**432** PITUITARY-THYROID AXIS FUNCTION IN THE LOW BIRTH WEIGHT INFANT (LBW) WITH INTRACRANIAL HEMORRHAGE (IC). J. Graeve and A. Erenberg, Dept. of Ped., University of Iowa, Iowa City, Iowa.

The incidence of hypothyroxinemia low serum thyroxine($T_4$) and normal serum thyroid stimulating hormone (TSH) levels in the LBW with an IC is significantly greater than in the LBW without IC. The significance of this observation is not clear. The purpose of the study was to assess pituitary-thyroid axis function in the LBW with IC by examining the pituitary and thyroid gland response to thyrotropin releasing hormone(TRH).

Twenty-four LBW weighing < 2.0 kg were screened for IC by ultrasonography between days 1 and 7 of life. On day 3, samples were drawn for serum $T_4$ and TSH levels immediately prior to and 30 and 180 minutes after 20 µg/kg TRH IV.

Six LBW were identified as having IC. Compared to the LBW without IC, the mean birth weights, 1 and 5 minute Apgar scores and incidence of RDS were similar in both groups. The mean ± SEM gestational age was significantly lower in the LBW with IC (29.5 ± 0.8 vs. 31.2 ± 0.3 weeks, $p<0.025$). The mean baseline serum TSH and $T_4$ levels were similar in both groups. The mean serum $T_4$ level was significantly greater at 30 and 180 minutes in the LBW without IC. The mean serum TSH level at 180 minutes remained significantly higher in the LBW with IC (51.4 ± 13.1 vs. 21.9 ± 4.0 µu/ml, $p<0.01$). Conclusion: 1) In response to TRH at 3 days, the mean serum TSH level at 180 minutes in the LBW with IC remains significantly elevated. This response is similar to that seen in patients with hypothalamic hypothyroidism.

**435** HYPERESTROGENISM IN CHILDREN WITH CAH: PERSISTENCE DESPITE GOOD CONTROL. James P. Gutai, David J. Watson, Edward O. Reiter. ECU School of Med., Dept. of Peds., Greenville, NC and Baystate Med. Ctr., Dept. of Peds., Springfield, MA.

We studied the relationship between Estrone (E1), Estrone sulfate (E1S), Estradiol (E2) and androstenedione (Δ4) concs. in 32 children and adolescents with 21-OH def. adrenal hyperplasia (CAH). Concs. were measured in 23 normal prepubertal children, 8 normal adolescent males, and a pop. of normal adult males. There was a sig. ($p<.01$) correlation coefficient between E1, E1S, or E2 and Δ4 in subjects with androgen hormone excess. CAH patients were divided into 2 groups: I. prepubertal male and female children in good metabolic control based upon Δ4 conc. and II. adolescent males in good control and compared with previously described control groups.

| | E1 pg/ml | E1S pg/ml | E2 pg/ml | Δ4 ng/dl |
|---|---|---|---|---|
| Group I (n=11)† | 27 ± 13* | 165 ± 76** | 11.8 ± 6.2* | 28.7 ± 13 |
| Control (n=23) | 10 ± 4.3 | 103 ± 55 | 3.8 ± 1.5 | |
| Group II (n=11) | 85 ± 56* | 1104 ± 801* | 27 ± 17** | 91 ± 89 |
| Control (n=8) | 24 ± 13 | 222 ± 140 | 8.5 ± 4.7 | |

* $p< .005$ ** $p< .05$ † Mean ± SD

The correlation of the estrogen profile and Δ4 in patients with adrenal androgen excess may reflect peripheral aromatization of Δ4 to E1 rather than increased adrenal secretion of E1. The sig. elevated conc. of E1, E1S, and E2 in CAH patients, despite good metabolic control, is surprising. Increased conc. of these hormones during the prepubertal years may in part explain alterations in pituitary gonadal function in older patients.

**† 433** COMPLICATIONS ASSOCIATED WITH THIOUREA THERAPY. Alice B. Granoff (sponsored by Dan M. Granoff), Washington University School of Medicine, St. Louis Children's Hospital, St. Louis, MO.

