# 29

HALF LIFE AND METABOLIC CLEARANCE RATE (MCR) OF GROWTH HORMONE (GH) AFTER GH-RH IN PREPUBERTAL CHILDREN WITH SHORT STATURE. M. Ciaccio, E. Charler, M. Maceiras, MA. Rivarola y A. Belgorosky. Lab. de Invs. Hosp. Garrahan. Bs. As. Argentina.

It has been reported that the half life (HL) and MCR of endogenous GH is similar in normal male and female adults and in normal children and that children with short stature without GH deficiency (ST) show no differences. To reevaluate these studies, HL and MCR of GH were studied after a GH-RH bolus in 8 prepubertal children with idiopathic ST, chronological age (X±SD) 11.3±2.75 years (y), bone age 8.75 ± 2.76 y and height SDS -3.14 ± 0.77, and in 14 normal adults (c). After overnight fasting, GH secretion was stimulated with a single dose of 3 ug/Kg(iv) of GH-RH followed by 250 ug of somatostatin(S) 30 min later. Three basal samples, were obtained at 15 minutes intervals and , after GH-RH, samples were collected every 5 min for 90 min. GH HL was calculated monoexponentially after S injection from at least 3 descending values. Basal GH levels were similar in ST and C (2.66 ± 1.66 and 3.62 ± 5.35 ug/ml) HL in ST (24.0 ± 8.12 min) was significantly longer than in C (16.6 ± 4.41, $p < 0.02$) and MCR in BT (2.62 ± 0.76 ml/min.Kg) significantly lower than in C (3.73 ± 1.01, $p < 0.02$). The data suggest that in prepubertal children with ST, GH clearance would be slower than in normal children. According to these findings, after each secretory pulse in vivo, GH probably enters into target cells at a rate slower than in children with ST.

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COMPARISON AND REPROducIBILITY OF GROWTH HORMONE (GH) SECRETION TESTS. G. Ropelato, A. Martínez, JJ. Heinrich C. Bergadá. CEDIE. Div. de Endocrino. Htal de Niños R. Gutierrez. Bs. As. Argentina.

There is not agreement on which is the most useful and reproducible test to diagnose GH deficiency. To asses the degree of reproductiveness of physiological and pharmacological test we studied 15 prepuberal childre(14 ♂; 1♀;CA (X±SD)10.5±2.0 years; BA 7.75±2.3 years with short stature(Height SDS -1.9to -3.6) and abnormal growth rate. In all children spontaneous overninght GH secretion (SGH)was performed,followed by clonidine test(Clo)in 8 children and arginine test(Arg)in 7.The same protocol was repeated a week later. GH was measured by RIA. Variability was expressed as the coefficient of variation (CV) of all repeated tests. Results: CV for mean SGH were significantly lower than those for Clo and Arg ($p<0.02$). No significant difference was found between the CV of both pharmacological tests. For the same patients correlation between CV of Clo/Arg and CV of SGH could not be found.GH response to Clo or Arg was always ≥10 ng/ml in 5 children(Group A),6 children had a GH response ≥10 ng/ml only in one test (Group B variable responses) and 4 children did not respond to pharmacological repeated tests (Group C).Thirteen out of 15 patients had mean values for SGH >2.5ng/ml in both oportunities(5 of GA;5 of GB and 3 GC),1 patient showed values <2.5 ng /ml in two ocassions (GC) and 1 had variable means of SGH (GB).

Conclusions: This study shows that SGH is most reproducible test. The lack of correlation between CV indicates that variability may be characteistic of each test. Normality of the GH secretory status could not be stablished with the tests used.

# 31

HEIGHT AND GROWTH VELOCITY IN CHILDREN WITH CHRONIC RENAL FAILURE (CRF) AFTER RENAL TRANSPLANTATION (Tx). M. Castellano, A. Turconi, MA. Rivarola y A. Belgorosky. Serv. de Endocrinología y Nefrología, Hosp. J.P. Garrahan, Bs. As., Argentina.

Height and growth were evaluated in 31 children of both sexes after Tx:16 clinically prepubertal (PP) with a mean(X±SD) chronological age(CA) of 11.5±4.16 years (y) and a bone age (BA) of 6.91 ±2.17y, and 15 pubertal (P),Tanner's stages 2-4, with a CA of 16.4± 2.46 and a BA of 13.6±1.65 y. Height SD score(S) was -3.73 ±1.48 in PP and -3.54±1.66 in P. Height SDS was correlated with time of pre-Tx CRF (PP:6.06±4.19 and P: 6.99±4.05y), Post-Tx CRF (PP:2.28±1.59 and P: 2.15±1.67 y) and creatinine clearance (CrCl) (PP: 67.3±36.8 and 71.4±30.7 ml/min.1.73). An iverse significative correlation was found between height SDS and time of Pre-Tx CRF in PP(r:-0.50, $p<0.05$), but not in P, and between height SDS and time of Post-Tx GRF in PP and P(r:-0.61,$p<0.02$ and r: -0.52, $p<0.02$, respectively), and a direct one between height SDS and CrCl in PP and P (r: 0.71, $p<0.01$ and r: 0.54,$p<0.02$, respectively). Furthermore, in the 31 patients, CrCl was correlated with growth velocity and time post-Tx. It was found that the r had a direct significant correlation with growth velocity SDS(r:0.62, $p<0.01$) and an inverse correlation with time post-Tx (r:-0.41,$p<0.02$). There was no significatn correlation between dose of methyl prednisolone during the last 6-12 months (mean dose: 4.95±1.39 mg/m2 body surgace area) and growth velocity SDS. It is concluded that growth is one of most sensitive parameters of post-Tx altered renal function. Reduced CrCl is an important indicator in growth failure of children before and during puberty.

