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COMPAIRING APPLES WITH PEARS.

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GH administration in GH-deficient patients is a well established therapy. At present, a cut-off level of 10µg/l for GH is widely accepted for detection of GH deficiency. But are the available GH assays sufficiently reliable yielding comparable results? For this purpose we have examined 5 commonly used commercial GH assays: 1. PR: Pharmacia RIA, a 2-site IRMA using 2 polyclonal antibodies(AB) - 2. PD: Pharmacia Delphia, a 2-site fluoroimmunometric assay with 2 monoclonal AB.- 3. HY: Tandem-R HGH Hybritec, a 2-site IRMA with 2 monoclonal AB.- 4. SE: Seria hGH Kit Serono, IRMA with 2 monoclonal AB.- 5. ME: hGH-IRMA Medgenix, with several monoclonal AB.

Results: Assay sensitivity was 0.01 µg/l for PD, 0.04 for PR, 0.075 for HY, 0.08 for ME and 0.25 µg/l for SE. The dilution of a plasma containing 20 µg GH/L resulted in a linear decline in GH levels in all assays except for a small deviation in HY. For determination of assay precision 5 pooled plasmas were used with GH concentration of 2-4 µg/l, 4-8, 8-14, 9-19 and 12 to 28 µg/l: the interassay coefficient of variation (CV) was 5-8.7% for ME, 3.6-9.9% for PR, 5.6-13.3% for PD, 4.95-8.4% for HY and 2.1-5.97% for SE; the intrassay CV was 2.8-6.2% for ME, 3.3-5.5% for PR, 3.7-8.5% for PD, 3.3-5.5% for HY and 1.3-2.5% for SE. Three commercial control sera ("Lyphochek",Bio-Rad) were run in 8 assays for each of the 5 kits. The values varied with the kit used: serum 1: 2.6-3.95 µg/l in PR, SE, ME, but 1.9 and 1.99 in HY, PD, serum 2: 7.1-9.3 µg/l in PR, SE, ME but 3.9 and 5.5 in PD, HY, serum 3: 16.1-18.4 µg/l in PR, ME, SE but 8.6 and 11.6 in PD, HY. In addition, recovery of 5,10,20,40 µg/l pituitary GH (received from the NIH, USA) added to serum was highly variable: it was high with PD(88.9-99.7%), ME(85.9-91.4%), SE(98.1-106.3%), but markedly lower with PR(71.6-79.8%) and HY (55.8-65.4%). Data from HY and SE, PD correlated significantly (r = 0.98-0.99, p<0.001).

In conclusion: The diversity of GH levels determined with different assays emphasize the necessity of assay- adjusted normal ranges.

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THE EFFECT OF GH AND IGF-I ADMINISTRATION ON GROWTH DURING MATURATION. R.R. Richman, M. Lu, M.R. Benedict, Department of Pediatrics, SUNY Health Science Center, Syracuse, NY 13210, USA

To evaluate the growth promoting effects of GH and IGF-I in normal animals, we infused vehicle (0.1 M acetic acid), ovine GH (3.3 mg/kg/day), or recombinant human IGF-I (1.2 mg/kg/day) (n = 5 per group) for 2 weeks via indwelling osmotic minipumps to Fischer 344 male rats, aged 2 (immature) and 8 mo (mature). Regardless of the treatment, all immature rats grew rapidly, gaining approximately 40 g per week. Mature, control and IGF-treated rats gained about 10 g/wk; GH-treated rats exhibited virtually no growth. Basal serum IGF-I levels had increased by 20% between 2 and 8 mo. Following infusion of IGF-I, the levels increased 24% and 43% in immature and mature rats, respectively, while GH administration resulted in an 8% and 26% decrease in IGF-I levels. The pattern of the IGF binding protein (BP) bands observed using ligand blotting were typical for rodent serum. In mature control animals, BP-3 levels more than doubled and BP-2 levels had tripled compared to immature rats. While IGF-I administration had little effect on BP-3 levels, it tripled BP-2 levels at 2 mo, but suppressed the expected age-related increase. GH administration had little effect on the BPs at either age. In conclusion, during maturation, there was a striking inverse relationship between growth rates, which fell sharply, and IGF BP levels, which rose; serum IGF-I increased only slightly during this period. IGF-I infusion resulted in a differential increase with age in total serum IGF-I levels, suggesting that the clearance rate of exogenous IGF-I, and perhaps, its bioavailability, may decrease towards the end of the period of rapid growth. If so, then the rise in BP levels may play a role in the deceleration in growth which occurs during maturation.

