389 LONGITUDINAL STUDY OF TESTICULAR VOLUME DURING EARLY INFANCY.

Fernando G. Cassorla, Stephen M. Golden, William M. Heroman, Roger E. Johnsonbaugh, D. Lynn Loriaux and Richard J. Sherins. DEB, NICHD, NIH and National Naval Medical Center, Bethesda, Maryland 20014.

In an attempt to correlate possible changes in testicular volume with the rise in gonadotropins and testosterone which occurs during early infancy, we followed the testicular volume of 10 normal infants during the first 5 months of life. Using a calibrated orchidometer with reference beads of 0.5, 1.0, 1.5, 2.0, 2.5, and 3.0 ml, a single observer performed testicular measurements at birth and at monthly intervals thereafter. Infants with hydrocele or undescended testes were excluded from the study. The mean testicular volumes for each side are shown in the following Table:

	Age (months)											
	Birth		1		2		3		4		5	
Side	L	R	L	R	L	R	L	R	L	R	L	R
Mean vol. (ml)	1.1	1.1	1.8	1.6	2.0	2.1	2.1	2.0	1.9	1.8	1.7	1.7
S.D.	0.5	0.3	0.4	0.3	0.4	0.3	0.5	0.4	0.4	0.4	0.3	0.3

The mean testicular volume increased from birth to one month of age, reaching a peak at 2 to 3 months and decreased thereafter. Mean testicular volume at 1 month of age was significantly higher than at birth ($p < 0.0025$), and at 5 months significantly lower than at 2 months of age ($p < 0.05$). We conclude that changes in testicular volume closely parallel the known rise in gonadotropins and testosterone which occurs during early infancy.

390 HORMONAL-METAL ION INTERACTION IN TESTICULAR FEMINIZATION.

Wai-Yee Chan, Kyung W. Chung, Jim Bates, LeAnn Blomberg and Owen M. Rennert. University of Oklahoma Health Sciences Center, Department of Pediatrics, Biochemistry and Molecular Biology and Anatomical Sciences, Oklahoma City, Okahoma.

Testicular feminization syndrome, an X-linked recessive disorder in humans, is caused by the insensitivity of target organs such as testes to the stimulation of androgens. Two animal models are available, the tfm mouse and the tfm rat. In tfm rats abnormal androgen receptor binding and/or defective processing of testosterone occurs. Zinc has been reported to affect dihydrotestosterone-receptor binding in vitro. Our study reports an abnormal testicular zinc level in tfm rats. Copper and zinc concentrations in liver, kidney, adrenals, testes and plasma from tfm and control pairs were determined. Metal contents of the various tissues and plasma of tfm and normal control rats were comparable except testicular zinc which is lower in tfm testes.

	Normal Testes	tfm Testes	Difference
ug Zn/gm wet weight	29.89±4.65	17.16±4.56	s.d. >99%
ug Zn/mg dry weight	0.207±0.029	0.126±0.034	s.d. >99%
ug Zn/mg soluble protein	0.481±0.079	0.291±0.117	s.d. >99%
ug Zn/mg DNA	19.43±2.66	7.85 ±2.97	s.d. >99%

Testicular zinc content is primarily under the influence of luteinizing hormone (LH) whose concentration is higher in tfm rats. The present results support the proposed metal carrier role of steroid-receptor complex and suggest the LH effect on zinc metabolism may be mediated through this complex. These data also suggest that the action of zinc and androgens on normal testicular development is interrelated.

● 391 THE CIRCULATING PARATHYROID HORMONE (PTH) TO CALCITRIOL (1,25OH_2D) RATIO: A MEANS OF EVALUATING CALCITRIOL SYNTHESIS IN DISORDERS OF CALCIUM METABOLISM.

Russell W. Chesney, Alan Hamstra, Hector DeLuca. University of Wisconsin, Departments of Pediatrics and Biochemistry, Madison WI.

The circulating level of calcitriol is often considered abnormal without regard to the factors responsible for calcitriol synthesis: serum Ca, PO_4 and iPTH level. Using a precise assay for calcitriol and an antibody assay for C-terminal and intact PTH, a ratio of PTH to calcitriol was determined in several disorders.

GROUP	Ca(mg/dl)	PO_4(mg/dl)	PTH/1,25-D	N
Control	9.5±0.1 (SE)	3.9±0.1	0.74±.13	14
Mild renal Dx	9.5±0.1	3.9±0.1	0.26±.06	6
Moderate renal Dx	9.7±0.1	4.7±0.5	6.47±1.1*	8
Severe renal Dx	8.5±0.4*	5.5±0.4*	75.4±28.7*	13
Renal Dx & 1,25 Dx	10.0±0.1	4.8±0.2*	8.4±1.3*	24
Hypoparathyroid	7.4±0.2*	7.2±0.6*	0.15±.15*	6
Hypophos rickets	9.5±0.1	3.0±0.1*	2.70±0.6*	11
25OH-D deficiency	8.4±0.2*	1.6±0.4*	3.03±1.0*	4

(*p < .01 from controls). Normal PTH is 20-70 ulEq/ml and normal calcitriol is 43±2 pg/ml.

These data suggest decreased calcitriol synthesis in moderate and severe renal failure, hypophosphatemic rickets with vitamin D_2 and 25OH-D deficiency despite high PTH/calcitriol ratios. Hypoparathyroid subjects have a lower ratio. This ratio demonstrated the influence of calcitriol Rx in patients with renal failure. This ratio may prove useful in evaluating the vitamin D status of a patient, the response to therapy and a better understanding of pathogenic mechanisms.

392 THE CIRCULATING LEVELS OF VITAMIN D METABOLITES IN VITAMIN D DEFICIENCY: THE MEANING OF NORMAL CALCITRIOL (1,25OH_2-VITAMIN D) LEVELS.

