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HEIGHT VELOCITY STANDARD DEVIATION SCORES IN 105 PRE-PUBERTAL CHILDREN RECEIVING EITHER BECLOMETHASONE DIPROPIONATE OR BUDESONIDE

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Objective - To determine whether any difference in height velocity exists in pre-pubertal asthmatic children on equivalent doses of two commonly used inhaled steroids. *Setting* - a large asthma clinic in a Children's Hospital serving a population of approximately 1 million as a tertiary centre. *Subjects* - 105 asthmatic children attending the clinic known by early age or as a result of specific examination to be pre-pubertal; having no other growth-limiting condition: on no other steroid preparation at the time of observation eg. nasal sprays: not on regular oral steroids though, rarely, some had short courses to deal with exacerbations of their asthma; receiving only one of the drugs considered immediately before and throughout the period of observation. *Main outcome measures* - height velocity measured by a single trained observer on a wall-mounted stadiometer over a period of 6 to 18 months; reported dose of steroid taken at each appointment and averaged for the period of observation. *Results* - Multiple regression analysis demonstrates that both height velocity was reduced in both groups (mean HVSDS for group receiving beclomethasone -0.775: for group receiving budesonide -0.35). The effect is significantly more marked with beclomethasone ($p<0.05$). Beclomethasone demonstrates increasing growth suppression with increase in dose. *Conclusion* s- Growth can be affected at low doses of inhaled steroids and the effect may increase with increases in beclomethasone dose . No dose related effect was seen with budesonide.

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TESTICULAR FUNCTION IN PREPUBERTAL AND PUBERTAL PATIENTS WITH VARICOCELE. S. Gottlieb, M. Podestá, R. Medel, H. Chemes, G. Ropelato, E. Quesada and C. Bergadá. Divisions of Endocrinology and Urology, Hospital de Niños R. Gutiérrez, Buenos Aires, Argentina.

Fifty two patients with unilateral varicocele, aged 8 to 19 years were studied and grouped in 5 Grades of Puberty. Basal plasma testosterone (T), LH and FSH before and after GnRH administration were measured in all patients. Testicular histology was studied in 14.

	Grade 1 n=10	Grade 2 n=7	Grade 3 n=14	Grade 4 n=10	Grade 5 n=11
LH (B) IU/L	1.57±0.86	2.31±1.39	2.01±1.03	2.20±0.80	3.51±2.81
LH (Mx) IU/L	9.62±6.73	30.4±28.7	20.0±8.43	18.7±6.92	21.1±11.0
T. ng/dl	37.3±17.8	115 ±37.9	340 ±140	405 ±153	620 ±212
T. Vol. Right(ml)	2.40±0.56	4.21±1.07	8.57±1.50	15.5±3.43	20
T. Vol. Left (ml)	1.95±0.49	3.57±1.27	5.82±1.46	11.7±3.80	13.4±2.50

Prepubertal control (n=6) LH(B):< 1.00, (Mx):4.81±1.07.
Pubertal control (n=5) LH(B): 1.68±0.68, (Mx): 14.9±3.65.
Testosterone control ng/dl G1(n=10): 22.8±9.50; G2(n=6): 91.8±41.2; G3(n=9): 144±37.4; G4(n=6): 492±222; G5(n=3): 645±168.
Microscopical examination revealed normal development of germinal epithelium according to the grade of puberty. These results demonstrated that patients with varicocele have a tendency to increase LH and T secretion probably secondary to a metabolic disturbance induced by a higher intratesticular temperature detected even before puberty. FSH and germinal function remained normal, suggesting that small testicular volume could be due mainly to the abnormal metabolic interstitial process than to a seminiferous tubule damage.

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CORTICAL ADRENAL TUMORS IN INFANCY:PROGNOSTIC VALUE OF PCNA/CYCLIN VERSUS TUMOR WEIGHT. I. Bergadá, S. Maglio, H. Chemes & C. Bergadá. Division of Endocrinology, Hospital de Niños R. Gutiérrez,Argentina.