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GROWTH HORMONE INCREASES THE LIPOLYTIC SENSITIVITY FOR CATECHOLAMINES IN HUMAN ADIPOCYTES

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The lipolytic effect of growth hormone (GH) was investigated in adipocytes obtained during elective surgery from otherwise healthy adults, 18-40 years old. No lipolytic or antilipolytic effect of GH was found when the cells were incubated with GH alone during 30min-6h. When the cells were preincubated with GH during 3h, the lipolytic sensitivity for isoprenaline increased markedly without any change in maximal lipolysis. However, a full effect was only obtained if GH was also present during the incubation with isoprenaline. The effect of GH was reduced by cycloheximide. GH did not alter DB-CAMP, enprophylline, or forskoline-induced lipolysis in human fat cells. In conclusion, GH had no direct lipolytic effect on human fat cells but GH markedly increased the catecholamine sensitivity by a mechanism which involves protein synthesis. The site of the GH effect seems to be in the β-adrenoceptors or in the G_s coupling protein.

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SEXUALHORMONE-BINDING GLOBULINE (SHBG) AND FREE TESTOSTERONE (FTE) IN PATIENTS WITH ULLRICH TURNER SYNDROME(UTS) RECEIVING OXANDROLONE

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Our investigation showed that the concentration of SHBG decreased in healthy girls and boys at increased FTE concentrations. It was therefore the aim of the present study to examine the effects of anabolic steroid oxandrolone in SHBG and FTE concentrations in patients with Turner´s syndrome. The normal dose to promote growth in patients with UTS is 0,1 mg/kg/BW. Our patients received a very low dose of 1,25 mg oxandrolone/day. We analysed 21 sera of UTS patients. The determination of SHBG concentrations was performed with the IRMA (Famos diagnostica, Oulunsala, Finnland), the concentration of FTE was determined with the RIA (Immunchem.Corporation,Carson, USA). In 7 untreated UTS patients with the pubic hair stage I and II, there were no differences in the concentrations of SHBG (median 70,3 nmol/l) and FTE (median0,52 pg/ml) in comparison to the values obtained in patients of the comparison group (SHBG median: PI 82,1 nmol/l, PII 70,6 nmol/l; FTE median PI 0,22 pg/ml, PII 0,66 pg/ml). In 14 patients with oxandrolone therapy the SHBG concentrations (SHBG median 10,3 nmol/l) were significantly lower than in patients of the comparison group (p=0,0001). Consequently the increase in FTE concentrations was greater than in FTE concentrations of the comparison group. 6 boys with tall stature received testosterone therapy (500 mg testosterone depot/4weeks) in inhibition of growth. With this treatment the SHBG median decreased to only 20,4 nmol/l, although the FTE median increased to 48 pg/ml.

We conclude that the growth promoting effect of oxandrolone in girls with UTS is mainly due to the decrease in SHBG- and therefore to the rise in FTE concentrations.

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HIGH LEVELS OF GH-BP IN KWASHIORKOR AND MARASMUS. L.Tatò, D.Dufillot[a], R.Valentini, G.Gambaro, F.Tagliaro[‡], D.Gendrel[#], F.Antoniazzi, G.Francia[◊]. Clinica Pediatrica,[‡]Medicina Legale e [◊]Medicina Interna, University of Verona, Italy; [a]Hôpital Ped d'Owendo, Libreville, Gabon; [#]Hôpital St. Vincent de Paul, Paris, France.

