241 VASOPRESSIN RELEASE IN THE LAMB FETUS. Fred G. Smith, Richard Weitzman, Jean Robillard, Allen Erenberg, and Delbert Fisher, Univ. of Iowa, Iowa City and UCLA-Harbor General Hospital, Torrance, Calif., Depts of Pediatrics

Arginine vasopressin (AVP) release was studied in 16 chronic fetal preparations between 101 and 141 days gestation following the infusion of 5% NaCl. The mean baseline plasma AVP in fetuses from 101-120 (N=20) days was 1.90 ± 0.46 μU/ml with a plasma osmolality of 292.9 ± 1.75 mOsm/kg. In fetuses 121 days to 141 days gestation, the mean baseline plasma AVP (N=11) was significantly lower 0.77 ± 0.19 μU/ml (P= <0.05) whereas the plasma osmolality was similar to that in the younger fetuses (292.7 ± 1.9 mOsm/kg). The paired maternal baseline AVP concentrations at 101 and 120 days gestation were significantly lower (0.843 ± 0.17 μU/ml) than the mean fetal levels (1.59 ± 0.44 μU/ml) however fetal and maternal levels between 121-141 days were similar; 0.68 ± 0.27 μU/ml and 0.70 ± 0.22 μU/ml respectively. A linear regression of the logarithm of baseline plasma AVP and plasma osmolality in 30 fetuses showed a significant correlation (P= <0.001, r=0.62). Plasma AVP was elevated after 5% NaCl infusion in 16 of 19 experiments. Studies of the relationship between steady state plasma AVP and plasma osmolality in adult sheep show a slightly flatter slope (adult 0.0282, fetal 0.0395). This observation suggests that the fetal osmoreceptors are more responsive to changes in tonicity than the adult sheep. Furthermore, the response to 5% NaCl as measured by the difference in the log plasma AVP divided by the difference in plasma osmolality was greater in the fetus.

242 THE NATURE AND SIGNIFICANCE OF AMNIOTIC FLUID (AF) GLUCAGON. Mark A. Sperling, Ronald A. Christensen, Raul Artal, Paul Mies. UCLA - Harbor General Hospital, Department of Pediatrics and Obstetrics, Torrance, Calif.

We have identified immunoreactive glucagon (IRG) measured by "specific" radioimmunoassay, in AF collected during the first 10-20 W for genetic screening or third trimester (30-40 W) for assessment of lung maturity. AF-IRG in the third trimester 117 ± 38 pg/ml (mean ± SEM) was significantly greater than in the first 10-20 W; 43 ± 10 pg/ml ($p < 0.05$). However no correlation was discerned between third trimester AF-IRG and type of pregnancy or course of neonatal glucose homeostasis in normal, premature, or infants of diabetic mothers (IDM), although spontaneous glucagon secretion following birth is obtunded in IDM. To investigate the nature of AF-IRG, selected samples were chromotographed on Biogel P10 columns calibrated with blue dextran, ^{125}I-insulin, ^{125}I-glucagon and ^{125}I, and IRG determined in all eluate fractions. Large peaks of IRG eluted with the void volume (MW > 20000) or in the region ahead of insulin corresponding to a MW of approximately 9000. A 3-fold concentration of AF was required to demonstrate a small IRG peak corresponding to its appropriate marker (3500 MW). Addition of crystalline glucagon to AF resulted in an elution profile corresponding to its appropriate 3500 MW position. Conclusion: Amniotic fluid IRG appears to reflect increasing gestational maturation, but fails to predict neonatal glucose homeostasis. This failure may be related to the nature of amniotic fluid IRG; "pro" or "big" glucagon rather than biologically active 3500 MW material.

243 CHARACTERISTICS OF VASOPRESSIN (AVP) RELEASE DURING ADRENOCORTICOTROPHIN (ACTH) INDUCED PARTURITION IN THE LAMB. Raymond Stark, Kazim Hussain, Salha Daniel, Jacques Milliez, Hisayo Morishima, L. Stanley James, Div. of Perinatal Med., Coll. of P & S., Columbia Univ., N. Y.

During premature parturition induced by ACTH there is a rise in fetal AVP only after the onset of labor. Fetal AVP levels which peak at delivery are not related to maternal levels which rise only during pushing. To investigate the characteristics of AVP release as measured by radioimmunoassay, 9 fetal lambs were instrumented at 121 days gestation. At 129 days, 7 fetuses were infused at 1.5 ml/hr with ACTH (10 mg/kg/hr) and 2 with saline. Delivery occurred after a mean of 74 hours of ACTH infusion.

During infusion fetal pH (7.36 ± .002 S.E.) and pCO_2 (42 ± 2 mmHg) remained constant while PO_2 decreased (22 ± 2 to 18 ± 2 mmHg, r = .96). Serum electrolytes and osmolarity remained stable through infusion and early labor (Cl 109.5 ± 1.5 meq/L, Na 145 ± 1.3 meq/L, K 4.0 ± .45 meq/L and osmolarity 289 ± 3.2 mOsm/L). Fetal AVP rose from prelabor mean values of 1.8 ± 1.8 pg/ml to 40 ± 73 pg/ml in active labor, 173 ± 404 pg/ml in the pushing phase and 720 ± 1470 pg/ml at delivery, then decreased 30 minutes after delivery to 360 ± 340 pg/ml. During labor serial fetal arterial AVP levels were compatible with pulsatile release unrelated to uterine contractions. In ACTH induced parturition the AVP rise is not related to the initiation of labor or changes in serum osmolarity but may be related to changes in fetal oxygenation. We speculate that the high levels of AVP may be instrumental in fetal cardiovascular adjustments to the stress of labor.

