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CYCLIC AMP AND cGMP: URINARY EXCRETION FROM BIRTH TO ADULTHOOD. Mary Newport and George Hug. Dept. of Pediatrics, University of Cincinnati, Cincinnati, OH 45229 USA.

1427 random urine specimens of 135 patients (age: newborn (NB) to 22 years) were analyzed for cAMP, cGMP, creatinine. Results in nanomoles/mg creatinine were on (*) single urine samples (-highest/lowest-values); others as mean values; and, for AGE; time of day -DAY:

		AGE		high-DAY-low		high-single-low	
Time	NB	7y	15y	0300h	1700h	urine	
cAMP	15.2	6.6	3.8	13.6	5.8	135.3*	0.0*
cGMP	3.3	2.0	1.0	4.3	1.6	23.4*	0.02*

By age 15y adult nucleotide concentration is attained at approx. 25% of newborn values. Statistical correlation between cAMP and cGMP for age was r = 0.96; for time of day r = 0.69; and none for sex. Extreme values occurred in complex disease states. cAMP high: intractable diarrhea; low: progressive CNS disease. cGMP high: multiple sulfatase deficiency; low: Reye's syndrome. Extremes may reflect pathophysiologic mechanisms in these conditions. Mean "normal" values served to assess nucleotide response (or lack of it) to glucagon or PTH in diseases such as glycogenoses or pseudohypoparathyroidism.

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EFFECT OF NUTRITION ON DEVELOPMENTAL CHANGES OF CARNITINE AND ACETYLCARNITINE PLASMA LEVELS IN NEWBORN INFANTS. Milan Novak, Paul B. Wieser, Maria Buch, Ellen Monkus, Univ. of Miami School of Medicine, Dept. of Ped., Miami, Fl., Peter Hahn, Univ. of British Columbia, Centre for Developmental Medicine, Vancouver.

In umbilical cord and maternal blood plasma free carnitine is significantly lower than in plasma of non-pregnant women. Acetylcarnitine but not free carnitine was elevated in cord blood from premature in comparison with full-term infants. In the first hours after birth plasma acetylcarnitine increases significantly but free carnitine remains unchanged. However, in infants receiving carnitine free diets (soy protein based formula) the levels of both free and acetylcarnitine are significantly lower than in infants receiving human breast milk or cow's milk based formulas which contain 50-200 nmol/ml carnitine. There was no correlation between the dietary intake of the amino acid precursors of carnitine, methionine and leucine, and carnitine blood levels. Soy formulas contain more methionine and leucine than cow's milk formulas and human breast milk; hence decreased carnitine in infants fed soy formula is not due to decreased synthesis because of a lack of precursor amino acids.

Carnitine functions to facilitate transport of fatty acids across the inner mitochondrial membrane. During the neonatal period the oxidation of fatty acids to produce energy is of great importance and less than optimal carnitine intake may have a detrimental effect on growth and development.

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THE DYNAMICS OF VASOPRESSIN RESPONSE TO BLOOD VOLUME DEPLETION IN THE LAMB FETUS. Jean E. Robillard, Richard E. Weitzman and Fred G. Smith, Jr., Dept of Peds, Univ of Iowa, Iowa City, Iowa, and Dept of Med, UCLA/Harbor General Hospital, Torrance, California.

Plasma arginine vasopressin (pAVP) release was measured before and during fetal hemorrhage (H) and 3 hours after fetal blood replacement (T) in 11 chronic fetal lamb preparations (103-138 days gestation). During H there were significant decreases ($p<0.05$) in fetal hematocrit (34.7±2.5 to 27±1.5%), arterial blood pressure (BP)(58.1±2.5 to 52.2±2.5 mmHg) and fetal pH (7.38±0.01 to 7.35±0.01), but no changes were seen in arterial blood gases (PCO_2 - PO_2), plasma electrolytes (Na^+, K^+, Cl^-) nor osmolality. After T all values returned to baseline levels. Fetal pAVP was measured at various levels of H until ≈30% of the total feto-placental blood volume (T-FPV) was removed. Fetal pAVP increased significantly ($p<0.01$) in all fetuses from mean basal values of 0.73±0.21 to mean peak values of 34.9±10.04 μU/ml. pAVP was returned to baseline values (1.77±0.67 μU/ml) 3 hours after T. No change in maternal pAVP was seen during H. When fetal pAVP was plotted against the percent of T-FPV removed, the correlation coefficient was 0.65; however, when the log of fetal pAVP was plotted against the percent of T-FPV removed, a correlation coefficient of 0.82 was observed. A multiple regression analysis showed that the decrease in fetal BP was not the primary factor explaining the increase in pAVP during T-FPV depletion. These data show that H is a potent stimulus for fetal pAVP release and suggest that this release is an exponential function of the degree to which T-FPV is depleted.

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DEHYDROISOANDROSTERONE (D) AND OVINE FETAL ESTROGEN PRODUCTION. Charles R. Rosenfeld, Richard J. Worley, Leon Milewich, Norman F. Gant,Jr., C. Richard Parker, Jr. Univ.Tex.Health Sci.Ctr.,Depts.of Ped.and Ob-Gyn,Dallas,Tex.

