**438** FREE T4 - NOT A PREDICTOR OF THYROID FUNCTION IN PREMATURE INFANT. P. Karna, E.A. Dolanski, D.Sciamanna, M. Netzloff. Michigan State University College of Human Medicine, Department of Pediatrics and Human Development and E.W. Sparrow Hospital, East Lansing, MI.

Thyroid screening is done in our center as recommended by AAP during the first week of life in all preterm as well as term infants in the NICU. During the past 6 months, 8 infants received complete laboratory evaluation due to low T4. The tests performed were T4 by RIA, TSH by RIA and Free T4 by RIA "Amersham Kit" method. Initial values revealed the following:

| GA(weeks) | T4(µg/dl) | TSH (µIU/dl) | *Free T4(ng/dl) |
|---|---|---|---|
| TA 28 | 2.0 | 3.7 | 0.6 |
| LA 28 | 2.1 | 4.0 | 0.3 |
| PB 27 | 2.0 | 8.1 | 0.4 |
| MB 30 | 2.0 | 7.2 | 0.5 |
| FB 30 | 2.2 | 3.4 | 0.6 |
| FA 27 | 2.0 | 2.5 | 0.5 |
| FB 27 | 2.0 | 8.3 | 0.4 |
| BB 29 | 4.3 | 5.5 | 0.4 |

*Normal Free T4 - 0.7 - 1.8 ng/dl

Further evaluation with time, including TRH stimulation test in two of these infants, suggested normal thyroid function. TSH increased from 5, 7 µIU/dl to 50.9, 32.0 µIU/dl at 30 minutes, and 46.4, 23.6 µIU/dl at 60 minutes, respectively after TRH stimulation in the two premature infants. This data suggests that Free T4 does not provide accurate evaluation of thyroid function in premature infants as it does in adults. This paper describes serum Free T4 values in very low birth weight infants.

**● 439** PROTEIN SYNTHESIS INHIBITORS INHIBIT 24,25-DIHYDROXYVITAMIN $D_3$ SYNTHESIS IN THE D-DEPLETED KIDNEY May Kung, Glenville Jones, Sang Whay Kooh, Donald Fraser Institute of Medical Science and Research Institute, The Hospital for Sick Children, Toronto, Canada

The final step of activation of vitamin D occurs in the kidney Depending upon the circulating levels of Ca, Pi and D, 24,25- and 1,25-dihydroxyvitamin D are produced in varying amounts by renal mitochondrial hydroxylases. 24,25-$(OH)_2D_3$, the major metabolite present under physiological conditions, may have a role in bone formation.

We have studied the biochemical control of 24,25-$(OH)_2D_3$ synthesis. When kidneys isolated from D-replete rats were perfused, they produced mainly 24,25-$(OH)_2D_3$. Kidneys from D-depleted animals produced 1,25-$(OH)_2D_3$. However, they began to synthesize 24,25-$(OH)_2D_3$ 2 to 3 hours after starting perfusion when the substrate was 10 ng/ml 25-hydroxyvitamin $D_3$ (25-$OHD_3$). We investigated whether the conversion of $^3$H-25-$OHD_3$ to $^3$H-24,25$(OH)_2D_3$ was dependent upon the synthesis of new protein. We added the protein synthesis inhibitor actinomycin D ($4x10^{-6}$M) or cycloheximide ($1x10^{-5}$M) to the perfusate. Addition of the inhibitors between 0 and 3 hours of perfusion abolished conversion of $^3$H-25-$OHD_3$ to $^3$H-24,25$(OH)_2D_3$ (control 2.76 ± 0.31 % vs inhibitor 0.30 ± 0.20%). However, when they were added 3 or 4 hours after starting perfusion, the synthesis of D metabolite was not inhibited (control 2.76 ± 0.31% vs inhibitor 3.95 ± 0.6%). The results suggest that the initiation of 24,25-$(OH)_2D_3$ production requires the synthesis of new protein.

**● 441** STUDIES OF GROWTH HORMONE BINDING AND ITS INSULIN-LIKE METABOLIC EFFECT IN ISOLATED RAT ADIPOCYTES. Stephen H. LaFranchi, Cheryl E. Hanna, Tony Torresani Eugene Schoenle, Ruth Illig. Oregon Health Sciences Univ. and Univ. of Zurich, Dept. of Pediatrics, Portland, OR and Zurich.

