443 DIURNAL VARIATION IN PLASMA CONCENTRATIONS OF SOMATOMEDIN C (SmC) IN CHILDREN. Allen W. Root, Alfonso Vargas and Catherine Livingston. Univ. South Florida

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In order to determine if plasma SmC levels fluctuate, this peptide was measured (Nichols Institute, San Pedro, CA) at 12 hour intervals (9-10 am, 9-10 pm) for 12-48 hours in 18 children (12 boys, 6 girls; 3-18 years) without organic endocrine dysfunction. At consecutive 12 hour intervals [SmC] were:

Time	PM(6)	AM(16)	PM(16)	AM(16)
$\bar{X}$	0.70	0.41	0.66	0.47
SEM	± 0.08	± 0.05	± 0.07	± 0.07

In this population the mean evening concentration of SmC (0.67 $\pm$ 0.06 U/ml; N=22) was significantly ($p < 0.01$) higher than the morning SmC value (0.46 $\pm$ 0.04 U/ml; N=37). In children with psychosocial deprivation or constitutional delay in growth and development associated with suboptimal nutrition, morning concentrations of SmC were often low, while evening values were normal. In two GH deficient children and one with bioinactive GH, SmC concentrations were low at all times. Diurnal variation in SmC concentrations was not observed in patients with gonadal dysgenesis (N=2) and hypogonadotropic hypogonadism (N=2). Conclusions: 1) There is a diurnal variation in plasma concentrations of SmC; SmC levels are higher at night than in the morning; 2) The diurnal variability in SmC values may be useful in distinguishing patients with low SmC concentrations not due to hypopituitarism from children with GH deficiency.

444 A COMPARISON OF INTRAMUSCULAR AND SUBCUTANEOUS INJECTIONS OF GROWTH HORMONE. Libbie J. Russo and Wayne V. Moore, University of Kansas Medical Center, Department of Pediatrics, Kansas City, Kansas

In the treatment of growth hormone deficiency, human growth hormone (hGH) injections are given intramuscularly (IM) since subcutaneous (SC) injections are considered to be immunogenic. We have demonstrated that antibody formation is likely secondary to aggregated hGH and individual susceptibility. Since GH preparations in the U.S. now contain $< 5\%$ aggregated hGH, we have compared the integrated hGH concentration, growth response, antibody response, and pain associated with either IM or SC injection of hGH.

Thirteen age-matched children received either IM or SC injections at a dose of 0.1 U/kg. The peak serum hGH concentration was not significantly different between IM and SC injections (38.6 and 41.8 ng/ml for IM and SC, respectively). The SC group had a significantly larger integrated growth hormone concentration ($p < 0.05$) SC being 125.1 ng/ml and IM being 92.5 ng/ml. Subsequent growth velocity measurement on a standard dose of 0.1 U/kg (maximum 2 U/kg) 3 times a week were identical (8.16 cm/yr). The antibodies to hGH was similar in both groups. There was one compliance problem in the IM group and none in the SC group. Subjective questioning of parents revealed an increased amount of pain and apprehension in the IM group over the SC group.

We conclude that there is no difference in peak value, growth velocity or antibody formation between the IM and SC groups. The lack of pain, ease of administration and the higher integrated hGH concentrations suggests that SC injection of hGH might be the preferred route of administration in GH deficiency.

445 RENIN-ALDOSTERONE (R-A) RESPONSES IN A BOY WITH DEFECTIVE RENAL K^+ EXCRETION. S. Sauder, R.P. Kelch, R.J. Grekin and R.C. Kelsch. Univ. of Mich., Depts. of Ped. and Int. Med., Ann Arbor, Michigan.

Hyperkalemia and acidosis were found in an asymptomatic 13/10/12 year old boy during evaluation of short stature and delayed adolescence (HA&BA=10 yrs). Renin activity was not evaluated in two similar reported cases. We studied the R-A system during changes in posture and diet to evaluate the effects of primary hyperkalemia. Hyperkalemic hyperchloremic metabolic acidosis was documented (Na 139, K 7.1, Cl 116, CO_2 19 mEq/l). Cortisol, thyroxine, GH and FSH/LH secretion were normal as well as inulin and PAH clearance. Urinary K^+ excretion was low when compared to the elevated serum K^+ , both before and after Na_2SO_4 infusion. Plasma renin activity (PRA) was low (Na^+ 120 mEq/day-supine(S) 0, upright(U) .06 ng/ml/hr). Although appropriate for normokalemic subjects, serum aldosterone was low for the degree of hyperkalemia (Na^+ 120 mEq/day-S 18, U 39 ng/dl). During Na^+ restriction PRA remained low, serum K^+ rose to 8 mEq/l, and the patient became tachycardic and hypotensive. After chlorothiazide treatment, electrolyte abnormalities corrected and PRA increased (S 3.2, U 7.8 ng/ml/hr). Our studies support the hypothesis that renal K^+ excretion is defective. These alterations in R-A responses may be attributed to the effects of hyperkalemia. Although it suppresses PRA, hyperkalemia directly increases aldo and thus partially compensates for decreased renin-angiotensin stimulation. We speculate that low PRA and resultant low angiotensin II caused decreased vascular tone, decreased Na^+ retention and the patient's symptoms during Na^+ restriction. CRC grant 5M01RR42

446 ENDOCRINE FUNCTIONS DURING CARDIAC SURGERY IN HYPOTHERMIA. Heinrich Schedewie, Astrid Seifen, Joycelyn Elders, Louis Pryor, Thomas Hart, Doyne Williams.

