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FUNCTIONAL HYPERSOMATOTROPISM IN SMALL FOR GESTATIONAL AGE NEWBORNS.

Basal plasma GH levels and response to an injection of 1ug/kg of synthetic 1-44(NH2) GHRH (SANOFI RECHERCHE - Toulouse) were prospectively studied at day 3 postnatally in 5 small for gestational age twin babies (SGA) compared to their adequate for gestational co-twin (AGA) and in 10 idopathic single SGA babies compared to 6 single AGA, under conditions approved by the Ethic Committee of Univ.Cl.Bernard. Means basal plasma GH were higher in SGA than in AGA but statistically different only for single ($p < 0.01$). Mean peak GH response to GHRH was markedly increase in SGA compared to AGA in both twins (202 ± 34 versus 116 ± 49 ng/ml) ($p < 0.05$) and single (190 ± 45 versus 80 ± 63 ng/ml) ($p < 0.01$).12 SGA retested at 1 month showed (compared to day 3) a decrease in basal,absolute increment and peak GH response to GHRH ($p < 0.01$). In 21 SGA as in 17 AGA serum IGF-1 was measured by RIA between 12 and 96 hours after birth. Mean serum IGF-1 value was significantly higher in SGA than in AGA (0.61 ± 0.29 versus 0.3 ± 0.14 U/ml) ($p < 0.001$). S-200 gel filtration chromatography of serum sample drawn at 3 days showed similar patterns in SGA and AGA, of both immunoreactive IGF-1 and 125-IGF-1 binding, with material eluting at 30-50 K and bearly detectable at 145 K (adult pattern) region. These data suggest post-natal functional hypersomatotropism in SGA compared to AGA babies. Regardless of the mechanism(s), this process could participate to the early post-natal catch up growth.

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PHYSIOLOGICAL GH SECRETION DURING THE RECOVERY FROM PSYCHOSOCIAL DWARFISM: THE PATTERN OF GH PULSATILITY IS REPRODUCIBLE.

We have studied 11 prepubertal children (5F, 6M) with subnormal growth velocities and adverse psychosocial factors within in the family; 5 patients had been sexually abused. Mean age was 8.0 yrs (range, 3.8 - 13.6). All were admitted to hospital for a 3 week period with only limited parental access. Serial serum sampling for GH at 15 minute intervals for 18 hours was performed on 3 occasions during each admission with sleep monitored by EEG.

4 patients had GH insufficiency which reversed between day 2 and day 6 of their admission. Two patients had GH insufficiency which did not alter during their admission; they both had an excellent anthropometric response to GH treatment. Five children had normal GH profiles which remained unaltered.

The recovery of GH secretion in psychosocial dwarfism was achieved by an increase in pulse amplitude with no alteration in pulse frequency. These observations provide further evidence that the control of GH secretion is by pulse amplitude modulation.

There was a variable relationship between slow-wave sleep and GH secretion. The patients who had irreversible GH insufficiency had 3 identical GH secretory profiles. In the patients who had normal GH secretion and in those after recovery from psychosocial dwarfism, the pattern of GH pulsatility, the size and timing of GH peaks, and the shape of GH pulses were reproducible for each individual patient.

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**RESPONSE OF PLASMA CONCENTRATIONS OF GROWTH HORMONE (GH), GH-RELEASING HORMONE (GHRH), AND SOMATOSTATIN (SRIF) TO PENTAGASTRIN INJECTION IN CHILDREN.**

Pentagastrin - the C-terminal pentapeptide of gastrin - has been shown to stimulate both plasma GH and SRIF. Immunoreactive GHRH in the gastrointestinal tract has been mainly found in the G cells of gastric antrum. Therefore we determined the effect of pentagastrin on the plasma levels of these tightly connected hormones.

6 µg/kg pentagastrin was administered subcutaneously to 10 short normal children. Blood samples were drawn at -30, 0, 5, 10, 15, 30, 45, 60, 90 and 120 min. Informed parental consent was given. GH, SRIF and GHRH were measured according to recently described methods (Acta Endocrinol 116 (1987):549).

Results (mean ± SEM): Following pentagastrin injection plasma GH levels increased within 15 to 90 min (1.1 ± 0.4 µg/l vs. 9.3 ± 1.2 µg/l; $P < 0.01$). Plasma GHRH values increased between 15 and 45 min (9.6 ± 0.6 ng/l vs. 19.6 ± 2.0 ng/l; $P < 0.01$). Plasma SRIF peaks occurred from 5 min to 30 min (11.7 ± 0.8 ng/l vs. 20.8 ± 1.9 ng/l; $P < 0.01$). The plasma SRIF peak preceded or coincided with that of plasma GHRH in any case and there was a negative linear correlation between the peak values of these two hormones ($r=0.67$; $p < 0.05$). No time relationship between GHRH plasma peaks and GH peaks was noticed.

