425 EFFECTS OF TESTOSTERONE ON ZINC METABOLISM IN RATS. Mariano Castro-Magana, Sanda Clejan, Shang Y. Chen, Vaddanahally T. Maddaiah, and Platon J. Collipp. Nassau Cty Med Ctr, SUNY, Stony Brook Health Sciences Ctr, Dept. of Ped., E. Meadow, NY 11554.

We have measured Zinc (Zn) levels in different tissues of castrated rats (CR) fed purified diet containing 100 pp Zn for 6 wks with and without injection of testosterone (T) enanthate (20 mg IM) 2 wks prior to sacrifice. CR had very low serum T (0.6 ± 0.1 ng/ml) as compared with the controls (8.2 ± 0.7 ng/ml) and T administration restored serum T to normal levels (9.1 ± 1.1 ng/ml).

	Serum Zn (mcg%)	Hair Zn (mcg/g)	Liver Zn (mcg/g)
CONTROL (15)	261 ± 23.8	250.7 ± 16.3	57.1 ± 4.5
CR (17)	146.7 ± 16.0	164.0 ± 9.0	35.7 ± 5.4
CR + T (18)	215.9 ± 39.0	270.0 ± 20.0	47.8 ± 9.7
	Pancreas Zn (mcg/g)	Jejunum Zn (mcg/g)	Urine Zn (mg/g creat)
CONTROL (15)	57.9 ± 9.7	41.2 ± 12.3	1.8 ± 0.5
CR (17)	38.9 ± 8.7	27.8 ± 9.8	2.1 ± 1.1
CR + T (18)	50.6 ± 8.5	35.7 ± 3.2	1.43 ± 0.3

After castration, serum and tissue Zn levels were significantly decreased with concomitant increase in urinary Zn (see Table). Administration of T to CR increased the serum and tissue Zn levels almost to the normal level. Since food intake was similar in all groups, T in CR may have increased Zn retention. These results strongly suggest a positive relationship between Zn and T metabolism.

426 HORMONES AND ZINC. Mariano Castro-Magana, Platon J. Collipp, Thulasi Cheruvanky, and Shang Y. Chen. Nassau Cty Med Ctr, SUNY, Stony Brook Health Sci Ctr, Dept. of Ped., E. Meadow, NY 11554.

We have shown that children with constitutional growth delay (CGD) have reduced zinc concentration (Zn C) in hair (160.6 ± 31.0 ug/g) and that oral testosterone (T) administration resulted in raising the Zn C (189.2 ± 10.4 ug/g). Furthermore, a linear relationship between serum T and hair Zn C (r=0.65) was found. Zn supplementation to children with low hair Zn C produced a marked improvement in their growth hormone (HGH) responses to standard stimuli and in their rates of growth, suggesting an influence of Zn in HGH synthesis or release. To further understand these relationships between Zn and hormones we have measured hair Zn C and urinary zinc excretion (U Zn E) in 30 children with HGH deficiency (HGH-D) before and after HGH administration (0.1 u/kg) three times a week x 3 months) and in 26 children with juvenile diabetes mellitus (JDM). Children with HGH-D and JDM had a significant lower hair Zn C (HGH-D: 147±32, JDM: 141±31 ug/g) than age-matched control children (185±23 ug/g). Following HGH administration to HGH-D children there was an increase in the hair Zn C (168.7±36.1 ug/g) with concomitant decrease in the U Zn E (514±170 ug/g creat. before, and 353±162 ug/g creat. after). U Zn E in children with JDM (1449±550 ug/g creat.) was markedly increased in spite of the lower hair Zn C. These results suggest that the anabolic hormone status (HGH, insulin, testosterone) is directly related to the zinc nutritional status.

427 IMPROVING GROWTH HORMONE RESPONSE WITH ORAL ZINC THERAPY IN RUSSELL-SILVER DWARFISM. Ziaadin Ghavami-Maibodi, Mariano Castro-Magana, Sanda Clejan, Shang Y. Chen, Vaddanahally T. Maddaiah, and Platon J. Collipp. Nassau Cty Med Ctr, SUNY, Stony Brook Health Sci Ctr, Dept. of Ped., E. Meadow, NY 11554.

Growth hormone deficiency has been reported in 10-20% of Russell-Silver dwarfs. Two siblings with all the classical features of Russell-Silver Syndrome were low in growth hormone (insulin-arginine stimulation test), and blood and hair zinc (Zn). They received 50 mg elemental Zn orally each day for 2 months and 50 mg weekly for 4 more months. Growth hormone and Zn determinations were repeated at 6 months:

	GH PEAK (ng%)		ZINC LEVELS	
Patient A	Insulin	Arginine	Hair (µg/gm)	Blood (µg%)
Before	11	20	94.7	80.7
After	29	31	175.0	140.0
Patient B				
Before	12.7	20	114.8	66.2
After	20.5	20.5	173.7	125.0

It appears there is a direct relationship between the growth hormone response and Zn nutritional status. We have data indicating that growth hormone therapy increases hair Zn and decreases urinary Zn in children with growth hormone deficiency. These two children provide new data indicating that there are patients whose growth hormone production is affected by their Zn nutritional status.

