211 DEVELOPMENT OF THE DIURNAL RHYTHM OF JEJUNAL SUCRASE ACTIVITY IN THE WEANLING RAT. Susan J. Henning and Harold E. Beam (Spon. Hope H. Punnett) Temple University, Department of Biology, Philadelphia, Pa. 19122.

In the adult rat, fed ad lib, the activity of jejunal sucrase shows a diurnal rhythm with a peak during the dark period. Ontogenically this enzyme does not appear until approximately the 16th postnatal day; its activity then rises rapidly and reaches adult levels by the 25th day. Our aim was to determine whether the diurnal rhythm is present from the outset or appears only after sucrase has attained adult levels. Rat pups were raised in litters of 9 with a light/dark cycle of 12h. Solid food and water were available to mothers and pups at all times and mothers were normally removed on the 21st postnatal day. Four litters were studied during the 24h period beginning at 8am on the 19th day. One pup from each litter was removed for assay every 3h. Jejunal sucrase showed considerable variation between pups, but there was no discernable pattern with time. In contrast, when the experiment was repeated with pups aged 22 days, there was a distinct peak in sucrase activity during the early part of the dark period. In order to determine whether the rhythm is cued by the process of weaning, two litters were raised on a feeding schedule which ensured that maternal milk was the only food available to the pups. When studied during the 24h period beginning on the 22nd day, the jejunal sucrase activity of these pups exhibited no rhythm. It is concluded that some component of solid food is responsible for the usual appearance of the diurnal rhythm of this enzyme. (supported by NIH Grant No. HD-10042.)

212 PSYCHOMETRIC STUDIES ON A GIRL WITH 47,XX,+21 DOWN'S SYNDROME AND NEAR-NORMAL INTELLIGENCE. Leonard Hersher, Elizabeth R. Lehr and Lytt I. Gardner. Dept. of Pediatrics, SUNY, Upstate Medical Center, Syracuse, New York.

Observations have been made on a 6 1/2 year old girl with 47, XX,+21 Down's syndrome on whom the following IQ scores have been obtained: 104 (Goodenough Scale), 80 (Stanford-Binet) and 77 (Wechsler Intelligence Scale for Children). Performance IQ on the Wechsler was 90. She was tested between kindergarten and first grade (public school) with the Wide Range Achievement Test and scored within the first grade level in spelling and reading. Concentration and short term memory were in the superior range! Performance subtest scores on the WISC ranged from 7 to 12 (12 on Coding). Her remarkable achievement on the WISC Coding A test was primarily the result of her memorizing quickly the five double symbol associations. She regularly defeats her mother in the card game "Concentration".

Twenty-five cells were analyzed from a leucocyte culture and all showed an extra chromosome in the G group. No euploid cells were seen. G-banding identified the extra chromosome to be a no. 21. A skin culture was unsuccessful. Appearance was quite typical of Down's syndrome with bilateral epicanthal folds, severe clinodactyly and hypoplastic ears.

More detailed psychometric studies seem indicated on those trisomy-21 children in the highest range of performance in order to define their areas of strength, as well as to aid in sorting out familial factors vs. environment in terms of the etiology of the "gifted" trisomy-21 child.

213 EFFECTS OF INORGANIC LEAD ON ISOLATED RAT BRAIN MITOCHONDRIAL RESPIRATION. David Holtzman, J. Shen Hsu, and Patricia Mortell. Stanford University School of Medicine, Departments of Pediatrics and Neurology, Stanford, CA.

Oxidative phosphorylation was measured polarographically before and after adding lead acetate to cerebral and cerebellar mitochondria isolated from two week old and adult rats. With glutamate and malate as substrates, lead acetate (0.25 mM) produced a transient increase in respiration followed by complete inhibition of ADP-dependent respiration. The inhibition was not relieved by dinitrophenol or by freezing and thawing the mitochondria. NADH-supported respiration, in frozen and thawed mitochondria, was not affected by these low concentrations suggesting that lead acts on substrate transport or dehydrogenases. With succinate as substrate, inorganic lead produced an increased respiratory rate, approaching State 3, and no respiratory inhibition. The enhanced respiration was inhibited by oligomycin. There were no differences in lead effects associated with age, two weeks vs adult, or with brain region, cerebral vs cerebellar. We conclude that there is an energy-dependent transport of inorganic lead in brain mitochondria. Low concentrations of lead inhibit oxidative phosphorylation with NAD-linked substrates but not with succinate. These in vitro lead effects are similar to those seen in cerebellar mitochondria from lead-treated immature rats (Holtzman and Hsu, Pediat. Res. 10:70-75, 1976). However, this in-vitro mitochondrial effect does not show the age and regional specificity seen in lead encephalopathy in the rat and the human.

