{.79}$
sup. colliculi	$0.42^{.05}$	$0.39^{.20}$	$1.12^{.14}$	$1.56^{.34}$	$3.33^{.31}$	$1.94^{.19}$*

These data confirm that 1) ME is greatest in the medulla, pons > inferior colliculi, superior colliculi and 2) except within the inferior colliculi, prenatal hypoxia is associated with decreased ME levels within brainstem regions at postnatal day 21. This decrease may reflect a direct effect on ME neurons or alternatively reflect changes in transmitters that regulate ME. ME is inhibitory to respiration; thus, long term effects of hypoxia may accelerate control mechanisms.

247 PREDICTIVE VALUE OF UMBILICAL CORD PLASMA PROSTAGLANDINS E1, E2, AND 6-KETO F1α ON FUTURE PATENCY OF THE DUCTUS ARTERIOSUS. Harley G. Ginsberg and W. Michael DeVoe (Spon. by John Lewy). Tulane University School of Medicine, Dept. of Pediatrics, New Orleans, Louisiana.

The placenta is a well known source of many prostaglandins (PG) including E1, E2, and 6-Keto F1α. PGE1 has been used to maintain patency in the ductus arteriousus in infants with ductal dependent congenital cyanotic heart disease. Various plasma prostaglandin levels have been measured at birth in term as well as preterm infants but none of these reports discussed their relationship to any future development of a hemodynamically significant patent ductus arteriousus (PDA). We measured venous umbilical cord plasma PGE1, PGE2, and PG 6-Keto F1α levels by radioimmunoassay to determine if any of these might serve as predictors of future ductal patency. All three of these PG's have been implicated in maintaining or causing ductal patency. Levels were measured at birth in 36 infants weighing less than 1750 grams and having a gestational age of under 35 weeks. Thirteen infants (36%) were subsequently diagnosed by either two dimensional echocardiography or physical parameters (or both) as having a PDA. While there tended to be marked elevations in PG 6-Keto F1α levels in some infants prior to diagnosis, these as well as other PG levels were not found to statistically correlate with ductal patency (p=.05 for PGF1α). These findings do not support the hypothesis that umbilical cord PGE1, PGE2, or PG 6-Keto F1α levels may serve as predictors of future ductal patency. Instead, patency may be determined by primarily local or intracellular factors which may or may not be oxygen dependent.