325 EXPERIENCE WITH A NEW RADIOIMMUNOASSAY FOR SOMATOMEDIN-C.

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Using a highly sensitive radioimmunoassay (RIA), serum somatomedin-C (Sm-C) concentrations were determined in a variety of clinical conditions. Relative to a pooled serum standard containing 1.0 u of Sm-C activity/ml, levels for normals were lowest in cord serum (0.38±0.05[SEM]u/ml), rose rapidly in early life, and approached adult levels (1.50±0.10u/ml) by 5 years of age. Evidence that the substance measured is growth hormone (hGH) dependent includes the finding that 14 acromegalics had a mean value of 6.28±0.37 u/ml, while 19 hypopituitary children all had levels below 0.2 u/ml. Serum Sm-C concentrations rose significantly in 9 of 10 hypopituitary patients within 12 hours following hGH administration. Four children with psychosocial dwarfism had low Sm-C levels prior to hospitalization and showed significant increases concurrent with accelerated linear growth. Concentrations were normal in 10 patients with achondroplasia (1.19±0.14u/ml) and 7 children with non-hGH deficient dwarfism (1.55±0.50u/ml). Six children with hypothyroidism had a mean level of 0.80±0.23u/ml. The mean serum Sm-C concentration in 4 patients with cortisol excess was elevated (2.6±0.10u/ml). Five patients with protein calorie malnutrition and elevated hGH had low Sm-C levels. In three, significant rises were observed during refeeding. Evidence was obtained that a portion of the activity detected in bioassays and membrane receptor assays is not attributable to Sm-C and is less hGH dependent.

326 SERUM LEVELS OF T4, T3 and TSH DURING THERAPY OF NEONATAL HYPOTHYROIDISM.

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Neonatal screening of over 200,000 infants in Québec by filter paper spot T4 and TSH determinations has detected congenital hypothyroidism in 1/6,000 live births (85% primary). Hypothyroid infants were immediately started on combined L-thyroxine (T4), 25ug daily, and L-triiodothyronine (T3), 5ug TID for 2 wks when the T3 was discontinued and the T4 was increased to 50ug daily. Thereafter the dosage of T4 was adjusted according to serum levels of T4 and TSH or clinically. Serum hormone levels were determined after 2 & 6 wks of therapy, and then every 3 months of age. Results are:

Time	N	Serum Levels (mean±SEM)			Therapy (ug/kg)	
		T4(ug/dl)	T3(ng/dl)	TSH(uU/ml)	T4	T3
0	41	2.2±0.3	91±16	504±62	0	0
2 wk	18	8.7±1.0	324±64	148±79	5.14±.29	3.08±.17
6 wk	14	11.4±1.5	259±34	22±6	8.85±.42	0
6 mos	18	12.7±1.2	157±26	33±13	5.78±.25	0
9 mos	9	10.8±0.9	148±22	39±25	4.96±.20	0
12 mos	9	10.6±1.7	139±37	15±5	6.02±.73	0
18 mos	6	11.8±1.7	167±29	8±2	5.95±.98	0

These data suggest that a minimum T4 dose of 5 ug/kg/day (2.5 times the dose recommended in adult acquired hypothyroidism and 50% that usually recommended for infants) is required to maintain serum T4 above 10 ug/dl and serum TSH below 15 uU/ml. No serious toxicity has developed with this regimen and early clinical progress has been satisfactory.

327 SEXUAL PRECOCITY IN ASSOCIATION WITH SEPTO-OPTIC DYSPLASIA (SOD) AND HYPOTHALAMIC HYPOPITUITARISM.

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Sexual precocity arises frequently from a CNS disturbance but its association with hypothalamic hypopituitarism is most unusual. We report 5 girls with SOD and multiple tropic hormone deficiencies; all were GH and ACTH def. and 2/5 had sexual precocity while 3 were prepubertal and responded to IV GnRH. This finding contrasts sharply with other patients with multiple tropic hormone def. who have severely blunted or absent responses to GnRH. Case 1 diagnosed at 2 mos. with ADH def., presented at 7 4/12 yrs with midpubertal development, menarche, bone age 13.5 yrs, height age 9 yrs, and growth increment of 20 cm/last 2 yrs. GH and ACTH def. were documented by arginine/L-dopa and IV metapyrone tests. Basal serum Prl values were 31-42 ng/ml. Pelvic exam was normal and brain scan showed no mass. Case 2 presented at 16 yrs before GnRH testing was available, with short stature (HA 8 yrs), optic nerve dysplasia and regular menstrual periods since 10 yrs. Case 5 also was ADH def.; only case 3 was TSH def.

Table LH/FSH (mIU/ml) Responses to IV GnRH

Case	1	3	4	5	N1 (n=8)
Age(yrs)	(7 4/12)	(4 mos)	(6)	(5)	(3-7)
Max.	123/16	18/38	14/23	6/13	13 ± 3/44 ± 15
ΔMax.	114/14	12/31	4/20	3/11	11 ± 4/36 ± 13

These interesting cases illustrate selective retention of gonadotropin secretion despite presumed anterior hypothalamic dysfunction. Their congenital anomalies may have resulted in sexual precocity by interference with tonic inhibitory effects of the CNS.