We reviewed the clinical courses of 105 children with hyperthyroidism: 69 received propylthiouracil (PTU), 29 received Tapazole (TAP) and 7 were begun on one drug and later switched to the other (for purposes of analysis, these 7 were included in both groups). Choice of drug depended on the individual physician's preference. The mean ± 1 SD duration of therapy for PTU was 20± 16 months, and for TAP 16± 12 mos. Prior to therapy, there were no significant differences in the two treatment groups with respect to age, gender, family history of thyroid disease, mean T4 concentration,or mean goiter size. There were no significant differences in the clinical remission rates in the two groups (45.7% for PTU and 29.4% for TAP, p=0.11). However, hepatitis or collagen-like diseases occurred more frequently in children treated with PTU (14/76, 18%) than in children treated with TAP (0/36, $p<0.006$ by chi square). In contrast, there were no significant differences in the frequency of leukopenia (4.3 v. 2.9%) or rash (2.9 v. 8.9%, respectively, p=NS). The occurrence of hepatitis or collagen-like illness did not appear to be related to dosage or duration of therapy. In conclusion, the efficacy of the two drugs appears to be similar but serious complications occur more frequently with PTU. Therefore, TAP would appear to be the drug of choice in initial therapy of hyperthyroidism in children.

**● 436** CALCEMIC RESPONSES TO PHOTIC AND PHARMACOLOGIC MANIPULATION OF SERUM MELATONIN. D. O. Hakanson, R. Penny and W. H. Bergstrom Departments of Pediatrics, SUNY, Upstate Medical Center, Syracuse, NY and USC Medical Center, Los Angeles, CA.

We have reported decreased serum calcium(CaS) in human infants(HI) and in newborn rats(NBR) during exposure to white light(Photo). In NBR, bone Ca uptake increased. At wavelengths below 600nM (orange to blue), cranial light penetration fell sharply and CaS was unaffected. Occipital shields prevented hypocalcemia in both HI and NBR. Pineal melatonin synthesis is increased by isoproterenol and decreased by propanolol and by light (PNAS 69: 2547, 1972). In NBR we found serum melatonin to be 27±8 pg/ml during Photo and 122±32 pg/ml in shaded littermates (n=24, $p<.01$). Exogenous melatonin (20ng/Gm IP) gave serum concentrations of 383 pg/ml at 1 hr and 83 pg/ml at 2 hrs and prevented the hypocalcemic response to Photo. Propanolol reduced CaS in shaded NBR from 9.5±.1 mg/dl to 7.9±.2 mg/dl; after propanolol + melatonin, CaS was 8.8±.2 mg/dl. Isoproterenol ameliorated hypocalcemia during Photo (Shade 9.7±.1 mg/dl, Photo 8.8±.1 mg/dl, Photo + isoproterenol 9.4±.1 mg/dl). These findings support the hypothesis that hypocalcemia during phototherapy results from transcranial photic inhibition of melatonin synthesis.

**434** THE EFFECT OF THYROXINE(T4) AND DEXAMETHASONE(Dx) ON FETAL(F) HEART(H) AND BRAIN(B) INSULIN RECEPTOR (IR) P.F.Grim,III, S.Devaskar, N.Marino, F.Solomon and U.Devaskar (Spons W.J.Keenan) Dept. of Peds., St. Louis University School of Medicine, St. Louis, Missouri

Insulin mediated tissue glucose uptake and lipid synthesis as well as F lung and liver IR are modulated by $T_4$ and Dx. Using plasma membranes(PM) $^{125}$I-insulin binding(IB) per 100µg HPM/200 µg BPM and IR $x10^{10}$mg protein$^{-1}$ in two highly glucose dependent fetal organs (H and B), were studied under conditions of $T_4$ and steroid excess. Date bred rabbits(M) received T4 at 50µg/kgx5 IM from 21 to 29d. (term~31d.), while control 1(C1) received saline (T4↑F serum free $T_4$ from 0.2±0.02 to 0.8±0.1ng/dl↑, F plasma glucose from 47±5 to 69±5mg/dl↑) Dx at 0.09mg/kgx2 IM on 25 and 26d. was given to M, while control 2(C2) received saline IM. (Dx↑F plasma glucose from 57±5 to 124±12↑). In all groups, no change in plasma insulin and IR affinity was noted($p*<.05†<.02$,UD=undect.)