214 AMMONIA PRODUCTION BY THE PREGNANT SHEEP UTERUS. Ian R. Holzman, James A. Lemons, Giacomo Meschia, and Frederick C. Battaglia. University of Colorado Medical Center, Division of Perinatal Medicine, Denver.

It is generally assumed that, during gestation, nitrogen metabolism of the uterus and conceptus is directed exclusively toward the synthesis of new tissues. The finding of large quantities of urea excreted by the fetal lamb prompted us to question that assumption and to examine the role of ammonia as an excretory product of the pregnant uterus in sheep with chronically implanted catheters. Seventeen pregnant ewes (GA 47-155 days) were studied with uterine vein and femoral artery catheters; 7 fetuses (114-144 days) had umbilical vein and pedal artery catheters. Two nonpregnant sheep were also studied. After postoperative recovery, simultaneous fetal and maternal blood samples were obtained for NH_3 and O_2 content. Between-group differences in mean arterial [NH_3] (fetus 49.27 ± 2.35 μM; pregnant ewe 36.70 ± 0.93 μM; nonpregnant ewe 23.04 ± 1.01 μM) were statistically significant. In all cases, NH_3 was excreted from the gravid uterus into both the uterine and umbilical circulations by tissues other than the fetus. Thus, the placenta is the probable site of NH_3 formation. Quantitatively, at 70 days of gestation, the ratio of nitrogen excreted by the uterus as NH_3 to the combined total nitrogen requirements for both growth and NH_3 excretion is $\sim$ 44%. Toward the end of gestation, uterine NH_3 production represents $\sim$12% of fetal nitrogen requirements. Ammonia is an important metabolic end product of the ovine gravid uterus, especially in early pregnancy.

215 INHIBITION OF GROWTH AND DNA SYNTHESIS OF CELLS FROM AN ALVEOLAR CELL CARCINOMA BY GLUCOCORTICOIDS. Kenneth Lee Jones, Norman S. Anderson III, and Judith A. Addison. Departments of Pediatrics and Medicine, University of California, San Diego, La Jolla, California.

Glucocorticoids have been reported to inhibit lung growth and to induce differentiated function in fetal lung in many species. We have used the A-549 cell line, derived from a human alveolar cell carcinoma, to study corticosteroid-induced growth inhibition. We found that dexamethasone (DM) inhibits the growth of these cells and that this inhibition is concentration dependent, being identifiable at 10^{-9}M DM and near maximum at 4×10^{-8}M. Population doubling time of the cells was increased from 28.4 hours in control conditions to 66.5 hours in dexamethasone. DNA synthesis was also inhibited by DM with a concentration response similar to that seen with inhibition of cell growth. Several other steroids tested inhibited DNA synthesis, with their inhibiting potential corresponding to their known glucocorticoid potency (dexamethasone > cortisol > corticosterone > deoxycorticosterone). Testosterone and estradiol were not inhibitory. Cytosols from these cells bound ^{3}H-dexamethasone with high affinity and limited capacity. Other glucocorticoids decrease ^{3}H-DM binding in a pattern which correlates with their growth inhibiting activity and biologic activity. The corticosteroid induced growth inhibition in these cells is not cytolytic and may be characteristic of an anabolic pattern of growth arrest associated with induction of differentiated function.

216 ENZYMATIC STUDIES OF A NEW VARIANT OF GM_1 GANGLIOSIDOSIS IN AN OLDER CHILD. Parvin M. Justice, David A. Wenger, Sakkubai Naidu, and Ira M. Rosenthal. Abraham Lincoln Sch. of Med., Dept. of Ped., Univ. of Ill. and Dept. of Ped., Univ. of Colorado Med. Ctr., Denver, Colorado

The metabolic error in GM_1 gangliosidosis has been identified as a deficiency of acid β-D-galactosidase. A number of variants of the disease have been defined by clinical studies and by enzymatic differences with general classification into type I (infantile) and type II (juvenile). O'Brien has predicted identification of other mutants with varying phenotypes based on differences in activity of mutant enzyme for various natural substrates. Another phenotypic variant is reported in an 11 year old black girl whose symptoms began at age 6 years with extremity pain, and who has developed mild mental retardation and progressive ataxia. Focal and grand mal seizures developed at the age of 10 years. Intensive macula cherry red spots are present with evidence of deposition of storage material also in the stromal and epithelial areas of the cornea. There is no hepatomegaly or splenomegaly and no skeletal abnormality. Vacuolated cells are present in the bone marrow. Activity of β-D-galactosidase was 65 nmoles/mg protein/hr vs 389 as the average for control cultured skin fibroblasts (17% of normal). Using natural substrate GM_1 ganglioside, activity of the enzyme was 4% of normal, 9.5 nmoles/mg protein/hr vs 227.5 for controls. Enzymatic studies on leukocytes confirmed the deficiency in acid β-D-galactosidase activity. It is postulated that the affected child has a previously undescribed structural mutation of acid β-D-galactosidase.