189 EFFECT OF NALTREXONE, AN OPIATE ANTAGONIST, ON SERUM SOMATOMEDIN VALUES IN PREGNANCY.

Ilene Fennoy, Robin Marks-Kaufmann, Guy E. Barbato, Alisa Siegfield. College of Physicians & Surgeons, Columbia University, Institute of Human Nutrition, New York, NY.

The effect of naltrexone, a long-acting opiate antagonist, on pregnancy was studied by implanting Alzet osmo-minipumps on day 5 of gestation in Sprague-Dawley rats. The pumps contained either 100 mg/ml naltrexone hydrochloride in 0.9% saline delivering 5.6 mg/kg/hr of drug for a period of 14 days, or saline only. Somatomedin activity was determined on serum obtained from individual mothers, and on pooled blood from fetuses. Delivery occurred under ether anesthesia. Blood was collected by decapitation. A competitive protein binding assay using Multiplication Stimulating activity(MSA) as previously described by Moses, et. al(Endo,104:536,1979) was used to determine somatomedin activity. Samples were chromatographed on Sephadex G50 in 1M acetate to remove binding protein before assay. Maternal somatomedin activity was lower in drug treated animals (MD) = 28.0+ 51.3 (n=5) than in controls (MC) = 337+ 51.3ng/ml (n=5), p=.069. Fetal somatomedin acivity of control animals measured 3778+ 3785 (n=2) vs. 3148+ 1454ng/ml (n=2) in those that were drug treated. Maternal weight gain was also unaffected (MC=114.0+ 14 vs. MD=116.3 + 23.9g). However, drug treated animals had food intake decreased to 80% of control during the first week after pump implantation.

These data suggest that naltrexone impairs maternal somatomedin production without affecting fetal outcome. Studies are in progress to determine if this effect could be due to the alterations in food intake seen.

190 LONG TERM THERAPY OF PRECOCIOUS PUBERTY WITH THE SUPERACTIVE LH-RH ANALOGUE D-TRP-6-LH-RH.

R. Kauli, O. Kalter-Leibovici, A.V. Schally, A.M. Comaru-Schally, B. Szoke & Z. Laron, Beilinson Medical Center, Sackler Faculty of Medicine, Tel Aviv University, Israel & Tulane University Medical School, New Orleans, USA.

Five girls and one boy with precocious puberty have been treated for 2-4 yrs with D-TRP-6-LH-RH (0.45-1.5 mcg/kg/day s.c.). LH and FSH secretion assessed by LRH tests remained suppressed in 4 patients; in 2 "escape" FSH responsiveness was observed after 1½ and 3 3/4 yrs of therapy. In all girls E2 levels remained in the prepubertal range (< 20 pg/ml) with occasional transient increases up to 53 pg/ml. In the boy testosterone levels dropped from 245 to 45 ng/dl on starting therapy and starting 1½ yrs later showed some increase (mean testosterone during 3rd year of therapy: 88.11+36 ng/dl). Clinically all showed sustained arrest of gonadarche with adrenarche unaffected; 2 girls required additive antiandrogen therapy. In all growth slowed to prepubertal rate and the BA/CA was decreased, indicating an improved final height prognosis. There were no undesirable side effects and all patients showed good compliance. It is concluded that at present therapy with superactive LH-RH analogue is the treatment of choice for precocious puberty.

191 PLASMA LEVELS OF D-TRP-6-LH-RH (DECAPEPTYL) AFTER INTRAMUSCULAR INJECTION OF LONG-ACTING MICROCAPSULES IN CHILDREN TREATED FOR PRECOCIOUS PUBERTY (PP).

Najiba Lahlou, Marc Roger, Pierre Canlorbe, Jean L. Chaussain, Françoise Raynaud, Jean E. Toublanc and Andrew V. Schally. Fondation de Recherche en Hormonologie and Hôpital Saint Vincent de Paul, Paris, France, and Veterans Administration Medical Center, New Orleans, La, USA.

The efficacy of periodic administration of Decapeptyl microcapsules upon symptoms of PP has been previously reported (Roger et al., ESPE meeting 1984, abstract 22). A sensitive radioimmuno assay of the analogue was developped using an antiserum raised in rabbit which exhibited unsignificant cross reactivity with native LH-RH or LH-RH fragments (Mason-Garcia et al.,Proc.Natl. Acad. Sci., USA, in press). Iodinated D-Trp-6-LH-RH was used as a tracer. Fifty µl antiserum diluted at 1/2500, 50 µl tracer, 100 µl standard (or unknown plasma), 100 µl plasma pool (or phosphate buffer 0.01 M, pH 7.5) were incubated for 24 h. Free and bound were separated by PEG. NSB of the plasma pool and of 40 different child samples were respectively 6.2± 0.4 and 6.3± 0.4% (mean±SD). Bo was 20%. Intraassay CV were 12 and 7% for mean plasma levels of 100 and 370 pg/ml respectively. The detection limit was 57 pg/ml. Five children received intramuscularly (IM) on days 1, 21 and every 28 days thereafter, 1.5 mg Decapeptyl microcapsules. Plasma levels were on days 3, 7, 14, and 21 (pg/ml, mean±SEM) 312±57, 242±65, 145±78 and 171±87. Decapeptyl was undetectable in most of samples on day 28 after injection. This study demonstrates that significant Decapeptyl levels are maintained for at least 21 days after a single IM injection.