| GROUPS(gest.age) | $T_4$ (30d.) | | C.1 (30d.) | | Dx (27d.) | | C.2 (27d.) | |
|---|---|---|---|---|---|---|---|---|
| FH/FB (n) | FH(4) | FB(6) | FH(5) | FB(7) | FH(4) | FB(6) | FH(5) | FB(6) |
| %$^{125}$I-IB $\bar{X}$± | 5.8* | 12.5 | 3.6 | 11.7 | 3.4 | 10.3 | 3.5 | 9.2 |
| SEM | 0.1 | 0.5 | 0.7 | 0.6 | 0.2 | 0.4 | 0.4 | 0.5 |
| Total IR No. | 244.1* | 153.2 | 137.0 | 186.1 | | | | |
| | 39.2 | 10.0 | 3.9 | 14.8 | - | - | - | - |
| Glycogen µMo gluc U/mg prot. | 0.5† 0.01 | UD | 0.7 0.04 | UD | 0.7† 0.02 | UD | 0.8 0.03 | UD |
| Cholesterol µg/mg protein | - | 44.0 3.0 | - | 50.0 5.0 | - | - | - | - |

We conclude:1)$T_4$ has a trophic effect on FH IR while Dx does not; FB IR being unresponsive. 2)$T_4$ and Dx ↓ FH glycogen content.

**● 437** SOMATOMEDIN-C (SM) LEVELS IN PATIENTS WITH TRUE PRECOCIOUS PUBERTY: EFFECT OF TREATMENT WITH A POTENT LRF-AGONIST (LRF-A). David A. Harris, Dennis M. Styne, Guy Van Vliet, Selna L. Kaplan, Melvin M. Grumbach, Dept. of Pediatrics, University of California SF, San Francisco, CA

An interrelationship has been suggested between SM, growth rate, and sex steroid levels in normal puberty. We measured serum acid-ethanol extractable SM by RIA in 7 boys and 12 girls with central precocious puberty before and at 1 week (W), 2W, 6W, 12W, and then every 3 months (M) after starting treatment with 4 µg/kg daily SQ injections of the LRF-A, D-TRP$^6$-PRO$^9$-NET LRF, supplied by Drs. Wylie Vale and Jean Rivier. Gonadotropin and sex steroid levels at baseline and in response to an IV bolus of LRF were measured and correlated with changes in SM. Median ΔLH at 0, 1W, and 2W was 2.4, 0.6, and 0.7 ng/ml, respectively, in boys, and 7.9, 0.9, and 0.5 ng/ml in girls. Median testosterone (T) was 366, 403, 53, and 34 ng/dl in boys, and median estradiol (E2) was 61, 62, <5, and <5 pg/ml in girls at 0, 1W, 2W, and 6W respectively. The ΔLH, T, and E2 values remained prepubertal thereafter. SM was correlated with height velocity ($p<.005$) at 0, 6M, and 12M of therapy. SM rose from a pretreatment mean of 1.99±.17 (SEM) units/ml to 2.19±.16 u/ml at 1W ($p=.1$, Wilcoxon) and fell significantly to 1.6±.17 u/ml ($p<.05$) at 6M. Significant correlations were found between SM and E2 ($p=.005$) and T ($p<.001$). In 3 patients who had therapy with LRF-A discontinued, SM levels rose to pre-treatment values and decreased when therapy was restarted. The reversible suppression of T, E2, and SM by LRF-A treatment supports the assertion that SM is dependent on T and E2 levels in precocious puberty.