We conclude that gastrointestinal GHRH might play a role in the regulation of gastric acid secretion, but does not stimulate GH.

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**GROWTH-HORMONE (GH) NOCTURNAL PROFILE DURING SLEEP INDUCED BY ZOLPIDEM: A DOUBLE BLIND STUDY VS PLACEBO.**

Overnight blood sampling, regarded as the most physiological assessment of GH status, may cause some disturbances in patients' sleep. It is thus of interest to determine whether the nocturnal GH profile (GH peak, GH sum of peaks, time to first and max. GH peak, AUC, mean integrated concentration) relate with the clinically-recorded characteristics of sleep (sleep onset, sleep duration, number of awakenings), during overnight blood sampling .

We studied the influence of an hypnotic drug (zolpidem 10 mg) on nocturnal GH profile (blood sampling every 20 minutes from 8 P.M. to 6 A.M.) in a group of 12 young adult volunteers (27.9+/-4.3 years) and in a group of 12 children (10.8+/-2.8 years) with short stature and normal GH pharmacological tests. The adult volunteers were studied over 2 nights at 7 day interval in a double blind cross-over versus placebo design. The children were studied over one night in a double blind versus placebo parallel group design.

Mean GH profiles showed no difference between zolpidem and control in adults as well as in children. Furthermore, GH profile did not relate with sleep duration and number of awakenings in both populations.

Although, in these experimental conditions, sleep onset latency was significantly reduced with zolpidem in the adult population (-1.0+/-0.2 hour; p=0.004), the mean time to first GH peak remained unchanged.

We therefore conclude that sleep disturbances, induced by overnight blood sampling for physiological evaluation of GH status, do not alter the profile of GH nocturnal secretion which seems to be specific to each patient.

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AGE OF MENARCHE, ADULT HEIGHT (AH) AND TARGET HEIGHT (TH) IN GIRLS TREATED FOR ACUTE LYMPHOBLASTIC LEUKEMIA (ALL)

Several factors have been implicated to influence gonadal function and adult height in long term survivors of ALL. Age of menarche, AH with respect to TH have so far rarely been reported. 53 girls in 1. CCR reported their age of menarche. They constitute the total group of long term survivors of four different ALL protocols. In 7 pts (CA 11.6 ± 0.6 years, mean ± SD) menarche has not yet occurred. AH is available in 33 girls, parents' height in 29. TH was predicted using the Tanner method: MPH - 6.5 cm. Menarche was observed before therapy in 3 and during or after therapy in 43 girls. The menarcheal age was 12.76 ± 1.28 years ($n = 43$) and correlated closely with the CA at the end of therapy ($r = 0.75$). In addition, it was influenced by cranial irradiation and chemotherapy. Menarche occurred earlier, when pts received more than 2000 rads CNS irradiation ($p = 0.004$, log-rank test) or high doses of cyclophosphamide in their chemotherapeutic regimen ($p = 0.02$).

AH in 33 pts was 164.8 ± 6.4 cm with a TH of 164.5 ± 4.8 cm. AH corresponded closely to TH in girls with early as well as with late menarche.

We conclude, that several therapy related factors influence the age of menarche in ALL. AH is within the range of TH and thus not affected by the age of menarche, cranial irradiation and/or chemotherapeutic regimen.

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GROWTH AND PUBERTY IN SURVIVORS OF CHILDHOOD LEUKAEMIA.

Childhood leukaemia is often associated with impaired growth and disorders of puberty. To see how common this is we re-examined all 13 survivors (9f, 4m) of acute lymphoblastic leukaemia treated during childhood in our hospital 1964-1981. At diagnosis, aged 0.8 to 13.7 years, their mean height SDS was +0.9. They were given various chemotherapy, glucocorticoids and 11 had cranial irradiation (1600-2600 rad). During the first year after diagnosis the mean height velocity SDS was -1.4 (SD 1.2), and 6 of 13 lost >0.5 of their height SDS. By the end of therapy (7 years in 2, 3 to 3.6 years in 11) the mean height SDS was was +0.3 (SD 1.3) and 7 had lost >0.5 of their height SDS. After cancer therapy (follow-up 3 to 13 years) an improvement of height SDS >0.5 SD was seen in 4 and a deterioration in 1, due to scoliosis after paraplegia as a treatment complication. Of those 7 who had reached their final height, 4 were >1SD shorter than their midparent height SDS, 1 was 1 SD taller. Of those 6 still growing (aged 7.6 to 12.5 years) 3 were >1SD taller than their midparent height SDS and none was short. Five were obese with a relative weight for height of >120%, 2 were lean <90%. None of the girls had abnormal timing of puberty, and 2 had children. One boy was early in his puberty (G2 at 9.0 years). In conclusion, childhood leukaemia had impaired the growth of some of our patients, but their height deficit was not severe. Abnormal puberty was seen in only one of 13.