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Hyperglycemia and hypocalcemia frequently complicate open heart surgery (OHS) in hypothermia (HOTH). We have studied 21 children (8wks-6yrs) before, during, and after OHS in HOTH and determined serum glucose (G), insulin (IN), growth hormone (GH), calcium (Ca) calcitonin (CT), and thyroid concentrations:

	Baseline	Pre-Cooling	Re-Arrest	Re-Warming	Normo-thermia	1 Hour off pump
Temp., °C	37°	23°	15°	23°	37°	37°
G(mg/dl)	120	165	185	265	180	175
IN(uU/ml)	18	20	15	18	57	25
GH(ng/ml)	10	22	21	45	65	5
Ca(mg/dl)	9.1	8.3	7.0	7.8	10.0	10.5
CT(pg/ml)	21	15	18	25	17	18

IN conc. were suppressed during HOTH with an attendant increase in serum G levels. During rewarming, IN rebounded rapidly but transiently, suggesting insufficient hormone reserve. Ca declined during HOTH, but increased with rewarming. CT showed no variation with changing body temp. or Ca conc. GH increased with HOTH and post-arrest rewarming, but returned to normal within one hr of surgery. Preliminary thyroid studies suggested decreasing TSH and T4 with HOTH, which returned to baseline upon rewarming. CONCLUSION: OHS in HOTH is associated with profound endocrine changes. Their understanding may greatly aid in the management of OHS patients and improve surgical outcome.

447 GENETIC ASSOCIATION AND LINKAGE IN CONGENITAL ADRENAL HYPERPLASIA DUE TO 21-HYDROXYLASE DEFICIENCY. Douglas O. Sobel, James P. Gutai, William Smith, Diane

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Twenty-eight families of patients with congenital adrenal hyperplasia due to 21 hydroxylase deficiency (21 OH def.) were studied to evaluate specific HLA antigen association with the disease, & to further investigate the HLA linkage to 21 OH def. gene. The association of 21 OH def. & the HLA A3 antigen was established ($p < 0.01$) in our 28 affected families, & in combined reports of 54 families of North American-West European descent. In 23 unaffected siblings of children with 21 OH def., there was a significant correlation ($p < 0.01$) between the biochemical & HLA determined genotype assignments, providing further evidence of 21 OH def. gene linkage to the HLA complex. However, in one family, we detected the first case of recombination between the 21 OH def. gene & the HLA-B locus. Studies in this family suggest that the 21 OH def. gene is located between the HLA-B and glyoxylase loci. In addition, this suggests that in the genotype assignment of high risk families, both the hormonal and HLA methods of detection should be used.

448 INTERACTIVE EFFECTS OF ACTH AND GROWTH HORMONE ON ADRENOCORTICAL HORMONE SECRETION. Edna H. Sobel, Barnett Zumoff, Albert Einstein College of Medicine,

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The effects of ACTH and growth hormone (GH) on adrenocortical hormone secretion were studied in a 13-year-old girl with GH and thyrotropin deficiency but normal ACTH function. Cortisol secretion was measured by the sum of the urinary excretions of tetrahydrocortisol (THF), allotetrahydrocortisol (ATHF), and tetrahydrocortisone (THE). Adrenal androgen secretion was measured by the sum of androsterone (A) and etiocholanolone (E). The patient took a constant daily dose of desiccated thyroid (150 mg) during 5 successive periods: 3-day control, 3 days of I.M. ACTH (0.5 mg/kg daily), 12-day post-ACTH control, 6 days of I.M. human GH (3.5 mg daily), and 3 days of ACTH + GH at the previous doses. Control excretion of THF + ATHF + THE was 6.0 mg/g creatinine and of A + E was 2.9 mg/g creatinine; these values confirm normal endogenous ACTH function. Taking these levels as 100, excretion of cortisol and androgen metabolites rose to 240 and 190 respectively during ACTH and decreased to 107 and 105 respectively during the last 3 days of the post-ACTH control period. During the GH period, they fell to 66 and 72 respectively. When ACTH was added to GH, they rose to 170 and 103 respectively. Thus GH given alone depressed secretion of both cortisol and adrenal androgens; this could be due to depression of endogenous ACTH secretion or to interference with the effect of ACTH on the adrenal. The data from the combined GH-ACTH period are compatible with either mechanism.