Russell W. Chesney, Jerry Zimmerman, Alan Hamstra, Hector DeLuca. University of Wisconsin Medical School, Clinical Science Center, Departments of Pediatrics and Biochemistry, Madison, Wisconsin.

Using a specific vitamin D metabolite assay, the serum levels of various metabolites were measured in 3 children with a history of decreased dietary intake of vitamin D and sun exposure; two had rickets, aminoaciduria and elevated iPTH levels. In some osteomalacic adults, calcitriol levels are said to be normal (Eastwood et al, Lancet 1:1377, 1979; Rasmussen, Am J Med 69:360,1980).

PATIENT	Ca (mg/dl)	PO_4 (mg/dl)	25OH-D (ng/dl)	24,25OH_2D (ng/dl)	Calcitriol	iPTH (ulEq/ml)
1	8.6	2.6	9.3	Not found	52	98
2	7.9	0.8	7.0	Not found	47	82
3	8.4	1.6	5.6	Not found	50	120
normal	9.4-10.2	3.5-5	34±5(SD)	1.71±0.5	43±12	20-70

Despite reduced 25OH-D levels, calcitriol levels are in the normal range. Nonetheless, the combination of hypocalcemia, hypophosphatemia and increased iPTH should result in even higher calcitriol levels. The ratio of PTH/calcitriol is significantly higher in these patients with reduced 25OH-D levels 2.00 vs. 1.06 suggesting actually reduced synthesis of calcitriol in these patients. Non-detection of 24,25OH_2D can be explained by high iPTH and low PO_4 levels rather than reflecting the inability to synthesize this metabolite. The evaluation of vitamin D deficiency should include the measurement of all metabolites.

● 393 THE NATURE OF HYPOTHYROXINEMIA IN SICK PRETERM INFANTS.

Parveen Chowdhry, Richard Auerbach, John Scanlon and Val Abbassi. Georgetown University School of Medicine, Department of Pediatrics, Washington, D.C. 20007.

To evaluate the nature of hypothyroxinemia in small sick preterm infants, the hypothalamic-pituitary-thyroid axis was evaluated by determining the thyrotropin-response to TRH. Preterm infants of gestational ages 26-28 weeks, with T4 < 4µg/dl on two occasions and low TSH (<20µu/ml) were included in a double blind study. Following a TRH test, 20 µg/kg IV babies were assigned to a therapeutic regimen of either T4 (10µg/kg) or placebo. Nine babies were tested prior to therapy, 3 from T4 group and 6 from placebo group. Four babies, 2 from each group were tested 1-2 wks post therapy and 4 were not tested. In untreated babies the baseline TSH of 7.25±1.4 rose to 23.7±4.1µu/ml at 30'. This response was slightly, but not significantly greater than that in full term babies, 23.7±4.1 vs 16.6±0.97, P>0.05. In 2 babies treated with T4, TSH response was completely suppressed. Serial T4 assay showed normalization of T4 in both groups at about the same time interval, 22.9±4.1 vs 23.8±4.9 days, P>0.5. There was no beneficial effect of T4 therapy on head growth 23.0±0.5 vs 31.2±0.6cm, P>0.05, length 42.5±0.6 vs 42.0±0.7cm, P>0.05, weight 1987±100 vs 1951±105gms, P>0.05, or duration of hospitalization 98.8±8.5 vs 110±8.3 day, P>0.05.

In conclusion: hypothroxinemia in sick preterm infants is not caused by hypothyroidism. The physiological pituitary responses to stimulatory effect of TRH and suppressive action of T4 negate such a possibility. Based on these observations routine supplemental T4 therapy in preterm infants with low T4 is unwarranted.

394 HYPERTHYROIDISM IN HYDRALAZINE INDUCED LUPUS.

Chris T. Cowell, C. Phillips Rance, F. John Holland (Spon by Robert M. Ehrlich). Hosp. Sick Child., Dept. Peds.Tor.

Hyperthyroidism is most commonly seen in Grave's disease, Hashimoto's thyroiditis, or following inflammation of the thyroid. We have identified a patient in whom transient hyperthyroidism presented during the acute phase of an Hydralazine-induced lupus erythematous (LE) syndrome. This association has not been previously described. A 15 year old female with pyelonephritis and hypertension on Hydralazine, Propranolol and diuretics presented with a one month history of 20 lbs weight loss, amenorrhea and polyarthralgia. On physical examination: HR 110/min, non-tender, symmetric goitre (3X N), and synovitis of wrists and knees. On investigation: ESR 103, LE Prep positive, DNA binding positive, ANF >1:1280, and complement levels normal. Serum T4 was 17 µgm/dl (N 4-12), total T3 160 ng/dl (N 90-220), T3 resin uptake 37% (N 25-35), TSH <1 µU/ml (N <10). I^{131} uptake was depressed: 2 hrs, 2.1% (N 3-9); 24 hrs, 4.9% (N 5-25). The patient's serum was negative for thyroid stimulating immunoglobulin (TSI), antithyroglobulin and anti-microsomal antibodies. Off Hydralazine, the synovitis rapidly resolved and three months later without anti-thyroid therapy, she appeared completely normal with regain in her weight and reappearance of menses. Her T4 was 5.8 µgm/dl, TSH 4.2 µU/ml. The parallel courses of the LE syndrome and the hyperthyroidism imply a common etiology. Depression of I^{131} uptake and absence of TSI suggest an inflammatory process, while absence of specific thyroid antibodies make Hashimoto's disease unlikely. We conclude that hyperthyroidism may be a feature of the LE syndrome caused by Hydralazine.