463

CLINICAL RELEVANCE OF THE INSULIN-LIKE GROWTH FACTORS
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We have reviewed our experience with radioimmunoassays of the insulin-like growth factors, IGF-I and II, to determine their utility in the evaluation of short stature. IGF-I and II were measured in normal (NL) (height 5-95%), normal short (NS) (height > 2 s.d. below mean, GH peak < 7 ng/ml) and growth hormone deficient (GHD) children by radioimmunoassay using the NIADDK anti-serum for IGF-I and a specific antibody to the C-peptide region of IGF-II. An age-related boundary for IGF-I and a level of 300 ng/ml for IGF-II were used to classify values as normal or low. Results are given in the table as [low values]/[total per group].

	IGF-I (N=265)	IGF-II (N=263)
NL	10/194 (5%)	9/195 (9%)
GHD	60/65 (92%)	33/59 (56%)
NS	9/10 (90%)	5/9 (55%)

IGF-I is a far better indicator of GHD than IGF-II. Using a criterion of either low IGF-I or II, 62/65 (95%) of GHD cases and 18/195 (9%) of NL would have been identified. 5/7 false positives for IGF-I occurred below age 5 and 4/5 false negatives occurred above age 8. Interestingly, the proportion of low values for both IGF-I and II in the NS group are similar to those observed for the GHD group. We conclude that IGF-I and to a lesser extent IGF-II levels are useful in identifying a child with possible GHD. Our data also demonstrate significant overlap in IGF-I and II levels in GHD and NS children, suggesting that a subset of NS has abnormalities in physiologic GH secretion which are not revealed by provocative testing.

464

TESTOSTERONE (T) BUT NOT OXANDROLONE (OX) INCREASES SPONTANEOUS GROWTH HORMONE (GH) AND SOMATOMEDIN-C (SmC) CONCENTRATIONS IN BOYS WITH CONSTITUTIONAL DELAY OF GROWTH AND ADOLESCENCE (CDGA). Kathleen M. Link, Robert M. Blizzard, Alan D. Rogol, Department of Pediatrics, University of Virginia Medical Center, Charlottesville, Virginia.

The effect of T and OX on GH and SmC concentrations was studied in boys with CDGA. Ten boys received OX (0.1 mg/kg/d) for 65±5 d and 5 boys received T propionate (7.5 mg IM x 7 d) followed by T enanthate (100 mg IM q mo for 3 mo). Serum GH was measured in samples obtained q 20 min for 24 hr before and 65±5 d into therapy. SmC levels were measured twice during the same 24 hr period before and 65±5 d into therapy. The 24 hr integrated concentration of GH (ICGH) was obtained from the mean of 72 samples and compared to that obtained from a pooled sample (p=NS). A pulse of GH was recorded if the peak level rose > 5 ng/ml. We found no differences in the ICGH, in the number of GH secretory episodes, or in the SmC levels in boys treated with OX. However, in boys treated with T there were significant increases in the ICGH, the number of GH secretory episodes and in the SmC levels.

We conclude that testosterone therapy doubles the amount of GH secreted daily, although OX at 0.1 mg/kg/d is without effect. This increase in GH secretion may contribute to the increased growth rate at puberty.

465

CORTISOL LEVELS AND SKIN FOLD THICKNESS IN BPD
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Some babies with BPD, a chronic disease causing significant metabolic stress, have been noted to take on a cushingoid appearance. We postulated that this appearance is a result of stress induced elevated cortisol levels and altered body fat distribution (central/peripheral skin fold thickness). 29 infants were prospectively studied with 8am serum cortisol levels between days 4 to 10 (wk 1) and during weeks 4 and 6. Subscapular, periumbilical, and triceps skin fold measurements (SCF, PUF, and TF) were taken at wks 4 and 6. Central to peripheral fold ratios (SCF/TF and PUF/TF) were calculated. At wk 6, the patients were divided into 4 groups. Gr 1, (N=7) "well infants", $\pm F_{102} < 24$ hrs; Gr 2 (N=2) "non-pulmonary illness", $\pm F_{102} < 24$ hrs + non-pulmonary illness > 48 hrs duration; Gr 3 (N=6) "acute pulmonary illness", $\pm F_{102} < 2$ wks duration, $\pm$ other illness; Gr 4 (N=14) BPD, $\pm F_{102} > 2$ wks duration plus xray signs of BPD $\pm$ other illness. Data are presented as mean $\pm$ S.D.

Group	Cortisol (Mcg/dl)			SCF/TF (mm)		PUF/TF (mm)	
	WK 1	WK 4	WK 6	WK 4	WK 6	WK 4	WK 6
1,2,3	6.9±2.6	7.4±7.4	8.0±6.0	1.1±.13	1.1±.16	.99±.15	.94±.12
1	5.1±4.0	8.4±9.8		1.2±.15		.95±.01	
3	11.3±4.4	5.5±5.4	1.3±6.3	1.1±.10	1.0±.23	.90±.10	
4	7.1±5.8	5.2±4.1	5.3±5.6	1.1±0.2	1.2±.29	.92±.22	.89±.15

Group 2 does not have enough data for statistical analysis. Babies with BPD were compared to all non-BPD babies and groups 1 and 3 alone. Statistical analysis revealed no significant difference, $p < .05$, in cortisol levels or skin fold ratios.

