343 THE ROLE OF AGGREGATED hGH IN THERAPY OF hGH DEFICIENT CHILDREN, Wayne V. Moore (Spon. by Cheng Cho), University of Kansas Medical Center, Department of Pediatrics, Kansas City, Kansas 66103.

These studies were designed to define the growth promoting and immunogenic potential of aggregated hGH contained in clinical grade hGH[1] used in the therapy of hGH deficient children. Samples of clinical grade hGH were fractionated into aggregated and monomeric components by Sephadex gel filtration. The absorbance at 280 nm of the gel filtration fractions indicated that various lots of clinical grade hGH contained between 38.4-60.9% polymeric hGH (P1), 29.6-12.8% dimeric hGH (P2) and 26.3-43% monomeric hGH (P3). The radioimmunoreactivity of P1, P2 and P3 was 5, 30 and 100% of an hGH standard, respectively. One group of patients receiving clinical grade hGH (2 U, M-W-F) had growth rates of 1.6± 0.3 and 8.1±0.6 cm/yr before and during therapy, respectively. A second group of patients receiving an amount of P3 (monomeric hGH) contained in 2 U of clinical grade hGH (28.2% P3) had growth rates of 1.6±0.6 and 10.9±0.6 cm/yr before and during therapy, respectively. Antibodies to monomeric hGH were detected in sera of 54% of the first group and in 0% of the second group of patients within 9 months of onset of therapy. We conclude that 1) the growth promoting potential of clinical grade hGH resides solely in the monomeric hGH fraction, and 2) aggregated hGH stimulates formation of antibodies to monomeric hGH during therapy with clinical grade hGH.

[1]Clinical grade hGH was generously supplied by NIAMDD, NIH and National Pituitary Agency.

344 ISOSEXUAL PRECOCIOUS PUBERTY AND HYPERTENSION IN A FEMALE WITH AN ADRENAL ADENOMA. Eleazar H. Noriega, Neville J. Howard, John D. Bailey. Hospital for Sick Children, Endocrine Division, Department of Paediatrics, Toronto.

A 6.4 year old Chinese female, who presented with breast development and vaginal bleeding, was found to be hypertensive on physical examination. Her height was 123 cm. (90th percentile) and weight 25.1 Kg. (85th percentile), blood pressure 155/110 supine. Her breasts were Tanner stage 3 with pigmented areolae. The uterus was enlarged for age. During investigation acne developed on the face but no axillary or pubic hair was present. 24 hr. urine, 17 ketosteroids and 17 hydroxysteroids were 6.1-7.2 mg (<2 mg) and 6.8-7.1 mg(<5.6 mg) respectively. Urine pregnanetriol was 0.7 mg/24 hr. and Compound S 5.4 mg/24hr. Dexamethasone suppression test was negative. Serum testosterone was 35.3 ng/dl, androstenedione was 352 ng/dl, and estradiol 9.5 ng/dl. FSH was <2.5 and LH 2.5 mIU/l. Serum electrolytes were normal and plasma renin activity values were low. Urine aldosterone was elevated. A left adrenal tumor was identified by computerized axial tomography and arteriography. After left adrenalectomy with a well encapsulated adenoma, the child became normotensive, the 24 hr. urine for 17 KS. and 17 OH. were 1.2-2.8 mg. and 2.3-2.4 mg. respectively. Pregnanetriol was < 0.1 mg/24hr; compound S was 0.8 mg; estradiol <3.0 ng/dl. and testosterone <9 ng/dl.

This patient is the first described case of an adrenal adenoma producing female isosexual precocity and hypertension with laboratory confirmation of estrogen, androgen, and mineralocorticoid hypersecretion.

345 TREATMENT OF DIABETIC KETOACIDOSIS (DKA) WITH CONTINUOUS LOW-DOSE INSULIN INFUSION. Michael Nussbaum, Cyril A.L. Abrams, Robert Rappaport & I. Ronald Shenker, Sponsored by Philip Lanzkowsky. School of Med., Health Sciences Center, State Univ. of New York At Stony Brook and Long Island Jewish-Hillside Medical Center, Dept. of Pediatrics, New Hyde Park, New York.

Continuous low-dose insulin infusion was employed in 14 children aged 5 to 18 years with DKA based on the method of Kaufman et al. (J. Pediatr. 87:846, 1975). Regular insulin 0.1 unit/kg was given initially by IV push, followed by 0.1 unit/kg/hr by continuous infusion, piggybacked into the non-glucose containing rehydrating fluid. When blood glucose fell to 300 mg%, 5% dextrose was substituted and when it reached 250 mg% the insulin infusion was discontinued. If acetonemia persisted, the insulin infusion was continued at a 0.02 to 0.05 unit/kg/hr until acetonemia cleared.

Initial blood glucose levels ranged from 310 to 945 mg% and fell at a mean rate of 82.6 mg%/hr and normoglycemia was achieved 2.0 to 13.5 hrs after onset of treatment. When acetonemia persisted it was not accompanied by acidemia. No patients developed hypokalemia or hypoglycemia.

This method has several advantages over the traditional large-dose insulin regimens: (1) the rate of fall of glucose is steady and predictable (2) the risk of hypoglycemia and hypokalemia is minimized (3) clinical and metabolic recovery is rapid. Our findings also support the view that insulin resistance is not a characteristic feature of DKA.