192 β-HUMAN CHORIONIC GONADOTROPIN (β-hCG) PRODUCED BY A GRANULOSA CELL OVARIAN TUMOR CAUSING PSEUDOPRECOCIOUS PUBERTY.

Mauricio Llano, Jaime Urdinola, and Alfonso Vargas. Hospital Infantil Universitario and Universidad del Rosario, Facultad de Medicina, Dptos. de Pediatría, Bogotá, Colombia.

Production of β-hCG is commonly seen in non-gestational choriocarcinoma and considered a specific hormonal marker of this kind of neoplasm. More rarely ovarian germ cell tumors have been described producing β-hCG. A 4 11/12 yr old girl had a 2 yr long history of abdominal pain, bilateral breast development for 5 months and vaginal bleeding for 9 days. Examination showed a well developed girl with a height 112 cms, weight 21 kg (both at the 85th percentile), evidence of gonadarche (breast development Tanner 4, estrogenization of the external genitalia and vaginal bleeding), and no evidence of adrenarche (absent pubic hair= Tanner 1, not axillary odor nor hair). A large abdominal mass 15x20 cms was palpated. Bone age was 5 6/12 yrs. Pielography and ultrasound exams were consistant with an ovarian cystic mass. At laparotomy a 13x8x7 cms right ovarian cystic multiloculated tumor removed. By punction a citrine clear fluid was obtained which contained the following hormones: β-hCG >2,500 mIU/ml, LH 2.9 mIU/ml, FSH 2.0 mIU/ml, estradiol 220 pg/ml, progesterone 40 ng/ml, 17-OHprogesterone >12 ng/ml, DHEA.SO_4 54 ng/dl, and prolactin 9.8 ng/ml. The left ovary and uterus were reported "normal". Histology was that of a granulosa cell tumor. All the abnormal clinical findings disappeared. We conclude: 1- The estrogen production of this tumor was the cause of the pseudoprecocious puberty, 2-This neoplasm had a self stimulatory mechanism by producing β-hCG, and 3- β-hCG is a potential hormonal marker for some types of granulosa cell tumors.

193 CATECHOLAMINE EXCRETION IN PRECOCIOUS PUBERTY.

Jorg Winterer, Ora Pescovitz, Saul Malozowski, Gordon Cutler, Jr., DEB, NICHD, NIH, Bethesda, MD 20205

Catecholamine excretion, when corrected for creatinine excretion, decreases throughout childhood, reaching adult levels at age 15. To explore the hypothesis that the pubertal process may play a role in this decrease we measured catecholamine and vanillylmandelic acid (VMA) excretion in 24 hour urine samples from 39 normal children (N) and from 42 children with precocious puberty (PP). The results (mean ± SEM), grouped according to age and pubertal stage, are shown in the Table:

	Catecholamine (mg/gm creat./d)			VMA (mg/gm creat./d)		
Age	Normal	PP	P	Normal	PP	P
2-6	107 ± 7	81 ± 13	<0.05	8 ± .5	6 ± .5	<0.01
6-10	82 ± 4	64 ± 3	<0.01	9 ± .9	5 ± .3	<0.01
Stage						
I	96 ± 5	85 ± 13	NS	8 ± .5	7 ± .6	NS
II	63 ± 5	77 ± 7	NS	5 ± .7	6 ± .3	NS
III	57 ± 4	64 ± 7	NS	5	5 ± .4	NS
IV	45 ± 4	50 ± 6	NS	4 ± .4	5 ± .4	NS

Children with precocious puberty had significantly decreased catecholamine and VMA excretion compared to age-matched normal subjects. Catecholamine and VMA excretion in PP decreased with increasing pubertal stage, mirroring the pattern seen in normal puberty.

We conclude that puberty is associated with a decreased urinary catecholamine and VMA excretion and that children with precocious puberty have urinary catecholamine and VMA excretion that is decreased for age but appropriate for pubertal stage.

194 VARIABLE SECRETORY HORMONAL PATTERNS IN A PATIENT WITH MC CUNE-ALBRIGHT SYNDROME, LARGE OVARIAN CYSTS AND PRECOCIOUS PUBERTY

Jürgen H. Brämswig*, G. Schellong*, H.J. v. Lengerke*, E. Nieschlag* (Intr. by W.v.Petrykowski). University of Münster, Department of Pediatrics and Max Planck Research Group.

Precocious puberty (PP) in girls with Mc Cune-Albright syndrome has been attributed to autonomous ovarian function and premature activation of the hypothalamo-pituitary-ovarian axis. We report the clinical and hormonal findings in a 5 2/12 year old girl with Mc Cune-Albright syndrome, large ovarian cysts and PP. She initially presented with extremely elevated E_2- (1473 pmol/l) and suppressed LH- (11 ng/ml) and FSH-levels below the detection limit. 8 months after initiation of cyproterone acetate therapy, an intravenous LHRH-test showed LH- (56 and 324 ng/ml, basal and stimulated) and FSH-levels (6.8 and 12.6 ng/ml) well in the pubertal range. 23 days later complete suppression of gonadotropins again was demonstrated.
We suggest that the mechanism of PP in girls with Mc Cune-Albright syndrome might involve intermittent activation of the hypothalamo-pituitary axis followed by apparently autonomous ovarian function.