428 THERAPEUTIC INSULIN LEVELS FOR CHILDREN WITH DIABETES John I. Malone, Allen W. Root. University of So. Fla. College of Medicine, Dept. of Pediatrics, Tampa, FL.

Measurement of serum insulin levels by RIA in insulin dependent diabetes (IDD) is limited by interfering antibodies. Total circulating insulin (TI) can be measured after acidification of the serum to release bound insulin and treatment with polyethylene glycol (PEG) to remove binding proteins. Treatment with PEG before dissociation allows measurement of free insulin (FI). TI and FI did not correlate with the administered dose (U/kg) in 64 IDD. FI was present 24 hrs. after the first dose in 12% (7/61) of IDD taking twice a day insulin and 38% (76/202) of IDD taking a single dose. Circulating TI did not correlate with either coexistent fasting plasma glucose (FPG) or hemoglobin A_{1c} (HbA_{1c}). However, the FI levels for those with FPG <200 mg/dl and HbA_{1c} <8% were significantly greater than levels found in association with FPG >200 mg/dl and HbA_{1c} >8%. Five IDD youth had FI determined every 1 to 4 hrs. throughout 24 hrs. FI levels associated with FPG <150 mg/dl after an 8 to 10 hour fast were 20 to 30 µU/ml. Plasma glucose levels <150 mg/dl were achieved during the fed state with FI levels of 40 to 60 µU/ml. Ten IDD children with measurable TI (202.3±69µU/ml) had no measurable FI and moderate to large urine ketones. Forty of 196 children were noted to have moderate to large acetone in the first morning urine and had no FI. Ketosis is associated with absence of circulating FI even in the presence of supraphysiologic levels of bound insulin. The quantity of circulating FI is an important determinant for effective metabolic control of IDD.

429 INFANTILE HYPOGLYCEMIA DUE TO GLUCAGON DEFICIENCY. Peter Mamunes (spon. by Harold Maurer), VCU - Medical College of Virginia, Dept. of Pediatrics, Richmond,VA.

The course of the female infant herein presented indicates that glucagon (G) deficiency was the cause of severe hypoglycemia; only two such causes (from Europe) have previously been described. She presented acutely at age 5 mos. with an abnormal cry, inspiratory stridor, a blood sugar (BS,mg/dl) of 30, and serum insulin (I,µU/ml) < 5. Subsequently, BS was persistently 15-30 and simultaneous I = < 5-10. Growth hormone, cortisol, catecholamine, and thyroxine were normal and there was no ketoacidosis or hepatomegaly. Intravenous (IV) (G) induced a BS rise of 45 in 10 mins. and an I.V. push of alanine (250 mg/kg) did not cause a rise in the BS over a two hour period. After frequent feedings and diazoxide (to 30mg/kg/d) failed to control the BS, a 90% pancreatectomy was performed for suspected hyperinsulinism. The gross and microscopic appearance of the pancreas was normal except that immunofluorescence revealed reduced numbers of α and β cells. Serum G (by RIA after extraction) was undetectable in the only preoperative (pre-OP) value obtained, when BS = 18 and I < 5. Hypoglycemia presisted post-OP, and on two occasions no G was detectable when I was <5 and BS 30. Also, no G was detectable in q15 min specimens x 4 after an IV push of 250 mg/kg of arginine. IV G at 8 ng/kg/min stabilized the BS both pre-and post OP. After failure to respond to diazoxide post OP, nomoglycemia has been maintained with sub Q protamine zinc G (0.5 mg/kg/d in two divided doses) and supplemental carbohydrate feedings. G deficiency as a cause of infantile hypoglycemia should be ruled out prior to pancreatectomy for suspected hyperinsulinism.

430 INCREASE IN CAPILLARY BASEMENT MEMBRANE WIDTH IN PARENTS OF CHILDREN WITH TYPE I DIABETES MELLITUS. ASSOCIATION WITH HLA-DR4. J.F. Marks, P. Raskin and P. Stastny, Departments of Pediatrics and Internal Medicine, Univ. of Tx. Health Sci. Ctr. at Dallas, Dallas, Texas.

Hereditary factors related to HLA antigens play a role in determining risk for development of type I diabetes. Asymptomatic first degree relatives of diabetic patients were investigated to determine whether any abnormalities could be associated with HLA haplotypes. Muscle biopsies were performed to obtain measurements of the width of the capillary basement membranes in 16 type I diabetic children, 16 of their unaffected sibs and 38 parents. Two diabetic children had capillary basement membranes greater than 2000 A and the mean width of the capillary basement membranes was not different in affected compared to unaffected sibs. In contrast, the capillary basement membranes in the parents were considerably larger, with 14 of the 38 parents (37%) having measurements greater than 2000 A. The capillary basement membrane width in the parents correlated with the presence of the antigen HLA-DR4. The mean capillary basement membrane width in DR4+ parents was 2026 + 350; that of DR4- parents was 1642 + 333A. The difference was highly significant ($p < 0.001$). There was no correlation of capillary basement membrane width with HLA-DR3. The data suggests that a risk factor for type I diabetes associated with HLA-DR4 was linked in parents of type I diabetic patients with an asymptomatic increase in capillary basement membrane width in the absence of any clinical evidence of diabetes. The possible role of these abnormalities in pathogenesis of type I diabetes and its vascular complications must be considered.