244 PSYCHOLOGICAL DEVELOPMENT OF CHILDREN WITH X AND Y CHROMOSOME ANEUPLOIDY. D.A.Stewart, J.D. Bailey, and C. Netley, Dept. of Ped., Univ. of Toronto, The Hospital for Sick Children, Toronto, Ontario

Thirty-three children identified at birth as having aneuploidy of sex chromosomes were assessed with one to four annual examinations between four and eight years of age for general intelligence, verbal skills, perceptual functioning, motor ability, and educational attainment. Interviews, rating scales and symptomatic check lists provided information on temperamental characteristics of the children and also of parental attitudes. The psychological assessments were done "blind" and in the case of the rated variables, the use of two judges provided a basis for determining reliability of the raters. Findings follow in this table (all units are standard scores):

MEAN SCORES FOR SEPARATE PSYCHOLOGICAL VARIABLES

Karyotype	n.	Verbal	Perceptual	Quantitative	Memory	Motor
47 XXY	20	86.4	96.9	84.6	86.8	86.7
47 XYY	4	81.0	97.2	85.5	83.8	84.5
47 XXX	9	79.0	90.2	86.0	81.3	84.4

Inter-test variabilities are high implying that a single estimate of "general intelligence" is misleading. Perceptual skills generally fall within average limits while verbal ability is low. Deficits are most pronounced in 47 XXX children. Temperamental difficulties or overt behaviour problems have been encountered in all groups. The groups, thus far, do not differ in the incidence of behaviour problems nor do particular constellations of behavioural traits characterize any karyotype.

245 HUMAN AMNIOTIC MEMBRANE: A SOURCE OF ACTIVE FETAL GLUCOCORTICOIDS? A. Keith Tanswell, D. Worthington, Barry T. Smith (Spon. by H.W. Taeusch) Queen's Univ.,Dept.Paediatrics,Kingston,Ont.

We have recently shown that in both sheep and human pregnancies the ratio of the active glucocorticoid, cortisol (F), to its inactive 11-oxidized form, cortisone (E), in amniotic fluid increases with gestational age and is closely linked to lung maturation.

Samples (100 mg) of human amniotic membrane were obtained within 3 hours of delivery and incubated in the presence of equimolar amounts of ^{3}H-F and ^{14}C-E. F and E were isolated and their content of ^{14}C and ^{3}H allowed the calculation of %F→E and %E→F conversion. %F→E (inactivation) was arbitrarily given a negative value and the two results arithmetically summed to give the "C-11 activation index", a measure of the net gain (or loss) of glucocorticoid activity. We found that this index increases with gestational age (n=28, slope=0.671, r=0.674, p<.001), becoming positive at 30 weeks, and reaching values of 40-50% by term.

Since glucocorticoid introduced into the amniotic fluid reaches the fetal circulation, the amniotic membrane activity is a potential source of active glucocorticoid for the fetus. Further studies will be necessary to determine if the observed activity is related to lung maturity.

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246 INCREASES IN BRAIN GLUCOSE AND PLASMA GLUCOSE, GLYCEROL AND β-HYDROXYBUTYRATE AFTER AMINOPHYLLINE. Jean Holowach Thurston, Richard E. Hauhart, and John A. Dirgo. Dept. Pediat., Wash. U. Med. School, St. Louis.

Effects of aminophylline (100 mg/kg i.p.) on brain carbohydrate and energy metabolism were studied in 2 litters of normal 17-23-day-old mice (11 animals). Although no clinical effects were seen, 20 min after aminophylline plasma glucose increased 22% (11.79 ± 0.15 vs 8.90 ± 0.80 mM in controls, p = 0.025); plasma β-hydroxybutyrate was 242% of control (443 ± 75 μM vs 183 ± 28, p = 0.031) and plasma glycerol, 258% of control (570 ± 48 μM vs 221 ± 17, p <0.001). Since the methyl xanthines increase tissue cyclic AMP levels and/or catecholamine and glucagon release, these findings may reflect this action (increased hepatic glucose output and lipolysis).

Brain cyclic AMP increased 56%, p = 0.014. Brain glucose increased dramatically, 1.47 ± 0.12 vs 0.76 ± 0.08 mmol/kg in controls, p = 0.001. Brain ATP, P-creatine, glycogen and lactate levels were unchanged. In the face of an apparently normal cerebral metabolic rate, the increased brain to plasma glucose concentration ratio, 0.13 ± 0.01 vs 0.09 ± 0.01 in controls, p = 0.048, suggests increased brain glucose transport.

β-hydroxybutyrate is a major metabolic fuel of the brains of young animals and glycerol is an effective substrate for hepatic gluconeogenesis; furthermore, in anoxic brain, glucose is the only source of ATP. In view of these facts, the findings presented in this report may explain the mechanisms(s) of the beneficial action of methyl xanthines in apnea of prematurity.