33 BROMOCRIPTINE USED TO TREAT GIGANTISM IN A TWENTY-THREE MONTH OLD CHILD. L. Lyndon Key, Jr, Sonia Ehrlich, and John F. Crigler, Jr, Harvard Medical School, Department of Pediatrics, Boston, MA, USA

Bromocriptine (1.25 mg BID) was administered orally to a 23 year old asymptomatic female with accelerated growth and a parasellar tumor (tissue type unknown). Other forms of therapy were refused. Length increased from 76 to 95 cm (22 cm/yr) and weight increased from 10 to 16.25 kg between ages 13 and 23 months. Bone age was 2 years at a chronological age of 18 months. Somatomedin C level was 4.3 U/ml (n=2; normal 0.8 to 2.2 U/ml). Thirteen growth hormone values during overnight monitoring averaged 4.7 ng/ml, range 1.8 to 7.9 ng/ml. Suppression to 5.0 ng/ml was seen during an OGTT. Other neuroendocrine functions were normal. No evidence of isosexual precocity was noted. Somatomedin C levels were 3.2, 2.6, 2.5, 2.4, and 2.2 U/ml on days 1 to 5 of therapy, 2.5 U/ml at 14 days and 2.7 U/ml at 56 days. Length increased from 95 to 97 cm (4.8 cm/yr) during the first 5 months of therapy. CT scan at 5 months shows no change in tumor size. The patient remains asymptomatic.

The decrease in levels of somatomedin C associated with a reduction in the growth rate may have resulted from decreased GH production; however, other effects of bromocriptine, such as blocking the peripheral action of somatomedins may be involved.

34 EXPERIMENTAL EVIDENCE FOR CENTRAL NERVOUS SYSTEM CONTROL OF CATCH-UP GROWTH. H. David Mosier, Jr., Regina A. Jansons, Karl F. Swingle, Charles A. Sondhaus, and Lyle C. Dearden. Department of Pediatrics, University of California, Irvine, CA. 92717.

In rats permanent stunting follows neonatal head-irradiation (Head-X); during the post-weaning period full catch-up growth (CU) occurs after fasting (F); failure of CU occurs after cortisone treatment (C); and superimposition of F or C on Head-X results in similar responses in the stunting after Head-X. In this study growth hormone (GH) secretory profiles were determined in rats treated with Head-X, F or C. Superior vena cava blood was sampled at 15 min intervals during the light phase in chronically cannulated undisturbed animals. Sampling duration was 9 h in Head-X, 6 h in F, and 12 h in C. The results, expressed as area units/15 min under the curve of plasma GH concentration vs. time, are as follows:

	(N) X-IRRAD	(N) FAST	(N) CORTISONE
EXPERIMENTAL	(14) 69.5±7.3	(21) 110.6±10.4	(7) 100.9±18.7
CONTROLS	(13) 98.4±11.9	(16) 84.6±10.9	(7) 55.3±7.4
P	<0.025	<0.05	<0.025

Normal pulsatile GH rhythm existed in all three models. The data indicate that GH controls are linked to the CU control. That GH secretion is decreased in Head-X is compatible with the concept that brain injury has reset growth controls for a smaller body size. We conclude that GH release is linked to the putative CU control through a mechanism which senses the discrepancy between actual body size and normal body size for age.

35 CHANGES IN BODY COMPOSITION DURING GROWTH HORMONE THERAPY IN CHILDREN WITH GROWTH HORMONE DEFICIENCY - M. D. Urban, W. C. Chumlea, Department of Pediatrics, Wright State University, Dayton, OH

Ten children with documented Growth Hormone Deficiency had their body composition determined before and during Human Growth Hormone treatment. Body composition was determined by underwater weighing and selected measures of subcutaneous fat thickness. The measurements were obtained before the onset of Human Growth Hormone therapy and subsequently every 6 months during the treatment.

During the first 6 months of treatment, most patient's demonstrated an increase in body fat without significant increase in lean body mass. During the second 6 months and subsequent periods of treatment, a decrease in body fat and increase in lean body mass was observed in most of the patients.

These data tend to indicate that for children receiving Human Growth Hormone therapy changes in body composition are not uniform. Body fat appears to increase in the first 6 months and lean body mass increases during subsequent periods of treatment.

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GROWTH HORMONE RESPONSE TO A STANDARDISED EXERCISE TEST RELATED TO PUBERTY IN SHORT, TALL AND NORMAL CHILDREN.

