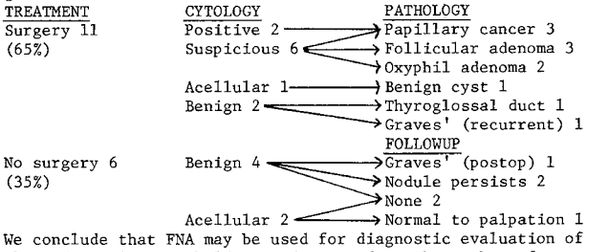
## 475 FINE NEEDLE ASPIRATION BIOPSY OF THE THYROID NODULE IN CHILDHOOD AND ADOLESCENCE.

Teresa J. Nelson and Donald Zimmerman. Spon. by Morey W. Haymond. Mayo Clinic and Mayo Foundation, Department of Pediatrics, Rochester, Minnesota.

Surgical biopsy has been recommended for all thyroid nodules in children because of the risk of thyroid cancer. Our 3-year experience with fine needle aspiration biopsy of the thyroid (FNA) was reviewed to determine whether some patients with thyroid nodule could be safely followed without surgical biopsy. 17 patients, ranging in age from 5-17 years, received FNA. Based on cytologic and clinical findings, it was determined whether surgery or observation was indicated. The following diagram illustrates the results.




We conclude that FNA may be used for diagnostic evaluation of thyroid nodules in children and may reduce the number of patients requiring surgical biopsy.

## 478 A THYROID HORMONE BINDING INHIBITOR (THBI) IN CORD SERA OF PREMATURE, TERM AND POST-TERM NEONATES.

L.V. Oberkotter, G.R. Pereira, L.C. Farmer, M. Farber. Dept. of Ob-Gyn, Albert Einstein Med. Ctr. No. Div., & Dept. of Peds., Univ. of Pa. Sch. of Med., The Children's Hosp. of Phila., Phila., PA.

A thyroid hormone binding inhibitor (THBI) which affects the ability of thyroxin binding globulin (TBG) to bind T4 was first described by Chopra et al as a possible explanation for the low T4 levels observed in some adults patients with non-thyroidal illness. Because low T4 levels are likewise a common clinical feature of prematurity, we examined THBI activity in 30 neonates (GA 26-43 weeks, BW 930-4360 grams) using a competitive ligand binding assay in order to determine whether increased THBI levels might be responsible for the hypothyroxinemia of prematurity. Serum concentrations of T4 and TBG were measured by RIA and the free T4 index calculated. THBI activity was expressed as the % CPM T4 $I^{125}$ displaced from serum binding protein in the absence of THBI. A THBI index was then calculated, normalizing patients' samples relative to a baseline (control value of 1.0). Significant positive correlations between THBI activity and birthweight ($r=0.76$, $p<0.0001$) and gestational age ($r=0.74$, $p<0.0002$) were noted in infants born between 26 and 39 weeks of gestation, but not in more mature infants. No significant correlations were observed between THBI activity and TBG, T4 and free T4 index in these infants. The results of this study indicate that: 1) increased THBI activity is not a likely etiology for the hypothyroxinemia of prematurity; 2) the activity of THBI increases with fetal maturation until term gestation, and then it appears to decline; 3) the relationship between THBI activity, birthweight, gestational age, and systemic illness needs to be further investigated.

## ● 476 LOW DOSE ESTRADIOL ACCELERATES ULNAR GROWTH IN BOYS

Manuela Caruso Nicoletti, Fernando Cassorla, Marilyn Skerda, Judith Levine-Ross, D. Lynn Loriaux and Gordon B. Cutler, Jr. (Spon. by J. Sidbury) DEB, NICHD, NIH, Bethesda, MD 20205, and Hahnemann University, Philadelphia, PA 19102.