Adipocytes isolated by collagenase digestion from normal rat epididymal(EP), subcutaneous(SC), or retroperitoneal(RP) locations were selected for a study of human growth hormone(hGH) binding and metabolic activity. Scatchard analysis of 125-I-hGH binding was linear; binding affinities ranged from 2.1-3.5 x $10^9$ $M^{-1}$ and were not different, but the number of binding sites per cell were highest in EP(8,300), followed by SC(6,700), $p<.05$, and then RP fat(2,700), $p<.01$. The metabolic response of fat cells was evaluated by the incorporation of 14-C(U) glucose into adipocytes(without pre-incubation). With pituitary hGH, basal and maximally stimulated glucose incorporation was: EP=202±9 to 265±18 (31% increase, $p<.05$), SC=97±6 to 111±8 (17% increase), and RP=96±10 to 104±9 nMoles/$10^6$ cells(7% increase). Similar studies following biosynthetic hGH (supplied by Kabi Vitram) showed: EP=243±13 to 301±21(24% increase, $p<.025$), SC=120±17 to 139±31 (18% increase), and RP=110±10 to 104±12 nMoles/$10^6$ cells. Addition of hGH antibodies blocked the glucose incorporation in EP adipocytes using both pituitary and biosynthetic hGH, while insulin antibodies did not prevent this increase. We conclude that this insulin-like metabolic effect is caused by hGH, not an insulin-like impurity. EP fat cells demonstrated the highest number of binding sites and glucose incorporation, followed by SC and then RP fat cells. These results suggest different metabolic responses to hGH for adipose tissue from different locations.

**442** THYROTROPIN (TSH) RESPONSE TO THYROTROPIN RELEASING HORMONE (TRH) IN CHILDREN & ADOLESCENTS WITH OBESITY. Vinod Lala, P. Jamias & C.S.Yogananda (Spon. by T.W. AvRuskin) N.Y. Medical College, Lincoln Hospital, Division of Pediatrics Endocrinology. Bronx New York.

A number of abnormalities in hypothalamic pituitary functions have been reported in non-endocrine obesity. No reports are available on hypothalamic pituitary-thyroid status in children with obesity. TSH response to TRH was studied in 47 obese patients (Gr.A) (mean age 12.4±0.5 range 5.1-19.2 yrs; ♂ 25, ♀ 22) & was compared with 24 short-normal controls (Gr.B) (mean age 12.3±0.6 range 5.2-17.5 yrs; ♂ 18, ♀ 6) Mean % overweight 64.8±6.1 range 11.3-226.0. TRH test was done with IV bolus 4ug/kg/BW (maximum 250 ug) of TRH after overnight fast of 10 hrs. There was no significant difference in basal levels of T4, T3, free T4 & TSH. 34.0% of Gr.A had augmented TSH response (Peak TSH > 20uIU/ml). Mean TSH response was significantly higher in Gr.A vs Gr.B.

TSH u IU/ml mean ± S.E.

| | Time in minutes | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Gr | Basal | 15 | 30 | 45 | 60 | 90 | 120 | Peak |
| A | 3.8 ±0.2 | 18.2 ±1.1 | 19.3 ±1.3 | 16.0 ±1.1 | 12.6 ±0.8 | 8.5 ±0.5 | 6.2 ±0.4 | 20.5 ±0.4 |
| B | 3.0 ±0.3 | 12.6 ±0.7 | 14.3 ±0.8 | 11.9 ±0.7 | 10.1 ±0.6 | 7.3 ±0.5 | 5.6 ±0.4 | 14.4 ±0.8 |
| P | N.S. | < 0.001 | < 0.005 | < 0.005 | < 0.02 | N.S. | N.S. | < 0.001 |

The higher/augmented TSH response to TRH in obese children could be a evidence of hypothalamic pituitary dysfunction, of partial peripheral resistance to thyroid hormone, or of minimal thyroid insufficiency.

**440** MINIMAL THYROID INSUFFICIENCY (MTI) IN CHILDREN WITH CONSTITUTIONAL DELAYED GROWTH (CDG). Vinod Lala, P. Jamias, B.Hermosa & Ashit Ray. (Spon. by T.W. AvRuskin) N.Y. Medical College, Lincoln Hospital Department of Pediatrics, NY.