Controversy exists to determine which variable is a reliable predictor of clinical outcome of adrecortical tumors in children. We analyzed retrospectively 17 patients with functional adrenal tumors, and assessed their clinical outcome by comparing tumor weight,classical histologic features and percentage of proliferating cell nuclear antigen (PCNA)/cyclin in their tumor cells in order to delineate which variable correlates best with clinical outcome. Ten patients had Cushing Syndrome and 7 a pure Virilizing Syndrome. Mean age at diagnosis was 5.5±4.3 years(range 0.4-14). Thirteen patients with a benign course have been followed for 10.1±4.3 years(range 3.5-18). All these patients but one(185 gr) had a tumor weight of less than 100 gr(mean 60.8±52 gr). Two patients had a malignant course,one died 5 months after surgery with metastasis and the other presented lung metastasis 18 months after surgery. Their tumor weights were 1000 and 780 gr respectively. All the histology parameters such as cellular pleomorfism,neocrosis,calcifications,capsular and vascular invasion, were randomly found in all patients and did no correlate with clinical outcome. In the former 13 patients staining with PCNA/cyclin was found in 16±25% of the tumor cells(median=15, range=0 to 90%); the two who had malignant course had values of 60 and 70%. We found a positive correlation between tumor weight and PCNA/cyclin($r=0.60$, $p=0.015$). Our data shows that PCNA/cyclin could be a further aid to predict clinical behavior on these infrequent tumors althought the occasional presence of small tumors with high PCNA/cyclin values, indicates that this parameter should not be used alone.

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NITRIC OXIDE: A POTENTIAL MODULATOR OF ADRENAL HORMONE SECRETION. P. A. Zimmerman, J. A. Betz, and M. Poth. Department of Pediatrics, Uniformed Services University of the Health Sciences, Bethesda, MD 20814, and Walter Reed Army Medical Center, Washington, DC 20307, USA

Nitric oxide (NO) is a novel and exciting compound with activities in many biologic systems, playing roles in neurotransmission, in immune system activation, and as endothelial derived relaxation factor. Tumor necrosis factor (TNF) is believed to exert many of its effects by the elaboration of NO. The enzyme that catalyzes the production of NO, NO synthase, has been identified in the adrenal gland but its function there is not known. Arginine analogs such as N-monomethyl-L-arginine (L-NMMA) have been used as competitive inhibitors of NO synthase to investigate effects of NO. We have previously reported that TNF inhibits ACTH-stimulated glucocorticoid secretion, and we hypothesized that NO may mediate this effect of TNF. To test this hypothesis, we measured ACTH-stimulated corticosterone (CS) secretion from rat adrenal cells after 1 hour incubation with and without TNF in the presence or absence of 1 mM L-NMMA. Results are expressed as % baseline ± SEM (*$p<0.01$, control v L-NMMA).

	without ACTH	ACTH 300 pg/ml		
	without TNF	without TNF	TNF 100 pg/ml	TNF 300 pg/ml
Control	100.1±4.0	591.9±69.5	327.2±11.8	360.6±19.0
L-NMMA	100.2±2.3	619.4±95.8	627.0±73.7*	695.5±40.5*

Inhibition of NO production did not affect basal or stimulated CS secretion, but L-NMMA blocked TNF inhibition. These data implicate NO as a second messenger of TNF effect in the adrenal gland. This may have important implications in adrenal regulation, as the amount of glucocorticoid secreted may be dependent not only on ACTH but also the relative amounts of TNF and NO at any given time. This mechanism of control could be particularly relevant in states of immune activation such as Gram negative sepsis, in which TNF and NO are known to be elevated.

