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 < 7ng/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 300ng/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 cri-
terion 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 DE-
LAY OF GROWTH AND ADOLESCENCE (CDGA). Kathleen M. Link, Robert
M. Blizzard, Alan D. Rogol, Department of Pediatrics, University
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The effect of T and OX on GH and SmC concentrations was stud-
ied 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) follow-
ed by T enanthate (100 mg IM q mo for 3 mo). Serum GH was measur-
ed 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 con-
centration 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.

Rx	n	ICGH (ng/ml)		GH Pulses		SmC (U/ml)	
		Pre Rx	Post	Pre Rx	Post	Pre Rx	Post
OX	10	2.9	3.0	4	4.2	0.71	0.76
T	5	3.0	7.2	3.4	6.8	0.91	2.34

We conclude that testerone 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. Sub-
scapular, 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", ↑F₁O₂ <24hrs; Gr 2 (N=2) "non-pulmonary illness",
↑F₁O₂ <24hrs + non-pulmonary illness >48 hrs duration; Gr 3 (N=6)
"acute pulmonary illness", ↑F₁O₂ <2 wks duration, + other ill-
ness; Gr 4 (N=14) BPD, ↑F₁O₂ >2 wks duration plus xray signs of
BPD + other illness. Data are presented as mean + 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	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 AB-
NORMALITIES 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 ar risk of Pb-associated
thyroid dysfunction. 16 children, 6 years of age or less, re-
ferred 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 quali-
fied 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 mo-
ment correlations were calculated:

Results	T4 range	n	bPb/T4	EP/T4	uPb/T4	uPb/EDTA/T4
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
(x̄ = 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 (↑Pb, +EPT) on serum T4 concentra-
tions. 2) These data provide additional evidence to indicate
that clinical and biochemical toxicity of Pb differs in child-
ren compared to adults.

467 MARSHALL-SMITH SYNDROME: ANDROGEN ABNORMALITIES.
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Lawrence J. Fenton) University of South Dakota School
of Medicine, Department of Pediatrics, Sioux Falls.

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 fe-
male, hormonal evaluations have been normal. We present a male
with Marshall-Smith Syndrome with abnormal adrenal androgen pro-
duction. 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 hirsut-
ism, prominent forehead, low set ears, shallow orbits with promi-
nent 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 abnormal-
ity 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 RECO-
GNITION. Wendy J. Maury, Alan D. Rogol, Thaddeus E.
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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 result-
ing mutants in a eukaryotic expression vector. Two clones with
alterations in the DNA sequences encoding amino acids 93-96 with-
in 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 mut-
ants and standard human pituitary GH or hGH produced by the nor-
mal 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 re-
activity may retain normal biologic activities in certain assays.