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GLUCOSE ENTRY INTO THE FETAL HEPATOCYTE (FH) REQUIRES NON-INSULIN DEPENDENT GLUT-1 AND GLUT-2. Q. Zheng, L. Levitsky, D. Rhoads, K. Mink, Pediat. Endo. Unit, Children's Service, and Lab. Tumor Biology, G.I. Unit and Cancer Ctr., Mass. Gen. Hosp., Harvard Med. School

Low Km glucose transporter GLUT-1 mRNA and protein is found in vivo in adult hepatocytes (AH) only with starvation and diabetes. In contrast to AH, hepatic glycogenesis during fetal life is dependent upon glucose entry into hepatocytes at low glucose concentration. We have quantitated low Km GLUT-1 mRNA as well as high Km GLUT-2 mRNA in cultured rat FH compared to male AH, as % of FH at isolation.

| GLUT-1 | Time 0 | 2h | 16h | 45h | |
|---|---|---|---|---|---|
| FH | 100*** | 287±63** | 698±120* | 479±77 | *p<.05 |
| AH | 0 | 116±48 | 379±46 | 341±80 | **p<.01 |
| GLUT-2 | | | | | ***p<.001 |
| FH | 100*** | 183±40* | 101±42*** | 355±96* | FH vs. AH |
| AH | 473±149 | 503±158 | 571±97 | 815±183 | |

GLUT-1 protein (immunoblot) is not present in AH at isolation, but is weakly present at 16 and 45h of culture. GLUT-1 protein is present in large amount in FH at isolation, 16 and 45h. However, 3-*O*-methyl glucose transport activity (1 - 30 mM) in AH and FH at 45h demonstrates the presence of two transporters (Eadie-Hofstee plot, standard enzyme kinetic assumptions). One has a Km of 23 mM, and is presumed to be GLUT-2. The second has a variable Km approximating 6-8 mM presumably related to accelerated exchange phenomena typical of GLUT-1. The Vmax at 45h culture (nM/min·mg$^{-1}$protein) for GLUT-2 was 198 in FH and 92 in AH and for GLUT-1 was 105 in FH and 35 in AH. Therefore, activity of both GLUT-2 and GLUT-1 is greater in FH compared to AH, facilitating glucose transport at low ambient glucose levels of fetal life.

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PREGNANCY LACTOGENS IN THE RAT CONCEPTUS: CIRCULATING LEVELS, DISTRIBUTION OF BINDING, AND EXPRESSION OF RECEPTOR mRNA. M. Freemark, K. Kirk, K. Pihoker, P. Driscoll, M. Robertson. Departments of Pediatrics and Cell Biology, Duke University Medical Center, Durham, NC 27710, USA

The roles of the pregnancy lactogens in the growth and development of the fetal rat are poorly understood. We measured the concentrations of placental lactogen II (rPL-II) in fetal rat serum and examined the distribution and mRNA expression of lactogenic receptors in embryonic and fetal tissues. The concentration of rPL-II in fetal serum (day 20 gestation) was 28.3±0.8ng/ml (n=6), ≈ 1/10th that in maternal serum (398.3±45.3 ng/ml). At physiological concentrations, rPL-II bound specifically to the fetal adrenal, kidney, intestine, liver and pancreas. rPL-1, expressed on days 10-12, bound to chorion and mesometrial decidua. The binding of rPL-I & II were blocked by rat prolactin (PRL) but not by rat GH, suggesting a common PL/PRL receptor. Fetal tissues expressed four PRL receptor mRNA transcripts (12, 6.6, 4.2, 1.8 kb). The relative intensities with which fetal tissues bound rPL correlated with levels of the 4.2 and 1.8 kb transcripts. The observation that rPL-1 binds to chorion and decidua suggests a paracrine role for rPL-1 in the regulation of maternal decidual function. The demonstration that rPL-II circulates in fetal blood and binds to lactogenic receptors in fetal tissues implicates a role for the pregnancy lactogens in fetal development.

# 406

STEROID INDUCED SUPPRESSION OF BONE GROWTH IN THE PREMATURE NEONATE - SILVERMAN REVISITED

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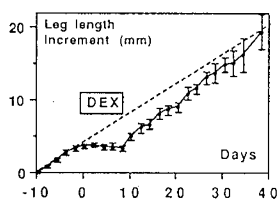
In 1951 Silverman reported significant growth disturbance in premature infants who received ACTH for the treatment of retinopathy. Despite the dramatic response that was demonstrated the effects of steroids on growth in this age group remain poorly understood. We have used the neonatal knemometer to assess bone growth in 26 babies who received a total of 32 nine day courses of dexamethasone for the treatment of chronic lung disease. Growth of the lower leg and weight gain were assessed for 10 days before, during and 30 days after the course. There was a decrease in leg length velocity in all subjects during steroid administration and actual limb shrinkage occurred in 15. There was then catch-up growth to the estimated pre-steroid length by 30 days. Oxygen requirements fell and calorific intake rose during steroid treatment. Dexamethasone has a profound effect on cartilage and bone growth even in the preterm neonate. The long term consequences of this effect are no clearer today than they were for Silverman more than 40 years ago.




