● **431** MOLECULAR CLONING OF DNA COMPLEMENTARY TO BOVINE PROLACTIN MESSENGER RNA. Walter L. Miller, Doris Coit, and Joseph A. Martial. Department of Pediatrics and Medicine, University of California, San Francisco, California.

Prolactin (PRL), growth hormone (GH) and chorionic somatammotropin form a family of protein hormones derived from a common evolutionary ancestor. To facilitate study of the structure,regulation, and evolution of this set of related genes, we have previously cloned complementary DNA (cDNA) for bovine GH (J. Biol. Chem. 255:7521). We now report the cloning of cDNA to bovine PRL. A previously cloned bPRL cDNA fragment (Endocrinology 107:851) was labeled with 32P by nick-translation and used to identify clones containing bPRL sequences. All clones were originally derived from bovine pituitary cDNA cloned in the PstI site of pBR322 by the dC.dG tailing technique. One of these clones contained cDNA corresponding to all 199 AA'sof bPRL, plus 10 AA's from the pre-sequence and 75 Bases from the 3'untranslated region. The sequence of the entire 702 nucleotides was determined and compared to the sequence of rat and human PRL cDNA's. The bPRL cDNA sequence permitted identification of 10 AA's in the pre-sequence and of 16 AA's where glutamic and aspartic acids had not been differentiated from their amides by AA sequencing. The homology between bPRL and rat PRL is 60.5% for the AA sequence and 70.8% for the nucleotide sequence. The corresponding values for a comparison of bPRL and human PRL are 74.0 and 79.7%, respectively. 59.5% of bPRL codons end in G or C, whereas this value is 81.7% for bGH. Such codon choice appears to be a characteristic difference between GH and PRL genes.

**432** CHONDROCYTE FUNCTION IS DISTURBED IN RATS WITH STUNTED GROWTH FOLLOWING NEONATAL X-IRRADIATION LIMITED TO THE HEAD. H. David Mosier, Jr., Charles A. Sondhaus, Oscar F. Zuniga, Regina A. Jansons, Cynthia S. Biggs, and Rosalinda C. Roberts. Department of Pediatrics, University of California, Irvine, California.

Stunted growth after irradiation of the head only of the neonatal rat is unexplained. Prior studies show no relationship to food intake and no response to growth hormone and/or thyroxine. Male and female rats were X-irradiated with 600 rads limited to the head at 2 days of age. Controls were non-irradiated littermates. Irradiation resulted in retarded growth of body weight and tail length beginning prior to weaning; catch-up growth did not occur. Costal cartilage at ages 21 days (d), 40 d and 70 d was incubated 20 h at 37C in serum-free medium (M) consisting of phosphosaline buffer, pH 7.4, amino acids, glucose and antibiotics or in medium with 10 percent pooled normal rat serum (MS). $^{35}$S-sulfate (S), $^{3}$H-thymidine (T), $^{14}$C-leucine (L) or $^{3}$H-proline (P) were added to media. In M irradiated rats had significantly increased incorporation of P at 21 d and 40 d and L at 40 d; there was no change in S. In MS irradiated rats had significantly increased incorporation of S and L at 21 d and 40 d. T incorporation was not increased over controls at any age in M or MS. We conclude that in stunted head-irradiated rats synthesis in cartilage of sulfated proteoglycans and collagen is increased and/or hyperresponsive to normal serum. That T incorporation is not increased is compatible with the possibility that failure in catch-up growth of bones after head irradiation results from inhibition of mitosis of chondrocytes.

● **433** ADRENAL GLOMERULOSA FUNCTION IN DSH. S.E.Oberfield, L.S.Levine, D.Chow, S.Lee, E.Lightner,M.Witte,M.I.New Cornell Univ Med Col,NY; Ariz. Health Sciences Ctr.

