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EFFECTS OF MATERNAL IRON STATUS ON THE SUBSEQUENT DEVELOPMENT OF IRON DEFICIENCY IN THE INFANT. A. Harold Lubin, Judith L. Bonner, Ruth O. Shrock, Albert L. Caffo, The Ohio State University College of Medicine, Children's Hospital, Columbus, OH.

5.5% of pregnant women (309) enrolled during the 2nd trimester in a longitudinal study determining effects of maternal nutrition and environmental factors on the infant's subsequent growth and development were iron deficient (<42mg%; %Sat <16%) despite receiving adequate prenatal care, including prophylactic iron. Women whose Fe status was deficient during the 3rd trimester were compared with women with adequate Fe status (serum Fe >140mg%; %Sat >30%).

Mothers	#	X Fe	P	X %Sat	P	X Hb	P	X Hct	P
Fe Def	17	34.4	.001	6.6	.001	11.4	.05	36.2	
Fe Suf	17	184		42.1		12.4		37.6	N.S.

At birth, infants' wts, APGAR scores, gestational ages, Hb and Hct were similar irrespective of their mother's Fe status. At 6 mos of age, 73% of infants of Fe def mothers were Fe def (%Sat <15%) compared to only 36% of infants of Fe suf mothers. Differences in race, parity, or feeding habits could not explain differences in serum Fe and %Sat between the 2 groups of infants.

Infants	#	X Fe	P	X %Sat	P	X Hb	P	X Hct	P
Fe Def	12	48.9	.05	13.2	.05	12.5	N.S.	36.6	
Fe Suf	12	65.0		18.3		12.7		37.5	N.S.

Despite data which indicates that maternal iron is transferred against a placental gradient, our data suggests that Fe deficiency during pregnancy is associated with an increased incidence of Fe deficiency during the 1st 6 mos of the infants' lives. Hb's and Hct's appear to be inadequate parameters to detect Fe deficiency in pregnancy or infancy.

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EXOGENOUS ARACHIDONIC ACID IS NOT CONVERTED TO PROSTAGLANDIN E₂ BY THE LAMB DUCTUS ARTERIOSUS.

Lynn Mahony, Ronald Clyman. Univ. CA, Cardiovasc. Res.

Inst. and Dept. Peds., and Mt Zion Med. Ctr., San Francisco. Prostaglandin (PG) E₂ regulates the patency of the ductus arteriosus (DA) in the fetus and preterm neonate. Numerous investigators have used exogenous arachidonic acid (aa), a precursor of PG synthesis, to study the biological effects of endogenous PG production. We have shown that 0.2 µg/ml aa relaxes isometrically-constricted rings of lamb DA in vitro. Since inhibitors of PGE₂ production block this relaxation, we postulated that the conversion of exogenous aa to PGE₂ causes the relaxation of the DA. To test this hypothesis, we incubated rings of DA from 8 fetal lambs in buffer containing 0.2 µg/ml aa: 47±25 pg immunoreactive PGE₂/mg wet weight/90 min incubation (±SEM, n=8) was measured. This is consistent with the above hypothesis. To see if the measured PGE₂ is formed from the exogenous aa added to the incubation media or from the endogenous aa pools within the tissue, we incubated another group of rings in buffer containing 14C-labeled aa. We measured the conversion of 14C-aa to PGE₂ and tissue phospholipids by radiochromatographic analysis. Only 0.048±0.019 pg radiolabeled PGE₂/mg wet weight/90 min incubation (±SEM, n=9) was measured. Thus, only 0.1% of the PGE₂ produced when aa is added to rings of DA is formed from the added aa. Although PGE₂ mediates the relaxation caused by exogenous aa, the exogenous aa is not converted to PGE₂. Rather, exogenous aa appears to be a potent stimulator of phospholipid breakdown in the DA; the subsequent endogenous aa released is the actual source of the PGE₂ produced.

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IMPAIRED FETAL GROWTH FROM AMINO ACID IMBALANCE. Jack Metcalf, Timothy Cole & Richard Luff.

University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma and Dunn Nutrition Laboratories, Cambridge, England.

Whether fetal growth retardation (FGR) could be induced by diets imbalanced relative to a single amino acid, was investigated. Pregnant rats were fed either a 6% casein "basal" (B) diet supplemented by L-MET & a 5% mixture of essential, plus 4.5% small neutral dispensable amino acids, (4 kcals & 0.16g protein-equivalent/g diet, complete in essential nutrients), an "experimental" (E) diet (same, except 0.4% L-THR supplement omitted) or a "control" (C) diet, like B, but containing 20% casein. 343 fetuses with placentas were delivered by Caesarian section usually on day 21 but occasionally on day 20 or 22. Food consumption was similar in all groups (kcal/100g rat/d); protein intake of the B & E rats was about half that of the C group. Net maternal weight gain (excluding conceptus) was +8% in C, 0% in B & -12% in E group dams. Body weight, length, volume, brain & placental weights, adjusted by multivariate analysis to control for maternal prepregnant weight, length, litter size, net weight gain & days of gestation, were significantly reduced in 156 B vs 32 C & in 155 E vs B fetuses. Net maternal weight loss did not prevent FGR. Of the total variance in birth measures, protein restriction accounted for 30-59% in the B vs C group fetuses; & the THR amino acid imbalance for 36% between the E & B groups. Thus, diets with excess dispensable amino acids during pregnancy induce FGR, especially when THR is limiting.