# 32

PITUITARY SENSITIZATION AFTER CHRONIC TREATMENT WITH GROWTH HORMONE RELEASING FACTOR (GRF). R. Silva, H. García, A. Avila, F. Cassorla. Instituto de Investigaciones Materno Infantil, Facultad de Medicina, Universidad de Chile, Santiago, Chile.

The majority of growth hormone deficient children (GHD) have a positive response to the acute administration of GRF. This suggests that their problem is an absence of the hypothalamic signal to release GH. A negative response to GRF suggests a pituitary deficiency, but chronic underestimulation of the pituitary might cause the poor response. To test this hypothesis, we administered GRF (20 ug/kg/day) during 7 days,to 5 prepubertal children with GHD (3 girls and 2 boys)with ages between 4, 9/12 and 12, 1/12 years. We performed 2 GRF tests (1 Ug/kg/iv)in these patients, one before GRF treatment and one after treatment. GH levels for each patient during both tests are shown in the table:

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| GRF TEST 1 | GH BASAL ng/ml | < 1.0 | < 1.0 | < 1.0 | < 1.0 | < 1.0 |
| | GH PEAK ng/ml | < 1.0 | < 2.6 | < 1.0 | < 1.0 | < 1.0 |
| GRF TEST 2 | GH BASAL ng/ml | < 1.0 | < 1.1 | < 1.0 | < 1.0 | < 1.0 |
| | GH PEAK ng/ml | 7.0 | 7.0 | 2.9 | < 1.0 | < 1.0 |

We observed a positive response to GRF in 2 of 5 initially unresponsive children (40%) after chronic GRF treatment. We conclude that an initial negative response to GRF does not exclude an hypothalamic disorder, since repeated administration of GRF can stimulate the somatotropes to respond.

# 33

HIPOTHALAMO-PITUITARY AXIS (HPA) BY MAGNETIC RESONANCE IMAGING (MRI) IN GROWTH HORMONE DEFICIENCY. TC. Segura, BB. Mendonca, MGF. Osorio, V. Estefan, IJP. Arnhold, LS. Lo, AC. Magalhaes, W. Bloise, W. Nicolau. Div. Endocrinol. and Dep. Radiol., HC-FMUSP, SP,Brazil.

Structural abnormalities of the HPA have been detected by MRI in GH deficient patients. We studied 29 children(18 boys and 11 girls) between 5-21 yr of age with GH deficiency: isolated(IGHD) or associated with multiple pituitary deficiencies (MPD). 10 cases refered abnormal deliveries. All children had GH peak levels less than 4.5ng/ml during clonidine and insulin tests, and submitted to combined TRH 200ug, GnRH 100ug and insulin 0.1 U/kg tests. Absence of TSH and PRL increment after test defined the GH deficiency as pituitary, and elevated basal TSH levels and/or high peak TSH and prolonged response defined GH deficiency as hypothalamic. MRI was performed using a 1.5 Tesla (Sigma GE) system, using spin echo sequences. The anomalies observed were:total transection of the stalk (TTS), thin stalk (TS), reduced pituitary parenchyma (RPP) and ectopic neurohypophysis (ENH).

| GROUP | n | NORMAL | NEUROHYPOPHYSIS | | | TTS | TS | RPP |
|---|---|---|---|---|---|---|---|---|
| IGDH | | | ECTOPIC | TOPIC | NON | VISUALIZED | | |
| Type A | 2 | | 2 | | | 2 | 2 | |
| Idiopathic | 15 | 1 | 8 | 5 | 2 | 7 | 2 | 12 |
| MPD | | | | | | | | |
| Pituitary | 2 | | 2 | | | 2 | | |
| Hypothalamic | 10 | | 10 | | | 10 | | 10 |

Reduced pituitary parenchyma was seen in 82.7%, ectopic neurohypophysis and total transection of the stalk in all cases of MPD and in 53% of idiopathic IGHD. The findings suggest that IGHD and MPD were related to transection or compression of the stalk.

# 34

DIFFERENTIAL REGULATION OF GROWTH HORMONE RECEPTOR EXPRESSION BY ESTRADIOL AND TESTOSTERONE. HM. Domené, YM. Yu, G. Marín, J. Sztein and F. Cassorla. Developmental Endocrionology Branch, NICHD, NIH, Bethesda, Maryland, USA.

Estradiol (E2) and testosterone (T) can stimulate growth by increasing GH secretion. Sex steriods can also regulate growth affecting GH receptor (GHR) expression in target tissues. In order to stydy the effect of physiological concentrations of E2 and T on GHR expression, we measured liver GHR mRNA by solution hybridization-RNase protection assay in rabbits treated with E2 or T. Three to five immature rabbits in each group received a s.c. pellet containing placebo, E2 (0.1; 0.5; 1.5; or 5.0 mg) or T(15, 50, or 100 mg). Liver RNA samples were hybridized to a 32 P labelled GHR antisense riboprobe and digested with RNase. After gel electrophoresis a specific 370 base long protected band, corresponding to GHR mRNA, was quantitated by autoradiography and densitometry. Liver GHR mRNA levels were significantly lower than that in controls in animals treated with 1.5 (62%; $p < 0.025$) and 5.0 mg of E2 (13%; $p<0.003$), and significantly higher in those treated with 100 mg of T (230%; $p<0.01$). From these findings we conclude that E2 and T, at physiological concentrations, have an opposite effect on GHR expression. The decrease on GHR expression by E2 might explain the inhibitory effect of moderate dose of estrogens on growth.