Therapeutic trial c̄ thyroid preparation in absence of clinical & laboratory evidence of hypothyroidism has been reported in children c̄ short stature. (J.Ped. 80,988,72). Patients c̄ MTI have normal T3,T4,& TSH levels but an augmented TSH response to TRH. (Peak TSH response > 20uIU/ml). TSH & T3 response to TRH was assessed in 20 children (mean age 11.7 range 7.9-15.8 yrs ♂ 18: ♀ 2) c̄ CDG. TRH test was done with IV bolus TRH 4ug/kg/BW. after an overnight fast of 10 hrs. 5 had augmented TSH response (Gr.B) 15 had normal (Gr.A). There was no significant difference in basal levels of T3,T4, free T4 & TSH. Mean TSH reponse was significantly higher at all times in Gr.B vs Gr.A T3 % increase was lower in Gr.B 29.1±2.5(N3) vs Gr.A 41.9±4.0(N9) $p < 0.05$.

TSH u IU/ml Mean ± SE

| Group | Basal | 15 | 30 | 45 | 60 | 90 | 120 | Peak | |
|---|---|---|---|---|---|---|---|---|---|
| A(15) | 3.0 ±0.4 | 12.6 ±0.9 | 13.6 ±0.9 | 11.6 ±0.8 | 10.1 ±0.7 | 7.2 ±0.6 | 5.7 ±0.6 | 13.8 ±0.9 | 10.8 ±0.8 |
| B(5) | 3.3 ±1.0 | 24.4 ±1.8 | 30.5 ±3.0 | 25.8 ±5.5 | 18.1 ±3.5 | 12.4 ±2.0 | 10.0 ±1.7 | 31.7 ±3.4 | 28.4 ±2.5 |
| P | NS | < .001 | < .001 | < .05 | < .05 | < .05 | < .05 | < .001 | < .001 |

Augmented TSH response & lower T3 % increase in response to TRH was found in 25% of children c̄ CDG. This could be an evidence of minimal thyroid insufficiency or of hypothalamic pituitary thyroid dysfunction in children c̄ CDG. Treatment c̄ thyroxine in two patients for 5 months showed 140% increase in annual growth rate. Controlled therapeutic trial is indicated.

**443** IMPAIRED SOMATOMEDIN (SM) GENERATION TEST IN POORLY CONTROLLED INSULIN DEPENDENT DIABETES MELLITUS (IDDM). R. Lanes, B. Recker, P. Fort, F. Lifshitz. Department of Pediatrics, North Shore University Hospital, Manhasset, NY 11030, and Department of Pediatrics, Cornell University Medical College, New York, NY 10021.

Recent studies have suggested a partial block in SM production or growth hormone (GH) action in IDDM. Twelve diabetic children (9 males and 3 females with a mean age of 11.2 ± 3.3 years), six in good control (HbA1C 7.9 - 11.2%) and six in poor control (HbA1C 12 - 15.6%) were studied as follows: the GH response following 100 ug of oral clonidine and the SM generation capacity after i.m. administration of 0.2 u/kg/dose of hGH for 4 days. Poorly controlled diabetics had a significantly higher mean ± SD GH increase after clonidine than did well controlled patients (17.4 ± 4.9 vs 5.7 ± 6.0 ng/ml; $p<0.004$); the basal GH of both groups were similar (1.6 ± 0.7 vs 2.3 ± 1.4 ng/ml). In contrast the SM response to hGH was significantly decreased in poorly controlled children as compared to well controlled (Δ of 0.3 ± 0.3 vs 1.2 ± 0.4 U/ml, $p<0.002$). The basal SM levels of both groups were normal for age. ↗ GH and ↗ SM correlated with HbA1C levels ($r = +0.80$, $p<0.01$; $r = -0.79$, $p<0.01$, respectively); there was no correlation with plasma and urine glucose or serum cholesterol, cortisol and transferin. Our data indicate a blunted SM response to hGH in poorly controlled diabetes; this defect in SM generation is apparently not present in well controlled IDDM. A biologically inactive GH molecule seems unlikely, but circulating inhibitory factors or a still unclear metabolic derangement may be contributing to this defect.