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A ROLE FOR PROLACTIN, CORTISOL AND INSULIN IN PHOSPHATIDYLGLYCEROL SYNTHESIS BY HUMAN FETAL LUNG.

Carole R. Mendelson, John M. Johnston, and Jeanne M. Snyder (Spon. by Charles R. Rosenfeld), Univ of Texas, Southwestern Medical School, Depts Biochem, Ob-Gyn and Cell Biol, The Cecil H. and Ida Green Ctr for Reprod Biol Sci, Dallas, TX.

Late in human gestation, the fetal lung synthesizes increased amounts of phosphatidylcholine (PC) followed in time, by an increase in phosphatidylglycerol (PG) synthesis with concomitant decrease in phosphatidylinositol (PI) synthesis. We reported previously that prolactin (P), cortisol (F) and insulin (I), in combination, stimulate PC synthesis and surfactant secretion by mid-trimester human fetal lung explants cultured in serum-free medium. Therefore, we examined the effect of these hormones on the relative amounts of PG and PI in surfactant. Lung tissue explants from 20-24 wk human abortuses were maintained for 7 d in medium without hormones (control) or with P (2.5 µg/ml), F (0.2 µg/ml) and I (2.5 µg/ml) added alone or in various combinations. During the last 24 h of culture [¹⁴C]glycerol (1 µCi/ml) was added to the medium. A lamellar body (LB) fraction was isolated and the percent incorporation of [¹⁴C] into LB glycerolipids was measured using two-dimensional TLC. The incorporation of [¹⁴C] into PC was 74% in all groups. In control explants [¹⁴C] incorporation into PG was 3.9% and into PI was 7.1% (PG/PI = 0.7). P+F+I and F+I increased significantly [¹⁴C] incorporation into PG (11.9% and 10.9%, respectively) and decreased [¹⁴C] incorporation into PI (3.5% and 4.1%, respectively). These treatments increased the PG/PI ratio (F+P+I = 3.5; F+I = 2.7). F and F+P also increased PG/PI (2.2 and 2.0, respectively). These results are suggestive that PG and PI synthesis in human fetal lung are under multi-hormonal control.

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THE EFFECT OF EXOGENOUS INSULIN ON OVINE FETAL GROWTH.

J. Ross Milley, Michael S. Kappy, Leslie P. Plotnick, Anthony F. Philipps, Richard A. Molteni, M. Douglas Jones, Jr., and Michael A. Simmons. The Johns Hopkins University School of Medicine, Department of Pediatrics, Baltimore, Maryland.

Macrosomia in association with a hyperinsulinemic intrauterine environment is found in the fetus of the diabetic mother. We have studied the ovine fetus to demonstrate directly that exogenous insulin administration accelerates fetal growth. Seven mixed breed ewes with radiologically confirmed, nondiscordant twin fetuses were used. Insulin was infused at 90±50 µu/kg/day to one randomly selected fetus while the other twin was infused with saline as control. Infusion was continued for 14.9±1.5 days during which there were no differences in serum glucose, PO₂, PCO₂, pH or hematocrit between infused and control fetuses. Studies of insulin binding to erythrocyte receptors revealed no differences in maximum percentage binding, mean empty site binding affinity, receptor concentration or the concentration of insulin which inhibited (¹²⁵I) iodinsulin by 50%. Following infusion, analysis of fetal growth demonstrated no differences in weight, length or organ weights between control and experimental animals. No effects of insulin infusion were found on tissue water, protein, RNA, DNA or glycogen. We have demonstrated that small amounts of exogenous insulin do not alter the normal pattern or rate of ovine intrauterine growth over a 15 day infusion period. It is possible that insulin at physiologic concentrations has little role in the regulation of fetal growth.

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β-ADRENERGIC RECEPTOR IN MAMMALIAN PLACENTA: COMPARISON OF RAT, GUINEA PIG, RABBIT, HUMAN AND TROPHOBLASTIC TUMORS.

John Moore*, Jeffrey A. Whitsett U. of Cincinnati Coll. of Med., Dept. Peds.

β-Adrenergic receptor (βAR) has been previously demonstrated in human placental membranes. Its demonstration in placentas of multiple species and trophoblastic tumors might support its regulatory function on the trophoblastic cell itself. βAR in rat, guinea pig, rabbit and human placenta and trophoblastic tumors were therefore examined. Term placentas were obtained, dissected to remove decidua and processed in identical fashion. The β-adrenergic antagonist dihydroalprenolol, (-)-[³H]DHA bound to a single, saturable class of sites in all placental membranes. Placental βAR was coupled with catecholamine sensitive adenylate cyclase in all species.

	n	Bmax (fmol/mg)	K _D (nM)	CATECHO-SENSITIVE CYCLASE fold-stim	p
Rat	6	70±6.7	1.32±.05	1.87	<.05
G.P.	6	104±2.5	1.60±.07	1.31	<.01
Rabbit	5	315±28.2	1.28±.10	1.51	<.01
Human	9	112±9.1	2.23±.23	2.44	<.01

βAR was absent in two human chorioncarcinoma cell lines (JEG-3, BeWo) but was present in a hydatidiform mole obtained freshly from surgery (91 fmol/mg, K_D=1.31 nM). We conclude that 1) variable but consistently high density βAR is present coupled to adenylate cyclase in mammalian placenta; 2) the affinity (K_D) of the βAR is similar in all species; and 3) the presence of high density βAR on a hydatidiform mole containing almost totally trophoblast tissue suggests a βAR is located on trophoblastic cell membranes.