466

CHILDHOOD LEAD TOXICITY IS NOT ASSOCIATED WITH ABNORMALITIES IN SERUM THYROXINE (T₄) CONCENTRATIONS.
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Adult Pb poisoning has been associated with depressed thyroid function (Arch. Intern. Med. 143:220, 1983). We have examined whether Pb poisoned children are also at risk of Pb-associated thyroid dysfunction. 16 children, 6 years of age or less, referred for evaluation of mildly elevated blood Pb (bPb) and erythrocyte protoporphyrin (EP) concentrations (bPb 30-47 µg/dl, EP 56-160 µg/dl), underwent EDTA provocative testing (EPT). All had pre-EPT T₄ measurements performed. 10 children qualified for chelation Rx (uPb ≥ 200 µg/8 hr, and/or, uPb/EDTA ≥ .70). Post-Rx bPb, EP and T₄ measurements were repeated in these children. T₄ was measured by RIA; Pb by atomic absorption spectrophotometry and EP by fluorometry. Pearson product moment correlations were calculated:

Results	T ₄ range	n	bPb/T ₄	EP/T ₄	uPb/T ₄	uPb/EDTA/T ₄
Pre Rx:	9.0-14.7 µg/dl	16	.17	-.23	.15	.30
Post Rx:	9.7-15.0 µg/dl	10	-.54	-.41	-	-

No correlations were found to be significant ($P > .05$). There was no difference in the mean T₄ concentration pre- and post-Rx ($\bar{x}$ = 11.1 and 11.6 µg/dl, respectively) in the 10 treated children. Conclusion: 1) We failed to find a significant effect of mild Pb poisoning ($\pm$ Pb, $\pm$ EPT) on serum T₄ concentrations. 2) These data provide additional evidence to indicate that clinical and biochemical toxicity of Pb differs in children compared to adults.

467

MARSHALL-SMITH SYNDROME: ANDROGEN ABNORMALITIES.
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In 1971 Marshall et al described a syndrome consisting of markedly accelerated skeletal maturation, relative failure to thrive and dysmorphism. Since then 11 cases have been reported. With the exception of an elevated testosterone in a neonatal female, hormonal evaluations have been normal. We present a male with Marshall-Smith Syndrome with abnormal adrenal androgen production. A.S. was noted at birth to have a bone age of 2 yrs. At age 8 mos. the bone age was 6 yrs. Noted were generalized hirsutism, prominent forehead, low set ears, shallow orbits with prominent eyes, small triangular upturned nose, hypoplasia of facial bones, long, tapered fingers, inguinal testes, small scrotum and a penile length of 5¼ cm. The following were normal for age: T₄, FSH, LH, somatomedin-C, testosterone, testicular response to HCG, and androgen receptors in cultured skin fibroblasts. Seventeen hydroxyprogesterone (17-OHP) was elevated (840 ng/dl; nl 30-100) as was androstenedione (67 ng/dl; nl < 50). An ACTH stimulation test was done. A 30 min. increase in 17-OHP of 23.4 ng/dl/min. suggested an adrenal enzymatic defect and hydrocortisone 20 mg/m²/day was begun. The androstenedione decreased to 13 ng/dl and on therapy has remained normal. ACTH stimulation tests were performed on both parents. The 30 min. increase in 17-OHP was elevated in both (father-13.8 ng/dl/min; mother-8.9 ng/dl/min; nl < 6.5 ng/dl/min) suggesting a heterozygous state for congenital adrenal hyperplasia. It is speculated that an inherited abnormality in androgen production may be contributory to the osseous maturation seen in the Marshall-Smith Syndrome.

468

AMINO ACID RESIDUES 93-96 OF THE HUMAN GROWTH HORMONE MOLECULE ARE IMPORTANT FOR POLYCLONAL ANTISERUM RECOGNITION. Wendy J. Maury, Alan D. Rogol, Thaddeus E. Kelly, Christopher Y. Thomas, Departments of Biology, Pediatrics and Internal Medicine, University of Virginia School of Medicine, Charlottesville, Virginia.

The precise regions of the human growth hormone (hGH) molecule that mediate its biologic effects and immunoreactivity are not known. To address this issue, we have introduced mutations into the coding region of a cloned hGH gene and expressed the resulting mutants in a eukaryotic expression vector. Two clones with alterations in the DNA sequences encoding amino acids 93-96 within the hGH molecule were created by the insertion of Bam HI DNA linkers into the Mst II site. The hGH derived from these mutants had characteristics indistinguishable from those of wild type hGH in the NB-2 cell lactogenic assay, the IM-9 cell radioreceptor assay, and in the binding of four anti-hGH monoclonal antibodies. However, significant differences were observed between the mutants and standard human pituitary GH or hGH produced by the normal gene in the binding of polyclonal hGH antisera. Both mutants bound to the polyclonal antibody poorly but did not displace labeled standard hormone in a proportionate manner.

These results suggest that amino acids 93-96 of hGH regulate the expression of antigenic determinants that are detected by polyclonal antiserum, but these determinants are distinct from those recognized by the four monoclonal antibodies that were tested. Moreover, hGH molecules with abnormal immunologic reactivity may retain normal biologic activities in certain assays.