462 LARON TYPE DWARFISM IS NOT DUE TO A MUTATION IN OR NEAR THE HUMAN GROWTH HORMONE GENE. John S. Parks, Laura C. Sexton, Ruth Keret, Myrta Kalichman, Athalia Pertzelan and Zvi Laron. Emory University School of Medicine, Department of Pediatrics, Atlanta and Tel-Aviv University, Institute of Pediatric Endocrinology, Israel.

We have analyzed DNA restriction fragment length polymorphism to determine whether the mutation responsible for Laron Type Dwarfism (LTD) is linked to the human growth hormone (hGH) gene. An hGH haplotype represents the combination of presence or absence of variable restriction sites for Bgl II, Hinc II and Msp I at 5 locations in a single 55 kb hGH gene cluster. We studied 3 Israeli families with LTD. Different haplotypes are indicated by capital letters A-D:

Family I				II			III
Mother	LTD	LTD	Father	Mother	LTD	Father	LTD
A|A	A|B	A|C	B|C	D|E	D|D	D|A	D|B

The affected siblings in Family I have inherited different hGH genes from their normal father. LTD patients in 3 families show a total of 4 different hGH haplotypes. Discordance for haplotype between affected siblings and lack of association of LTD with a particular hGH haplotype indicate that LTD is not linked to the hGH gene. This result excludes mutation of hGH to an antagonist molecule as an explanation for hGH resistance and abnormal receptor function in LTD. If an hGH receptor gene is mutated in LTD, then this gene is not located in proximity to the hGH gene.

463 ULTRASOUND EVALUATION OF NEWBORN THYROID STRUCTURE: VISUALIZATION WITHOUT RADIATION. Matthew Pasto, Gary G. Carpenter. Thomas Jefferson University, Departments of Diagnostic Ultrasound and Radiologic Imaging and Pediatrics, Philadelphia, Pa.

Infants with suspect thyroid dysfunction need visualization of the structure of the thyroid gland in addition to the understood biochemical specific studies for diagnostic and follow up care. With the application of ultrasound real time (10 MHz high resolution real time, prototype ATL, Bellevere, WA) 8 evaluations have revealed information aiding diagnosis and counseling potential for parents. Infants with prematurity and low T4 studies compatible with the diagnosis of "sick euthroid" when seen to have a normal gland may be observed with less anxiety than those found to have no structure resembling thyroid. Gland size of infants whose mothers required antithyroid medication during pregnancy can be serially followed. Term newborns with screening values in the first weeks of life that indicate possible athyreosis can have rapid confirmation when the gland is found absent; those with dysgentic thyroid structure may be followed with or without treatment depending on other individual balances of thyroid studies. Parents have indicated appreciation of this newer visualization technique utilizing ultrasound.

The procedure of ultrasound evaluation of the newborn and premature infant thyroid gland may supply a needed technique in the optimum care of newborn and premature infant.

464 EVIDENCE FOR INDEPENDENT MUTATION OF THE 21-HYDROXYLASE DEFICIENCY (21OH DEF) GENE IN ALASKAN ESKIMOS WITH CONGENITAL ADRENAL HYPERPLASIA (CAH). GM Petersen, JE MacCracken, JI Rotter, D Trotter, MI New, MS Park, PI Terasaki, RS Sparkes, JI Ward. Harbor-UCLA Med. Ctr., Torrance, CA; PHS Hosp. Bethel, Alaska; NY Hosp.-Cornell Med. Ctr.; UCLA Med. Ctr., Los Angeles, CA.

Worldwide, the salt-losing form of CAH (21OH Def) has been reported to have the highest known prevalence in Yupik speaking Alaskan Eskimos. The annual incidence is 1/490 with an estimated gene frequency of .045. We analyzed the HLA phenotypes and inferred genotypes in 11 Eskimo children with CAH, representing 7 families. All CAH children had at least one HLA-B27 allele (6 homozygotes), at least one HLA-C4 allele, and all were homozygous HLA-DR4. HLA types obtained on 118 healthy Eskimo controls showed significantly different frequencies for these alleles:

Allele Frequencies:	CAH Cases	Controls	Significance
HLA-B27	.93	.14	p<.001
HLA-C4	.50	.10	p<.001
HLA-DR4	1.00	.33	p<.001

The inferred haplotypes which carry the 21OH Def gene include A24 B27 C4 DR4 and A2 B27 C2 DR4, plus A28 B61 C3 DR4, which occurs in only one family. The three haplotypes combined occur in .076 of the controls, a frequency only slightly greater than expected for CAH heterozygotes based on the observed CAH disease incidence, implying that most Yupik Eskimos with these haplotypes are heterozygous for 21OH Def. These results differ markedly from other HLA population studies, suggesting that the 21OH Def gene in Yupik Eskimos occurred by an independent mutational event.

† **465** DEFECTIVE TRANSFORMATION OF ANDROGEN-RECEPTOR COMPLEXES: A CLASS OF FAMILIAL, RECEPTOR-POSITIVE PARTIAL ANDROGEN RESISTANCE. Leonard Pinsky, Morris Kaufman. Lady Davis Institute and Centre for Human Genetics, McGill University, Montreal, Canada.