Factors controlling uteroplacental blood flow are vaguely understood,but estrogen appears of importance. Systemic infusions of D into pregnant ewes result in increases in maternal estrone(E1), estradiol(E2),and uterine blood flow. Although D is a substrate for ovine estrogen production during pregnancy,the conversion site and fetal role are unknown. To investigate this 10 pregnant ewes, 124-150 days of gestation,were prepared with catheters in fetal umbilical vein(γ),femoral artery(α),and vena cava(fv),and maternal uterine vein(v),femoral artery(A),and vena cava(V),permitting simultaneous arteriovenous(a-v) sampling from fetal and maternal placental circulations. Uterine artery flow probes were placed in 4 ewes. After the 4th postop day simultaneous samples taken from A,v,α and γ prior to and 7.5,15,30,60,90,120,150 and 180 min. after the infusion of 6mg D into fv. Uterine blood flow rose 22 ± 9%*(Mean ± SE) at 110 min. At 7.5 min. ΔE1(pg/ml)was:A=281*,v=653*,α=621*,γ=715*;ΔE2(pg/ml):A=51.6*,v=89.8*,α=307*,γ=295*;and Δdehydroisoandrosterone sulfate(DS,ng/ml):A=66.9*,v=125*,α=1040*,γ=730*. In 3 fetuses D was measured in α and γ at 0 and 15 min.; Δng/ml=73.6 and 4.94,respectively. All values returned toward control levels after 180 min. The results of these studies are consistent with conversion of exogenous D by the fetal-placental unit to DS,E1 and E2. Although estrogen levels seen at the onset of parturition were achieved,parturition was not induced by D. Moreover,fetal-placental aromatase activity does not appear to be rate limiting in ovine estrogen production. *$p < 0.05$

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DEVELOPMENTAL ASPECTS OF MALEIC ACID INDUCED INHIBITION OF SUGAR AND AMINO ACID TRANSPORT IN THE RAT RENAL TUBULE. K.S.Roth, D.R.Goldmann and S.Segal, Univ.of Pa.Sch.Med.,Children's Hosp. of Phila., Phila.,Pa.

The transport of alpha-aminoisobutyric acid and alpha-methyl-D-glucoside by isolated renal tubules from Sprague-Dawley rats at different stages of development follows a separate age-dependent pattern for each substrate. The effects of 6 mM maleic acid on transport processes differ for amino acids and sugars and become manifest at distinct points during development. Maximum inhibition by maleic acid occurs at a time subsequent to complete maturation of these transport systems. In an effort to explain these transport phenomena, the uptake and metabolism of ^{14}C-labelled maleic acid by the newborn and adult renal tubule was studied, showing significant binding by the tubule membrane, penetration of the cell by diffusion, and no conversion to $^{14}CO_2$. Maleic acid has no demonstrable effect on the membrane-associated enzymes which are thought to play a role in the transport of small molecules.

Though the mechanisms by which maleic acid inhibits the transport of sugars and amino acids in the adult rat tubule remains unexplained, it is clear that its effects are age-related and independent of the maturation of these transport systems. This observation is consistent with the delayed appearance of the Fanconi syndrome seen in human cystinosis and suggests that the progressive tubular dysfunction in this syndrome and in the maleic acid model is secondary to genetically directed intracellular metabolic changes expressed during development.

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PLACENTAL BLOOD FLOW AND TRANSFER OF NUTRIENTS IN SPONTANEOUS FETAL GROWTH RETARDATION IN THE GUINEA PIG. J. Saintonge and P. Rosso, Dept. Pediat. Inst. Human Nutr., Columbia Univ.,N.Y.

Reduced availability of nutrients due to reduced placental blood flow or placental insufficiency is considered the most likely cause of intrauterine growth retardation(IUGR). These two variables, however, have not been measured during spontaneous IUGR. Since the guinea pig has a high incidence of spontaneous IUGR, it was, therefore, selected as a suitable model to explore the mechanisms of IUGR. Simultaneous measurements of maternal placental blood flow, using microspheres, and placental transfer of 14C-α-amino isobutyric acid(AIB) and 3H-3-0-methyl glucose(MG) were made between 32 and 59 days of normal gestation. Small (S) and large(L) littermates were compared to mean litter values. Results are as follows:fetal weight:S-18%,L+12%; placental weight:S-16%,L+14%; blood flow: S-35%,L+27%; total AIB transfer:S-34%,L+29%; total MG transfer:S-18%,L+13%;AIB transfer/g placenta:S-20%, L+16%; AIB transfer/g placenta/ml blood flow(placental efficiency):S+17%,L-13%. Thus in the guinea pig fetal growth is correlated with placental blood flow. IUGR fetuses have a reduced blood flow without a concomitant reduction in the efficiency of the placenta to transfer nutrients.(Supported in part by USPHS, NIH Grant KO4 HD 00116-01 & by the R.S. McLaughlin Found.)