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RELATIONSHIP BETWEEN SEX STEROIDS AND BODY FAT IN OBESE GIRLS M. Wabitsch, E. Heinze, R. Benz* and W. Teller, First Department of Pediatrics and *Department of Gynecology, University of Ulm, D-7900 Ulm, Germany

Obesity is associated with increased production rates of androgens and estrogens as well as with increased peripheral conversion of androgens to estrogens. Aim of this study was to investigate the relationship between serum sex steroid concentrations and body fat distribution in 92 obese girls, age 15.1±0.7 (14.5-16.8) years, BMI 31.2± 4.5 (24.0-44.0) kg/m^2, all PH 5. Waist and thigh girths were measured to determine the distribution of body fat. Girls were divided into three subgroups according to tertiles of their waist-to-thigh ratio (WTR). Girls with abdominal obesity (WTR>1.33)(O1) had higher levels of estradiol (E_2)(82.4±28.3 vs 51.7±25.3 pg/mL), testosterone (T)(0.67± 0.22 vs 0.52±0.23ng/dL), androstenedione (2.02±0.52 vs 1.73±0.49μg/L), and DHEAS (4.22±1.52 vs 3.62±1.55mg/L) and lower levels of SHBG (6.66±4.23 vs 14.07±9.97ng/dL) than girls with gluteal-femoral obesity(O2)(all $p<0.05$,independent of BMI and % body fat). Interestingly, T/E2 was lower in O1 than in O2 ($p<0.01$) suggesting increased aromatization of T to E_2 in abdominal fat depots. In a linear regression analysis WTR correlated significantly with all the variables, BMI only with SHBG. During a 6-week regimen the girls lost 8.3±2.3 kg and reduced their body fat from 39.1±3.5 to 35.6±3.6%. In O1 but not in O2 WTR was reduced after weight loss (1.46±0.09 vs 1.51±0.10, $p<0.01$) indicating a preferential loss of abdominal fat. After weight loss E_2, T, DHEAS were reduced and SHBG and T/E2 were increased in O1 ($p<0.01$) with only minor changes in O2. These data show that the sex steroid profile in obese adolescent girls is more dependent on the distribution of body fat than on its total amount. Girls with abdominal obesity, easily detectable by measuring WTR, have higher E_2 and T levels but lower T/E_2 than girls with gluteal-femoral obesity.

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GONADAL FUNCTION AFTER BONE MARROW TRANSPLANTATION (BMT) FOR ACUTE LEUKEMIA: THE IMPACT OF HYPERFRACTIONATED TOTAL BODY IRRADIATION (TBI) BEFORE PUBERTY K. Sarafoglou, F. Boulad, C. Sklar. Memorial Sloan-Kettering Cancer Ctr, The New York Hosp-Cornell Med Ctr, NY, NY 10021 USA

There is only limited information on gonadal function after bone marrow transplant (BMT) during childhood. The existing data is based primarily on the use of single dose or fractionated total body irradiation (TBI). In the present study, we evaluated gonadal function in 33 patients (18 females, 15 males with ALL, n=18 and AML, n=15), treated with hyperfractionated TBI before puberty. Median age at diagnosis was 4.8 years (0.4-11.2 yrs), median age at BMT was 7.3 years (3.8-11.5 yrs) and median age at last evaluation of gonadal function was 17.1 years (9.3-22 yrs). Transplant cytoreduction consisted of hyperfractionated TBI (125 cGy TID for total dose of 1375 to 1500 cGy) and 120 mg/kg of Cytoxan; male patients received an additional 400 cGy testicular boost. Fifteen of 33 patients had received cranial irradiation as part of previous treatment of their underlying disease (1000-2400 cGy) but none of the males had received testicular irradiation. Five of 15 boys had elevated baseline LH, 9 of 15 had elevated baseline FSH, and 2 of 15 had elevated LH and low testosterone requiring testosterone treatment to complete pubertal development. Fourteen of 18 females had elevated baseline levels of LH and/or FSH; nevertheless, 8 females experienced spontaneous menarche at a mean age of 12.7 years (9.4-15.8 yrs). All 8 patients including 4 with elevated LH/FSH have regular menses. One female presented with precocious puberty. Eight of 18 females have required hormone replacement therapy. In conclusion, our data suggests hyperfractionated TBI results in preservation of Leydig cell function in males, while the incidence of germ cell dysfunction in males and ovarian failure in females appears to be similar to that reported after single dose or fractionated TBI.