We have analyzed the androgen (A)-receptor (R) system in genital skin fibroblasts (GSF) of 2 subjects with external genital ambiguity. Subject 1 has 5 affected maternal relatives in 3 generations. With a 2-h assay, his AR has a normal binding capacity (B_{max}) (receptor-positive), but an apparent equilibrium dissociation constant (K_d) of 1.2-1.4 nM for 5α-dihydrotestosterone (DHT) or the nonmetabolizable androgen, methyltrienolone (MT) (normal: 0.1-0.3 nM). His DHT- and MT-R complexes dissociate 3 and 6 times faster than normal (0.006 and 0.012 min^{-1}, 37°, respectively). Prolonged incubation with DHT or MT fails to augment (up-regulate) basal A-R activity. Subject 2's mother has sparse sexual hair. With DHT, his AR has a normal B_{max} but an increased K_d (0.6 nM) and k (0.012 min^{-1}), and prolonged incubation does not cause up-regulation. In contrast, with MT his AR is normal. Normal GSF yield higher K_ds (0.3-1.8 nM) for either ligand after 0.5- compared to 2-h assays, and the GSF of both subjects catabolize DHT to a normal extent. Conclusions: (i) normal GSF transform initial, low-affinity A-R complexes to higher affinity states by a process that is codependent on time and initial ligand concentration; (ii) subject 1 forms DHT- and MT-complexes that remain in the initial, low-affinity state; (iii) subject 2 forms complexes that transform normally with MT but partially with DHT; and (iv) A-R complexes must attain the highest affinity state to act as the «signal» for up-regulation.

466 CORD SERUM THYROID STIMULATING HORMONE (TSH) AND THYROGLOBULIN (Tg) LEVELS DECLINE WITH INCREASING BIRTH WEIGHT IN NORMAL FEMALE NEWBORNS. Robert Penny, Carole A. Spencer, John T. Nicoloff. Depts. of Pediatrics and Medicine, Univ. of So. Calif., Los Angeles, California.

Tg, TSH and T_4 were determined in cord serum and related to birth weight and sex in normal newborns, 20 females and 19 males. Mean + SD birth weight of female infants (3299 + 282 grams) was significantly ($p < 0.005$) less than that of male infants (3757 + 447 grams). Whereas, mean gestational age of female infants did not differ from that of male infants (40.1 + 0.5 vs 40.1 + 0.7 weeks). Mean Tg levels of female infants (31.1 + 8.9 ng/ml) was significantly ($p < 0.05$) greater than that of male infants (26.1 + 7.7 ng/ml). TSH (14.9 + 11.3 vs 14.8 + 13.4 μU/ml, $p > 0.1$) and T_4 (11.1 + 3.3 vs 11.7 + 3.5 μg/dl, $p > 0.1$) levels of female and male infants did not differ significantly. Further analysis indicated that Tg levels ($r = -0.401$, $p < 0.05$) and the log of TSH levels ($r = -0.576$, $p < 0.005$) correlated negatively with birth weight in female infants. Also, Tg levels correlated positively with the log of TSH levels ($r = 0.401$, $p < 0.05$) in female infants. In contrast, none of these correlations were significant for male infants. We conclude that the sex difference in cord serum values and their correlations may be principally related to changes in body composition that accompany increasing birth weight.

467 CORD SERUM THYROID STIMULATING HORMONE (TSH) AND THYROGLOBULIN (Tg) LEVELS DECLINE WITH INCREASING WEIGHT IN LOW BIRTH WEIGHT NEWBORNS. Robert Penny, Carole A. Spencer, John T. Nicoloff. Depts. of Pediatrics and Medicine, Univ. of So. Calif., Los Angeles, California.

Tg, TSH, free T_4 index, and free T_3 index were determined in cord serum and related to birth weight and sex in infants with weights of less than 2500 grams, 19 males and 19 females. Free index values are the product of the T_3 resin uptake ratio and the appropriate thyroid function indice. Mean + SD birth weight of male (1850 + 413 grams) and female (2032 + 301 grams) infants did not differ significantly ($p > 0.05$). Similarly, mean + SD cord serum Tg (124 + 49 vs 107 + 55 ng/ml), TSH (9.2 + 6.5 vs 7.1 + 2.7 μU/ml), free T_4 index (6.2 + 1.6 vs 6.1 + 1.0 μg/dl), and free T_3 index (47 + 12 vs 47 + 5 ng/dl) values of male and female infants did not differ significantly ($p > 0.1$). Free T_3 index values of male ($r = 0.570$, $p < 0.01$) and female ($r = 0.443$, $p < 0.05$) infants correlated positively with the free T_4 index values. Tg levels and the log of TSH levels correlated negatively with birth weight in male (Tg, $r = -0.849$; log TSH, $r = -0.660$) and female (Tg, $r = -0.891$; log TSH, $r = -0.600$) infants ($p < 0.005$). Also, Tg levels correlated positively with the log of TSH levels in male ($r = 0.412$, $p < 0.05$) and female ($r = 0.554$, $p < 0.01$) infants. These data are consistent with a hypothesis that changes in body composition accompanying increasing birth weight are associated with an increase in thyroid gland responsiveness to TSH or a decrease in T_4 clearance.