Silverman WA, Day RL, Blodi FC. Pediatrics 1951;8:177-191

# 407

ANTHROPOMETRY OF VLBW SURVIVORS AT 8-10 YEARS OF AGE

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Detailed anthropometric assessment was made of 124 VLBW [<1500g] survivors, and age, sex and social class matched controls, at 8-10 years of age. The controls were taller, with longer legs (mean HtSDS +0.37; mean LLSDS +0.65) than the current T&W standards and the VLBW group (mean HtSDS -0.2; mean LLSDS +0.05). The VLBW group also showed significantly reduced weight & lean body mass [p=0.0001], reduced head circumference [p=0.002] and increased cephalic index [p=0.0001]. The LL of the VLBW group was the measurement most likely to be abnormal, [relative risk compared to controls = 2.96]. There were also significant anthropometric differences within the VLBW cohort with ex-small for gestational age (SGA) infants being shorter [p=0.03], lighter [p=<0.01] and having reduced sitting heights [p=0.008] and smaller heads [p=0.0001] than ex-appropriate for gestational age (AGA) infants. TWII bone age was calculated for the VLBW children only and the bone age-chronological age gap was not significantly different to zero & there was no significant difference between the SGA and AGA groups.
The pattern of height and proportion in the VLBW group is similar, but less severe, to that exhibited by abused children and identical to children of the late 1950's.

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ANTI-MULLERIAN HORMONE IN EARLY HUMAN DEVELOPMENT Nathalie Josso, Isabelle Lamarre and JY Picard, INSERM 293, Ecole Normale Supérieure, Montrouge, France

Anti-Müllerian hormone (AMH), also called Müllerian-inhibiting substance or factor, is a dimeric glycoprotein, produced by immature Sertoli cells, and responsible for Müllerian regression in male fetuses. To study the ontogeny of AMH production in the male fetuses, we have measured, using an ELISA with antibodies raised against human recombinant AMH, the AMH concentration in 21 samples of amniotic fluid and 44 samples of fetal serum, initially collected for cytogenetical analysis in fetuses with sonographic abnormalities. No AMH was detectable in amniotic fluid, whatever the fetal sex. Mean ± SEM AMH concentration was 40.5 ± 3.9 ng/ml in the serum of male fetuses from 19 to 30 weeks, and 28.4 ± 6.1 ng/ml in older ones. The AMH concentration in the serum of an male XX fetus, aged 24 weeks, 48.3 ng/ml, was the only biological indicator of fetal sex. No AMH was detectable in female serum at any time, allowing easy discrimination between male and female samples, even during the perinatal period, when mean serum AMH concentration is decreased, compared to that of infants aged 2 months to 2 years (43.1 ± 3.7? P>0.05). AMH production in early fetal life was studied by *in situ* hybridization, using AMH-specific sense and antisense riboprobes. AMH transcripts were detected in the Sertoli cells of fetuses aged 8 weeks or older, but not in ovarian tissue. Negative results were also found in the sexually undifferentiated gonadal tissue of one 7-week-old fetus, with detectable DNA SRY-specific sequences, confirming that AMH expression in the testis begins only after seminiferous tubule differentiation.

# 409

ADRENAL FUNCTION IN PRETERM INFANTS. P.C.Midgley, P.Holownia, K.Russell, N.Oates, J.C.L.Shaw, J.W.Honour, Neonatal Unit & Department of Chemical Pathology, University College & Middlesex Hospital, London.

This study set out to observe changes in adrenal function in infants born prematurely. 22 infants of mean gestation 27.9 weeks and birth wt. 946 g were studied longitudinally between 170-360 days postconceptional age (PCA), by measurements of plasma cortisol (F), cortisone (E), DHEAS, urinary steroid metabolites, and adrenal ultrasound scans (USS). Mean plasma levels of cortisol (283 nmol $l^{-1}$) and cortisone (1353 nmol $l^{-1}$) at 180-199 days PCA were ten times those reported in the fetus. The low fetal F:E ratio persisted after preterm birth (<1), and even past term (280 days). Mean plasma levels of DHEAS were also similar to fetal values, but fell from 12.3 µmol $l^{-1}$ at 176 days to <1.0 µmol $l^{-1}$ at 350 days PCA, being barely detectable after term. Adrenal fetal zone steroids represented 97% of the metabolites in the urine and their excretion remained high (>1200 µg $kg^{-1}$. d) until term, declining between 280-300 days. Although cortisone metabolites were seen throughout, cortisol metabolites did not appear until after term. The length of the adrenal gland on USS remained constant. These data suggest maturation in adrenal gland function occurs at term rather than after birth. Changes in adrenal function did not correlate with adrenal length.