328 REVERSE TRIIODOTHYRONINE/TRIIODOTHYRONINE RATIO: A BIOLOGICAL MARKER FOR GESTATIONAL AGE.

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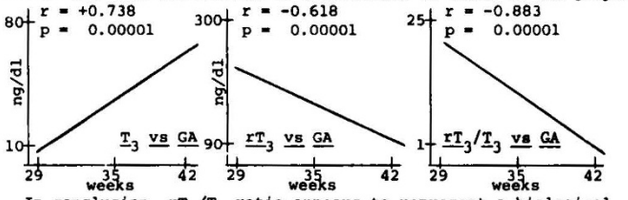
Biological significance of reverse triiodothyronine (rT_3) is yet to be identified. Cord blood values reflect the fetal thyroid state as one of rT_3 excess and triiodothyronine (T_3) deficiency. Postnatally, T_3 levels progressively rise and rT_3 levels fall.

In an attempt to correlate thyroid function and gestational age, TSH, T_4, T_3, and rT_3 concentrations were measured by RIA on 50 cord blood samples. Infant gestational ages (GA) ranged from 29-42 weeks by the Ballard criteria; birth weights from 650-3870 grams.

Results show a significant positive correlation between gestational age, T_3, and T_4, and significant negative correlation between gestational age, rT_3, and TSH. However, the rT_3/T_3 ratio offered the best coefficient of correlation as shown in the graphs



In conclusion, rT_3/T_3 ratio appears to represent a biological marker for gestational age.

329 ADRENAL HORMONES AND HYPOGLYCEMIA IN GROWTH HORMONE (GH) DEFICIENCY.

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The aim of this study was to evaluate the interaction of cortisol (C) and epinephrine (E) in the maintenance of carbohydrate (CHO) homeostasis in hypopituitary and normal children. The synthesis of E from norepinephrine (NE) in the adrenal medulla is dependent on phenylethanolamine-N-methyltransferase whose activity is induced by endogenous glucocorticoids. We hypothesized that recovery of blood glucose during insulin induced hypoglycemia (IIH) might be prolonged in GH-ACTH deficient patients because of reduced E production.

Three groups were studied--Group 1: GH deficient (N=9); Group 2: GH-ACTH deficient (N=5); Group 3: normal controls (N=9). Sequential blood samples were assayed for glucose, GH, insulin, glucagon (G) and C. Urine samples were assayed for E and NE.

	mean C (ug/100 ml)			mean E (ng/ml)			mean G (pg/ml)	
Group	-30(min)	0	+45	Pre	During	Post	-30	+30
1	14.8	10.0	19.0	1.5	15.5	6.2	108	188
2	5.9	5.1	6.1	0.8	8.8	4.8	115	275
3	15.9	10.5	19.8	0.9	16.1	6.4	73	165

Children in Group 2 had lower E and higher G levels in response to IIH. No differences in NE excretion were noted. All groups had similar rates of recovery from hypoglycemia.

Conclusions: In hypopituitary children (1) C and E are not essential for recovery of glucose following acute hypoglycemia or small amounts of these hormones are sufficient to restore CHO balance; (2) G is important in restoring normoglycemia.

330 PSEUDOHYPOALDOSTERONISM IN TRIPLETS,

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Premature female triplets were noted to have poor weight gain, end hyponatremia at age one week. Renal function, cortisols, sweat electrolytes and physical exam were normal. Urinary Na+ losses were initially high despite high plasma aldosterone(A). Hypernatremia, induced by p.c. Na+ supplementation, suppressed (A) and renin(R) transiently in only one of the triplets. They have maintained normal growth and normonatremia on a normal Na+ diet for the past two months, in the presence of high (A) and (R). (See table below):

Age	10 days	2 mos	4 mos	6 mos
Serum Na/K (meq/l)	128 130 128 5.1 7.4 8.7	133 129 132 5.1 5.8 6.0	147 150 140 4.8 5.7 6.0	143 130 138 5.1 5.4 4.6
Na+suppl.p.o.	5meq/kg/d	0 x 72 hrs	8 meq/kg/d	0 x 2 mos
(A) ng/dl	747,649,814	1197,1137,1518	782,812,80	368,318,417
(R)ng/ml/hr	not done	168,152,464	315,155,46	not done

The non-suppressability of (A) and (R) suggests two mechanisms:
1. Primary proximal tubular Na+ loss with compensatory hyperaldosteronism, unlikely alone in the absence of hypokalemia.
2. Partial distal tubular unresponsiveness to (A) which may improve with age and renal maturation. Measurements of (A) and (R) in infants with hyponatremia are necessary to distinguish pseudohypoaldosteronism from other electrolyte imbalances found in infants of low birth weight.