We have described a biphasic dose-response curve for ethinyl estradiol ($EE_2$) on short term growth in patients with Turner's syndrome. To investigate whether there is a similar phenomenon in boys, we evaluated the 3-week ulnar growth velocity (TUG) following the administration of different doses of $EE_2$ to boys with delayed adolescence. Basal TUG was determined in 5 prepubertal or early pubertal boys (Tanner stages I-II), ages 13 to 15 years. Subsequently, the boys received a 4-day i.v. infusion of $EE_2$ at each of 3 doses, 4, 20 and 90 μg/day, given double blind in a randomized sequence. The TUG was determined before and after each infusion, and was allowed to return to baseline before giving the second and third infusions. Results (mean ± SE) are shown in the Table.

| DOSE $EE_2$ | BASAL | 4μg | BASAL | 20μg | BASAL | 90μg |
|---|---|---|---|---|---|---|
| TUG(mm/3w) | .45±.11 | 1.38±.51[a] | .49±.11 | 1.0±.4 | .46±.1 | .84±.12 |
| $E_2$ (pg/ml) | <8 | 10±2.3 | <8 | 16±2.3 | <8 | 96±12 |
| Sm-C(U/ml) | .98±.12 | 1.21±.15 | 1.04±.37 | 1.41±.27[b] | .94±.11 | 1.24±.12[b] |

a $p<.05$ compared to basal value. b $p<.01$ compared to basal value.

We observed an inverse relationship between $EE_2$ dose and the increase in TUG. Mean TUG increased following all $EE_2$ infusions, but was significantly higher after the 4 μg/day $EE_2$ infusion. In contrast, somatomedin-C levels were significantly higher after the 20 and 90 μg/day $EE_2$ infusions. We conclude that small amounts of estrogen can stimulate ulnar growth in boys and may play a role in the male pubertal growth spurt.

## 477 USE OF NATIVE LHRH IN THE TREATMENT OF PRECOCIOUS PUBERTY.

Richard A. Noto, Maureen S. Rosati, Vinod Lala, Samuel S. Kasoff, Bruce Roseman and Ayse M. Yuceoglu. New York Medical College, Westchester County Medical Center, Dept. of Pediatrics, Valhalla, NY 10595

Long-acting LHRH analogues are known to be effective in the suppression of precocious puberty. We used native LHRH administered subcutaneously via a portable infusion pump in an 18-month old male infant with precocious puberty secondary to a hypothalamic tumor. The hormonal data in relation to the therapeutic management is summarized in the table below.

Table I: LHRH Treatment

| Week | testosterone ng/dl | FSH miu/ml | LH miu/ml | LHRH Stimulation Peak FSH | Peak LH | LHRH dose μg/kg/day |
|---|---|---|---|---|---|---|
| 0 | 650 | 0.5 | 8 | 6.9 | 46 | 0 |
| 2 | 250 | 1.0 | 5 | - | - | 5 |
| 4 | 134 | 1.0 | 2 | 4.0 | 10 | 10 |
| 6 | 240 | <1.0 | 10 | 3.0 | 19 | 10 |
| 10 | 292 | 5.0 | 14 | - | - | 15 |
| 12 | 433 | 6.9 | 13 | 10.0 | 39 | 25 |

The paradoxical rise in testosterone after almost full suppression can be explained on the basis of needle dislodgement because of the increased activity in this patient's age group. From our experience, we conclude and recommend that if LHRH analogues are not available to suppress puberty then native LHRH might be given provided it can be administered continuously.

## ● 479 IDENTIFICATION OF CALMODULIN IN HUMAN AMNION: ROLE IN PROSTAGLANDIN SYNTHESIS.

David M. Olson, Daniel P. Kramar and Zofia Smieja (Spon. by A. Keith Tanswell). Univ. Western Ontario, The Research Institute, St. Joseph's Hospital, Department of Paediatrics, London, Ontario.