To investigate the growth hormone (GH) response in children of varying stature to a physiological stimulus, we measured GH (mU/l) before and 10 min after a standardised bicycle exercise test (15 min) in 34 short (Group I), 14 tall (Group II) and 26 children of normal height (Group III). Mean height SDS ($\pm$SD) was different; (Group I -2.7 $\pm$0.55; Group II +2.86 $\pm$0.67; Group III -0.26 $\pm$0.82, $p < 0.0005$). Mean ($\pm$SD) chronological age (yr) was similar (Group I 12.4 $\pm$3.4; Group II 13.6 $\pm$2.0; Group III 13.4 $\pm$3.0), mean ($\pm$SD) bone age (BA, yr) however was delayed in Group I (10.4 $\pm$3.7) compared with Group II(14.1 $\pm$1.3) and Group III (13.4 $\pm$3.1) $p < 0.0005$. Results are expressed as mean $\pm$SEM. Pre-ex. GH was similar (Group I 6.5 $\pm$1.9; Group II 8.9 $\pm$2.6; Group III 9.0 $\pm$2.5). In contrast post-ex. GH was higher in tall (36.6 $\pm$5.5) compared with short (16.6 $\pm$3.1) and normal children (21.2 $\pm$3.5), $p < 0.005$. However, combining the three groups revealed a high post-ex. GH in relation to the pubertal growth spurt independent of height; GH at BA <10 yrs 13.1 $\pm$3.0; BA >10 yrs 25.5 $\pm$2.8, $p < 0.005$: GH at P3P4, 34.7 $\pm$4.5; at P1P2 15.2 $\pm$2.4 and at P5 20.7 $\pm$6.3, $p < 0.0005$). Raised post exercise GH in tall children appears to reflect a normal change in secretion of GH at puberty and this change is also present in short children.

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ASSESSMENT OF SLEEP-ASSOCIATED HGH SECRETION IN NORMAL CHILDREN AND IN ENDOCRINE DISORDERS: Sleep-associated hGH secretion was measured in 28 healthy controls and 218 children with endocrine disorders. HGH was determined every 30 min.through 5.5 hrs. Here only total hGH secretion is reported. Results. 1) In the controls in puberty stage P 1, ($\bar{x} \pm S$) for hGH was 4350 $\pm$ 1134, P 2 5905 $\pm$ 2536, P 3/4 9904 $\pm$ 1710 ng/ml x 5.5 hrs. Evidently, puberty induces a rapid increase of spontaneous hGH-secretion. 2) In 48 children (P 1) with pituitary dwarfism total hGH secretion was 934 $\pm$ 468 ng. 3) In 123 children with constitutional delay of growth and adolescence, total secretion in P 1, P 2 and P 3/4 was reduced by 43; 43; 67 %, resp., compared to controls. Differences were statist. highly significant. Hence, constitutional delay is caused by decreased spontaneous hGH secretion. 4) 6 of 10 children with IUGR showed values within ($\bar{x} \pm 2$ S), 4 values < ($\bar{x}$ - 2 S). IUGR is apparently no uniform disorder. 5) In 24 girls with Turner's syndrome, ($\bar{x} \pm$ S) was 2018 $\pm$ 1240 ng. In 17 girls total secretion was <($\bar{x}$ - 2 S) of the control group. 6) 3 girls with chronic inflammatory diseases under prednisone therapy had a total hGH secretion of 280; 595; 673 ng. Cessation of treatment caused normalization. Evidently corticoids strongly suppress spontaneous hGH-secretion. 7) In 9 children with severe obesity, 5 of them with Prader-Willi-syndrome, total hGH-secretion was 532 $\pm$ 275 ng - with no differences between simple obesity and PWS. Low hGH-secretion in PWS is rather due to excessive obesity than to impaired growth.

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EFFECT OF TRYPSIN AND ANTITRYPSIN ON SPECIFIC BINDING OF HGH TO HUMAN PERIPHERAL MONONUCLEAR CELLS.

A recently described method to investigate hGH receptors on circulating human blood cells has been used to study the effect of trypsin and antitrypsin on hormone binding to mononuclear cells. Trypsinization of cells lead to a considerable decrease of specific binding and of binding affinity (affinity constant after 60 minutes trypsinization 0.5×10^9 M^{-1} versus 1.5×10^9 M^{-1} in untreated control cells). Exposure of peripheral mononuclear cells to antitrypsin activities was followed by a steady increase of affinity and specific binding (affinity constants: with 10 KIU 1.9×10^9 M^{-1}, with 100 KIU 2.4×10^9 M^{-1}, with 1000 KIU 3.6×10^9 M^{-1}). This antitrypsin effect exceeds the binding values expected after blocking trypsin activities in the incubation medium. In a subset of experiments somatomedin-B was used as the antitrypsin moiety and was shown to increase specific GH binding in a similar manner as did antitrypsin (with 1000 ng SM-B affinity constant 12.0×10^9 M^{-1}, specific binding 9.7 % of total radioactivity). It is concluded that enzymatic factors and their inhibitors including partially GH dependent moieties like somatomedin-B modulate GH-induced action by regulating specific GH receptors in GH target tissues.