Dexamethasone-suppressible hyperaldosteronism(DSH),a form of low renin hypertension,is a familial disorder of aldosterone secretion which is transmitted by an autosomal dominant gene. With dexamethasone(DEX) administration there is a prompt suppression of aldosterone excretion to unmeasurable levels and return to normal blood pressure in young subjects. With prolonged ACTH administration, unlike normal subjects in whom aldosterone excretion decreases after an initial rise, the DSH patient demonstrates a sustained and continuous increase of aldosterone excretion.This unusual aldosterone response mimics that of cortisol(F). These findings suggest that in DSH, aldosterone may be a product of the adrenal fasciculata or that ACTH regulates aldosterone secretion by the adrenal glomerulosa. We studied adrenal glomerulosa function in ten patients with DSH treated continuously with DEX 2mg/d and studied on a regular Na+diet(87meq/m2)and on a 10meq Na+ diet. With DEX treatment all patients showed a prompt suppression of adrenal fasciculata function as evidenced by suppression of serum F,corticosterone,desoxycorticosterone and urinary 18-OH-desoxycorticosterone. The complete suppression of urinary pH 1 aldosterone by DEX was paralleled by a prompt suppression of urinary 18-OH-corticosterone. With continued DEX administration plasma renin levels rose to the normal range. Dietary sodium restriction resulted in a further rise in plasma renin activity and a rise in urinary pH 1 aldosterone and 18OHcorticosterone. Thus, in DSH the adrenal glomerulosa is responsive to the stimulation of renin-angiotensin II.

● **434** SEPARATION AND RADIOIMMUNOASSAY OF TRIIODOTHYRONINE ($T_3$) IN HUMAN BREAST MILK. Linda V. Oberkotter,Alfred Tenore, Otakar Koldovsky, John S. Parks. University of Pennsylvania, Children's Hospital of Philadelphia, Department of Endocrinology, Philadelphia. The purpose of this study was to identify and quantitate $T_3$ in human breast milk (HBM), and to elucidate the relationship of this radioimmunoassayable material with organified $^{125}$I in $Na^{125}$I-injected rats. The presence of thyroid hormone, and particularly $T_3$, in HBM has been poorly documented, and inconsistency in sample preparation and methods of quantitation have resulted in ambivalent data. Since thyroid hormones are routinely administered per-orally as corrective therapy for hypothyroidism, the presence of $T_3$ in milk has obvious implications for thyroid regulation in the suckling newborn, as the infant will consume ∿800 ml/day by 4-6 wks. of age if exclusively breast-fed. Aliquots of either HBM or rat breast milk (RBM) were extracted with acidic ethanol (H+EtOH) after overnight digestion with pancreatin. Samples were eluted from an LH-20 column (Pharmacia) using an ethyl-acetate based solvent mixture. Iodotyrosine and-thyronine standards were run, both in their native form, and after extraction. While the bulk of absorbance (HBM)and organified $^{125}$I (RBM) appears in the monoiodotyrosine (MIT) region of elution profiles, an absorbance peak in HBM in the region of the H+EtOH-extracted $T_3$ standard was observed which corresponds to a radiolabelled peak in RBM. $T_3$-RIA of this region revealed 625 ng/dl in HBM, equivalent to a dose of 5.0 µg/day (800 ml. day consumption in a 1 mo. old infant). We conclude from these data that HBM contains sufficient $T_3$ to be of therapeutic value in amelioration of hypothyroidism in infants.