Prostaglandin $E_2$ ($PGE_2$) production by human amnion increases with the onset of labor in women and may initiate myometrial contractions at term. Amnion $PGE_2$ synthesis is $Ca^{2+}$-dependent, but the intracellular mechanism of $Ca^{2+}$ action is obscure. The possibility that the intracellular $Ca^{2+}$ mediator, calmodulin, plays a role in $PGE_2$ biosynthesis was explored.

Calmodulin-like activity was identified in both the supernatant (cytosol) and pellet (microsomes) fractions of the 105,000xg amnion homogenate as assessed by their ability to stimulate the activity of cAMP phosphodiesterase (PDE). The activity of cytosol protein was greater consistently than that of microsomal protein in paired samples. Removal of $Ca^{2+}$ from the incubation medium by the $Ca^{2+}$ chelator, EGTA, decreased cytosol protein-stimulated PDE activity to basal levels. Three structurally different calmodulin inhibitors, trifluoperazine (TFP), calmidazolium and W7 each inhibited cytosol protein-stimulated PDE activity. The 50% inhibitory concentrations were: calmidazolium (0.11uM), TFP (6.7uM) and W7 (24.0uM). Basal $PGE_2$ output by dispersed amnion cells was inhibited also by calmidazolium and TFP (calmidazolium > TFP) but not by W7. The $Ca^{2+}$ ionophore, A23187 (10uM), stimulated $PGE_2$ output, and this was inhibited by TFP. It is concluded that human amnion contains calmodulin which may mediate, in part, $Ca^{2+}$-dependent $PGE_2$ biosynthesis.

Supported by Canada MRC.

## ● 480 ADRENAL CORTICAL FUNCTION IN CHILDREN WITH HYPOPITUITARISM SUGGESTS ACTH IS THE PITUITARY ADRENAL ANDROGEN STIMULATING TROPIC HORMONE

S. Pang, A. Legido, L.S. Levine, M.I. New, Dept Pediatr, New York Hosp-Cornell Med Ctr, New York 10021; Universidad De Zaragoza, Spain

Baseline and ACTH stimulated (40U IV infusion for 360 min) serum concentrations of deoxycorticosterone (DOC), cortisol (F), androstenedione (Δ4-A), dehydroepiandrosterone (DHA), DHA-sulfate (DS), and aldosterone (aldo) in prepubertal children with isolated growth hormone deficiency (N=5) and in children with two or more pituitary hormone deficiencies (def) without ACTH def (N=5) were similar to those of normal prepubertal children whose age matched to bone age of hypopituitary children. However in children with two or more pituitary hormone def including ACTH def (N=5) there was a markedly low response of DOC, F, Δ4A, DHA and DS to ACTH stimulation but normal response of aldo. Hormonal response to ACTH stimulation in hGH treated hypopituitary children did not differ from the untreated hypopituitary (Hyp) children. Thus, adrenal androgen secretory function is normal in children with multiple or single pituitary hormone def providing ACTH secretion is normal, while in ACTH deficient hypopit children, adrenal androgen secretion is very low. These data suggest that ACTH is the tropic hormone involved in the maturation of adrenal androgen secretion.

| | | ACTH STIMULATED SERUM STEROIDS | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | DOC | F | Δ4-A (ng/dl) | | DHA (ng/dl) | | DS (μg/dl) | | Aldo |
| Group | (n) | (ng/dl) | (μg/dl) | <7yrs | >7yrs | <7yrs | >7yrs | <7yrs | >7yrs | (ng/dl) |
| nl (7-17) | | 288±149 | 46±13 | 51±20 | 59±37 | 90±59 | 120±84 | 22±18 | 86±16 | 30±16 |
| Hyp, nl ACTH | (10) | 185±81 | 39±7 | 33±19 | 165±84 | 52±6 | 443±106 | 18±26 | 135±25 | 25±6 |
| Hyp, ACTH def | (5) | 104±45* | 24±5* | - | 18±7* | - | 23±29* | - | 6±2* | 20±11 |

*$p<0.05$ - 0.001 compared to normal or hypopit with normal ACTH