76 G.E. RICHARDS and R.N. MARSHALL, JR.* Dept. of Ped. , Univ. of Tex. Med. Schl. at Houston, P.O.Box 20708, Houston, Tx. 77025. Relationship between zinc and growth hormone (GH) in GH deficient children.

Previous studies suggest that GH may increase daily zinc requirements to meet the demands of growing bone and to replace increased urinary losses. Since zinc is a necessary cofactor in many enzymes concerned with growth, we tested the hypothesis that zinc might be a limiting factor in the response of children receiving GH replacement. 8 patients with GH deficiency were followed for GH induced changes in urine and serum zinc during acute (0.3 IU/kg/day x 5 days) and chronic replacement (0.1 IU/kg tiw). Zinc was measured in hair collected every 3 months. Zinc sulfate (220 mg/day) was given to half the patients during the second year of treatment. No significant changes in zinc concentration were observed with GH treatment: (all values mean±SEM)

	Pre-Rx	5 days Rx	6 mos Rx	12 mos Rx
Serum ug/dl	107±13	92±8	122±22	82±6
Urine ug/mgCr	0.6±.02	0.74±0.06	0.7±0.01	0.65±.06
Hair ng/mg	148±15		165±29	144±12

There was no evidence of zinc deficiency, and zinc supplements did not enhance growth response to GH during the second year. We conclude that GH treatment in children does not alter serum, urine or hair zinc, and zinc availability does not appear to be a limiting factor in the treatment of GH deficiency.
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Identifying the academic and emotional difficulties associated with short stature.

To determine if children with growth retardation are at greater risk for academic and emotional problems than those of normal stature, we compared twenty-five children of normal intelligence with constitutional short stature or growth hormone deficiency to a control group with normal height matched for age, sex and socio-economic status. On the Child Behavior Checklist, 44% of the short children scored in the 90th percentile or higher on the overall index of behavioral difficulty, a level typical of children referred for mental health services. Our patients had specific elevations on indices of somatic complaints, schizoidal tendencies, obsessive-compulsive traits and depression. They also had a disproportionate incidence of excessive clowning (45%), being teased (65%), unhappiness (48%), and underachievement (41%). Another striking finding was that the children had a high prevalence of grade retention, 28% having repeated at least one grade, in spite of having normal intelligence (mean full scale IQ = 105.3, S.D. 14.9). Furthermore, 30% of the subjects had a verbal IQ that was 20 or more points higher than the performance score, a discrepancy occurring in only 10% of the population. In conclusion, short children seem to be at increased risk for developing academic and emotional difficulties.

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Erythrocyte insulin binding studies in growth hormone deficiency.

Growth hormone (GH) is known to induce insulin resistance, although the mechanism of this action is poorly understood. To investigate whether GH or somatomedin (SM) may alter insulin binding at the cell surface receptor, we have studied in GH deficient (GHD) children the effect of acute and long-term GH therapy on erythrocyte insulin receptor binding (IRB). Fifteen GHD, ages 2-13 years, were evaluated before treatment, after short-term high-dose GH (2 mg bid x 7d), and long-term maintenance GH therapy (2 mg tiw x 2-12 mo). IRB was measured after fasting (16 hrs) and feeding (4 hrs). Fasting IRB was similar in GHD, control children and adults: 8.2±2.4, 7.4±2.4, and 8.2±2.3%, respectively. Corresponding concentrations of serum glucose were 78, 88, 82 mg/dl, those of insulin 12.2±3.4, 17.3±3.4, 11.2±2.8 µU/ml. There was no change of IRB in GHD with feeding vs fasting or short-term high-dose (7.3±2.9) vs long-term maintenance GH therapy (7.0±3.1). GH increased (<2 ng/dl to 22±4.3 ng/dl) and SM (0.36±.20 to 1.3±35 U/ml). A significant inverse correlation was noted between IRB and body weight:height ratios. Those patients with high weight: height ratios had elevated fasting insulin levels (>20 µU/ml), but very low IRB (3.1±1.2). IRB after GH treatment increased only in those patients in whom therapy was associated with a decrease in body weight:height ratios, suggesting IRB may be related more to changes in body fat than circulating GH or SM concentration.