● **435** A PILOT NEWBORN SCREENING FOR CONGENITAL ADRENAL HYPERPLASIA(CAH) AT NEW YORK HOSPITAL(NYH)AND ALASKA. S.Pang W.Murphy, L.S.Levine, D.Spence, A.Leon, S.LaFranchi, A.Surve, M.I.New. NewYork Hosp-Cornell Med.Ctr., Oregon Health Sciences Ctr., Oregon Dept. Health Resources, Alaska Dept. Health

A pilot newborn screening program for 21-hydroxylase deficiency CAH was conducted in Alaska using a 3mm disc filter paper elution technique of capillary whole blood for 17-hydroxyprogesterone (17-OHP)RIA. The highest values of 17-OHP in 4569 consecutively born normal neonates ages 2-14 d at NYH was 40 pg/disc. The range of values for 16 newborns with proven CAH was 57-980 pg/disc. Thus all Alaskan newborns with 17OHP of 57 pg/disc or greater were referred for diagnostic workup and those with 17OHP of 41-57 pg/disc were recalled for repeat specimen. In a 19mo period the Alaskan newborns screened on the 3rd day of life consisted of a total of 11,177 consecutive births (7802 Caucasians, 1207 Eskimo). Fifteen had 17-OHP values greater than 57 pg/disc, of which 3 (including 1 Eskimo) were proven to have CAH. Of the remaining 12, 8 were distressed premature infants including 1 infant who died with clinical symptoms of CAH, and 4 were unknown.Of the 21 newborns whose 17-OHP values were 41-56 pg/disc, 11 were recalled and proven to be normal, and 10 were unknown. Thus the neonatal Alaskan screening revealed an incidence of CAH of 1:3901 live births in Caucasians and 1:1207 live births in Eskimos. The predicted carrier rate is 1:32 in the Caucasians and 1:18 in the Eskimos. The false positive and recall rates were .088% and .25% respectively. The present study demonstrates the feasibility of a newborn screening program for CAH and indicates that the frequency of CAH is greater than previously reported by case assessment methods.

● **436** THE EFFECT OF MATERNAL AND FETAL COMPLICATIONS ON NEWBORN PLASMA LIPOPROTEIN-CHOLESTEROL (C) LEVELS. C. Richard Parker, Jr., Evan R. Simpson, Bruce R. Carr, and Howard Johnson (Spon. by C.R. Rosenfeld). U. Texas Southwestern Med. Sch., Parkland Mem. Hosp., Green Ctr. for Reprod. Biol. Sci., and Depts. Ob-Gyn., Biochem. and Physiol., Dallas.

The factors that contribute to unexplained (i.e., non-genetic) hypercholesterolemia in the newborn are poorly understood. Since the human fetal adrenal utilizes LDL-C as substrate for synthesis of the estrogen precursor-Dehydroepiandrosterone Sulfate (DS), the rate of adrenal utilization of fetal LDL-C could influence fetal plasma C levels. Therefore, we quantified C (total, LDL, HDL, and VLDL) and DS in umbilical cord plasma obtained at term of normal and abnormal newborns, and those delivered of mothers with various pregnancy complications. Results (C-mg/dl, DS-ng/ml; mean ± SE) are shown below:

| Subject | Total C | LDL-C | HDL-C | VLDL-C | DS |
|---|---|---|---|---|---|
| Normal | 47 ± 3 | 27 ± 2 | 18 ± 2 | 2.6 ± 0.7 | 2207 ± 689 |
| Diabetes | 54 ± 5 | 33 ± 4 | 20 ± 1 | 3.1 ± 1.9 | 1616 ± 873 |
| Chronic Hypertension | 58 ± 12 | 37 ± 12 | 17 ± 2 | 1.0 ± 0.8 | 1283 ± 404 |
| Severe PIH | 73 ± 5 | 45 ± 4 | 22 ± 2 | 5.4 ± 1.5 | 1001 ± 513 |
| Microcephaly, IUGR | 80 ± 9 | 56 ± 4 | 23 ± 5 | ≤1 | 880 ± 40 |
| Anencephaly | 112 ± 8 | 79 ± 6 | 27 ± 8 | ≤1 | 250 ± 49 |

We conclude that most instances of newborn hypercholesterolemia can be explained on the basis of impaired utilization of LDL-C by the fetal adrenal due to maternal disease or fetal anomaly rather than genetic predisposition for this disorder. (Supported in part by Grant HD14513).