Severe malnutritions are characterised by low IGF-I and high GH plasma levels. The reasons why high levels of GH do not stimulate IGF-I synthesis are not clear. With the aim of improving our knowledge of this problem, we assayed plasma basal GH (by RIA), GH-BP (by HPLC gel filtration), IGF-I (by RIA) and IGFBP-3 (by RIA) in 20 children (age range:1-2.2 yrs.). Of these, 6 were affected by kwashiorkor, 8 by marasmus and 6 were controls of the same ethnic group and age, hospitalised for minimal pathologies. At the same time the same parameters were evaluated in 5 acromegalic adults for comparison. All blood samples were taken after informed consent in occasion of routine samples. High basal GH levels were observed in kwashiorkor (14.6 ±5.3 ng/ml)(M±SD), marasmus (13. 5 ±2.5 ng/ml) and acromegalic patients (52.7 ±32.4 ng/ml); as expected in kwashiorkor and marasmus low levels of IGF-I (62.8 ±14.8 and 47.2 ±12.6 ng/ml respectively) and IGFBP-3 (1.37 ±0.8 and 0.81 ±0.6 mg/l respectively) were also found. In normal controls IGF-I was significantly higher (165.2 ±34.8 ng/ml, p<0.05 vs. both) and IGFBP-3 was higher but not in a significant way (3.3 ±1.6 mg/l). The specific binding of [^{125}I]hGH to peak II GH-BP was 22.17 ±2.53 % of radioactivity in normal controls, was significantly higher in marasmus (28.92 ±1.65 %; p<0.05), kwashiorkor (31.8 ±2.3 %; p<0.01) and acromegaly (27.3 ±2.2 %; p<0.05). Circulating GH-BP is known to be a part of GH cell receptor and his amount is correlated and controlled by GH levels. The high levels of GH present in acromegalic serum are known to decrease the specific binding of the added [^{125}I]hGH during HPLC gel filtration. Marasmus and kwashiorkor have high levels of GH but also significantly higher % levels of specific bound radioactivity. Therefore we can conclude that in these conditions the presence of high amounts of circulating GHBP is possible.

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PSYCHOLOGICAL IMPACT OF GROWTH HORMONE THERAPY IN CHILDREN WITH IDIOPATHIC SHORT STATURE. A. Andronikof-Sanglade, D. Castro, M.C.Frankard, E. Roeykens, R. Wetterwald, Department of Endocrinology, Hôpital des Enfants Malades, 75007 Paris, France.

In order to assess the potential psychological impact of growth hormone (GH) therapy on non-GH deficient short stature children, 44 children were investigated in a multicenter, multi-national clinical trial. The children were randomly assigned to a treated or non-treated group. Inclusion criteria were: strictly non-pubertal, normal growth velocity for chronological age (CA), height ≤ -2 SD for CA. Psychological assessment was performed twice, before random assignment and after 18 months. It included the Wisc-R (IQ), the Comprehensive System Rorschach Test (personality), the Goodenough's Draw-A-Person test (development and body image), the Rey Figure (development, cognition and neurological functions). At intake, mean age was of 8.4 (±2) with 23 males and 21 females, mean height of -2.9 SD (±0.6). IQs were of average range, body image was consistent with age, but learning difficulties, affective disturbances and cognitive deficits more frequent than average. There were no differences between the treated and control groups. Retest results indicate that (1) psychological development of children in the treated and control groups is identical in every aspect; (2) the whole group is significantly less depressed and less cognitively impaired; (3) a direct relationship is found between children's perception of the benefits of treatment and their basic attitude towards being small, of which three types are described. It is concluded that no objective data support the notion of a psychological impact of treatment itself nor of the self-perceived change in growth velocity. The very specific cognitive and affective disturbances of these children should be addressed with relevant psychological interventions.

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