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Academic achievement problems as a function of specific cognitive deficits in idiopathic hypopituitary dwarfs.

Intelligence testing (Wechsler Scales) and academic achievement testing (Wide Range Achievement & Peabody Individualized Achievement) were completed on 33 school-aged hypopituitary dwarfs with isolated growth hormone deficiency and 11 with multiple deficiencies.* Significant Verbal-Performance discrepancies (> 15 points) characterized the cognitive test pattern for 45% of the isolated group compared to an expected frequency of <15% in the normal population. Academic achievement was below grade level in 80% of the boys with V-P discrepancies compared to minor achievement problems in girls. Patients with multiple hormone deficiencies had significantly lower IQ's (Mean Full Scale = 79) than the isolated group (Mean Full Scale = 99). Academic achievement in the multiple group was commensurate with lower intelligence. These data suggest that (1) a difference in overall intellectual functioning may exist between children with isolated growth deficiency and children with multiple pituitary deficiencies and (2) poor academic achievement may be a function of specific cognitive deficits rather than secondary to low self-esteem and reduced parental expectations as suggested by previous investigations.
* 6 additional children with multiple deficiencies are being tested.

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Effect of chronic renal failure on insulin,GH,thyroid hormone,gluco- and mineralocorticoid,ACTH and gonadotropin levels.

Symptoms suggesting hormone disorders are frequently observed in uremic children. Hence endocrine studies were performed in 2 groups of azotemic patients. In group I (n=11,age 2.7-17.5 years, serum creatinine 3.1 ± 0.7 mg/dl) basal serum insulin levels were increased, peak insulin values after oral glucose load were higher and markedly enhanced following arginine infusion compared to normal controls. Nevertheless carbohydrate tolerance was impaired in 4 patients. Basal GH levels and peak values following arginine infusion were significantly above normal.TRH exerted no effect on GH levels.Markedly decreased T_3 values were found,T_4 and basal TSH levels were unchanged,but TSH response to TRH was delayed.Diurnal plasma aldosterone levels correlated closer with the extent of hypertension than with the degree of uremia.Normal baseline plasma cortisol values with normal diurnal fluctuation were found,but cortisol increase following insulin-hypoglycemia was reducted.Basal ACTH plasma levels were elevated,but ACTH response to insulin-hypoglycemia was impaired.LH-RH injection led to normal or above normal LH and FSH values.- Group II was studied during hemodialysis: n=10,age 6.1-17.3 years,serum creatinine prior to dialysis 10.5± 0.9 mg/dl. Higher basal levels of GH,insulin and ACTH were present. During hemodialysis ACTH,cortisol and insulin concentrations were increased.Despite high blood glucose GH levels were not suppressed. There was no definite change in TSH values during hemodialysis.

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Next year's growth (NYG) and all further growth (AFG) of short and tall children with RUS bone ages of 12 years and over.

How much will a child have grown this day twelvemonth, and when growth ceases? Longitudinal height and RUS BA data were used to calculate NYG and AFG for 49 HGH-treated hypopituitary children and 47 tall girls with or without oestrogen treatment. Centile standards for height velocity against RUS BA were derived from van Venrooij-IJsselmuiden (1978). As in normal children the highest NYG occurred during year following BA 11.0-11.9 in all groups of female patients and after BA 12.0-12.9 in males. In HGH-girls NYG varied from P50 to P10 at different BA's when puberty was spontaneous, and was below P10 in girls with gonadotrophin deficiency. In both types of HGH-boys NYG fluctuated around P50. In tall girls oestrogen treatment reduced NYG from P50-values to values at or below P10. AFG was calculated for 10 female and 10 male HGH-patients, and for 14 oestrogen-treated and 4 untreated tall girls. In HGH-girls with spontaneous puberty and in untreated tall girls average AFG values dropped sharply in one BA year from over 9 cm at BA 13.0-13.9 to less than 4 cm. In HGH-boys a comparable fall in AFG occurred following BA 14.0-14.9. Gonadotrophin deficient HGH-girls had very low AFG values, 5 cm at BA 12.0-12.9, 2 cm one BA year later. In tall girls high dose oestrogen treatment reduced AFG to 5 cm at BA 13.0-13.9. Results indicate growth potentials, relative to RUS BA at pubertal ages.