346 END ORGAN UNRESPONSIVENESS TO MINERALOCORTICOID HORMONES. Sharon Oberfield, Lenore Levine, Robert McVie, Robert Carey, and Maria New, Cornell Univ. Med. Col., New York, and Univ. Virginia Hosp., Charlottesville.

End organ unresponsiveness to aldosterone (aldo) in the kidney, colon, sweat and salivary gland was demonstrated in a 7 m.o. male infant who suffered recurrent episodes of severe salt-wasting and hyperkalemia. On a very high sodium intake (250 meq/d) he continued to waste sodium and manifested hyperkalemia (K+ 7.0 meq/l) unless dietary K+ was restricted. These abnormalities in electrolyte balance were observed in the face of very high plasma aldosterone often exceeding 500 ng/dl. Blood pressure measured 80/40 mmHg. Sodium wasting was documented in urine, sweat, and saliva. Administration of aldo, (0.6 mg/6 hr by infusion) did not result in conservation of Na+ by salivary glands or kidney. Colonic-rectal electropotential also did not change. Administration of 9αFF in doses as high as 3 mg/d was ineffective in producing changes in urinary, salivary or sweat Na+ and K+ concentration. Plasma aldo remained markedly elevated (586.6 ng%) and the elevated plasma renin activity did not suppress.

This patient represents the first report in which unresponsiveness to mineralocorticoids with excessive loss of Na+ and decreased excretion of K+ has been demonstrated in the kidney, colon, sweat and salivary glands. Since this patient probably has defective mineralocorticoid receptors in the major sodium conserving organs, the only therapy possible was administration of sodium to compensate for total sodium loss. This therapy is compatible with life and improved development.

347 ENDOCRINE FUNCTION IN THALASSEMIA. Gertrude Costin, Jorge A. Ortega, Carol B. Hyman, Maurice D. Kogut, Dept. of Pediat. Childrens Hospital of Los Angeles, USC Sch. of Med., Los Angeles, Calif.

Endocrine function was evaluated in 16 patients 5-28 yrs old on high transfusion therapy for 1-7 yrs. Growth hormone responses to insulin-induced hypoglycemia (ITT) and/or arginine were normal in 13/14. Serum TSH ranged from <1.7-8.2 μU/ml (normal <5); Adj T4 (RIA) was low in one and normal in the others; T3 (RIA) was elevated in 2 and normal in 8/10. Morning ACTH ranged from 21-118 pg/ml (normal 15-100) and cortisol (F) from 7.2-27.8 μg/dl. Peak F level after ITT and Cosyntropin (0.25 mg i.m) were normal (>18 μg/dl) in 8/13 and 16/16 respectively. Urinary 17 ketogenic steroids after Metyrapone were normal in 10/13. In 5 patients puberty occurred between 16-20 yrs; 1/5 developed secondary hypogonadism (LH and FSH < 2.0 mIU/ml, testosterone 50 ng/dl). In 5 patients, 18-26 yrs old with bone age > 14, LH and FSH were < 2.0 mIU/ml; 2/5 had a normal rise in gonadal steroids following human chorionic gonadotropin (1000 U x 10). Parathyroid hormone (PTH) ranged from 29-89 μlEq/ml, calcium and phosphorus from 8-10 and 2.8-5.6 mg/dl respectively. One patient had hypocalcemia and required vit D (PTH not measured). Glucose tolerance (OGTT) was normal in 6 patients and abnormal in 9. Of those with abnormal OGTT 4 developed insulin-dependent diabetes.

The data suggest that patients with thalassemia have: 1) pituitary/vs hypothalamic dysfunction with gonadotropin deficiency and possibly reduced ACTH reserve 2) primary gonadal failure and 3) increased incidence of chemical and insulin-dependent diabetes.

348 THYROID ABNORMALITIES IN TWENTY CHILDREN WITH TURNER SYNDROME. G.S. Pai, D.C. Leach, L. Weiss, C. Wolf and D.L. VanDyke. Henry Ford Hospital, Department of Pediatrics, Endocrine Research Laboratory, and Cytogenetics Laboratory, Detroit.

Hashimoto thyroiditis, Addison disease, and diabetes mellitus occurs with a greater than normal frequency among patients with Turner syndrome. Most studies demonstrating this have been of patients over 20 years old. Therefore, 20 pediatric patients with Turner syndrome were recalled to obtain subjective and objective data reflecting thyroid function. Thyroxine (T4) and thyroid-stimulating hormone (TSH) were measured in serum samples by radioimmunoassay, and the serum antithyroid antibody titer (Thab) obtained by the tanned red cell agglutination method. Hypothyroidism was diagnosed in the presence of a decreased T4 and an elevated TSH. Hashimoto thyroiditis was presumed when a hypothyroid patient had an elevated Thab.

Ten patients with Turner syndrome had structural abnormalities of the X chromosome. Three were hypothyroid, four had elevated serum Thab titers, and one had a goiter and low T4 without other evidence of thyroid dysfunction. Ten patients with Turner syndrome did not have structural abnormality of the X chromosome. None of these were hypothyroid, although five were considered to be at risk by virtue of an elevated serum Thab. One of these had a goiter. The Thab titer was elevated in nine of 15 patients over 10 years old, but in only one of five under 10 years. The three hypothyroid patients were over 10 years of age.

Screening of children with Turner syndrome for evidence of thyroid dysfunction is clearly indicated.