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REDUCTION OF FINAL HEIGHT IN TALL GIRLS FOLLOWING ESTROGEN ADMINISTRATION IS NOT DOSE DEPENDANT

Effects of Ethinylestradiol (EE) in girls with tall stature were assessed in a collaborative study of two centers comparing 38 girls (I), receiving 0.3 - 0.5 mg EE daily, with 44 girls on 0.1 mg EE daily (II). To minimize errors of height prediction (HP) bone ages (BA) were determined according to GREULICH and PYLE by using the mean of four determinations of both centers. Final height (FH) was predict according to the tables of BAYLEY and PINNEAU and was measured at a chronological age (CA) of 19.8±1.2 years (y). Prior to EE administration the following findings did not differ (I vs II): CA (12.5 vs 12.4 y), BA (12.4 vs 12.4 y), length (+3,2 vs + 3.2 SDS) and HP (+3.8 vs +3.8 SDS). Evaluation of the differences between SDS of HP and SDS of FH showed no difference with respect to dose, however, an increased BA at the onset was correlated with a smaller reduction (Table I).

	BA	10.5-11.5y	11.75-12.75y	13 - 14 y	12.5-13.5 post menarche
I	6.8/-1.22	5.45/-1.10	2.95/-0.46	5.52/-0.88	cm/-SDS(x)
II	6.6/-1.12	5.31/-1.08	3.72/-0.54	5.41/-0.99	cm/-SDS(x)

Cumulative dose (218±86 vs 64±20 mg), BA at the end (15±0.5 vs 15.9±0.5y) and growth after discontinuation of EE (2.7±T.8 vs 1.8±T.2 cm) did differ.

Conclusion: 0.1 mg EE is as effective as 0.3 mg EE daily.

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EFFECT OF SPINAL IRRADIATION ON GROWTH

The standing height, sitting height and leg length have been measured in 79 patients (age 16-30 years), who received cranio-spinal (c/s) irradiation (n=37) or cranial irradiation (n=42) in childhood for a brain tumour and had completed their growth. Their measurements were compared to the established standards for sitting height and leg length in British children (age 16-18 years) (Tanner and Whitehouse, 1978). To examine the effects of spinal irradiation (DXT) on spinal growth independent of GH deficiency we analysed the leg length (LL) minus sitting height (SH) SDS and utilised the cranial group as controls. There was an overall statistically significant difference ($p < 0.0001$) between the median c/s LL-SH SDS (1.98) and the median cranial LL-SH SDS (0.545). Within the c/s group there was a significant correlation with age at treatment (Spearman's $p=0.40$: $p < 0.02$) but no such correlation for the cranial group. After splitting age at treatment into 3 groups ($0 < 5$, $5 < 10$ and 10^+ years) there was a significant difference between the LL-SH SDS of the c/s and cranial groups for each of the age groups.

In conclusion spinal irradiation has a profound effect on spinal growth and the younger the irradiated child, the greater the subsequent skeletal disproportion. Our most conservative figures indicate that the eventual loss in height is 9cms if irradiated at one year, 7cms at five years and 5.5cms at ten years.

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PUBERTAL DEVELOPMENT IN GIRLS WITH CHRONIC RENAL FAILURE (CRF)

The introduction of dialysis therapy and renal transplantation (TP) for treatment of terminal CRF in children has produced a generation of young adults with late sequelae of pre- and transpubertal uremia. Whereas growth retardation has long been recognizid as a major problem of these pts the disturbances of sexual maturation have been neglected. We have followed 38 girls at different stages of CRF up to age 15-26 yrs. Breast and pubic hair development and the time elapsed between stage B2 to menarche deviated from the normal range in about half of the pts. Menarche failed to enter before age 15 in 45% and was associated with advanced bone maturation (mean TW2 bone age 14.0 yrs.). Menses rarely occured on dialysis but were often restored after TP. Plasma E2 measured in 31 girls was decreased according to age, but usually within normal limits when related to PH stage. However, in 7 girls with advanced CRF studied repeatedly E2 did not show the expected rise. Plasma LH was increased in 35% and prolactin in 26% of cases. Response of LH to LHRH was often blunted. We conclude that in CRF the activity of the hypothalamo-pituitary-gonadal axis is frequently disturbed resulting in hypergonadotropic hypogonadism.

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INTRACELLULAR REGULATION OF PLACENTAL LACTOGEN (hPL) SECRETION BY CULTURED HUMAN TROPHOBLAST

To study the regulation of hPL secretion, a monolayer culture of human term trophoblast was utilized. Time course of spontaneous secretion for 5 min to 21 hr showed a steady rate of secretion at 15±1.1 ng/10^6 cells/hr. Intracellular hPL was constant at 34±4 ng/10^6 cells. K^+ (21 mM) produced a slight but significant increase, from 457±13 to 584±15 ng/10^6 cells. GHRF (5×10^{-10} M) stimulated hPL secretion by 30±7%. Both dibutyryl cyclic AMP (dbcAMP) and Ca^{++} had inhibitory effects on secretion. dbcAMP inhibited secretion by 49±3%. This effect disappeared in the presence of verapamil, the Ca-channel blocker. Ca-ionophore A23187 inhibited secretion by 30±4%. EGTA and verapamil stimulated secretion by 116±11% and 16±1.1%, respectively. The Ca-calmodulin inhibitor trifluoperazine eliminated the A23187 effect. It also interfered with the inhibitory effect of dbcAMP. It is concluded that: 1) the secretory mechanism of hPL is a unique process in which both dbcAMP and calcium exert inhibitory action; 2) the two messengers interrelate: dbcAMP modifies calcium, which requires a calmodulin complex for its effect; 3) by analogy to other secretory mechanisms, the major amount of hPL is secreted by a constitutive mechanism with only small intracellular storage pools; and 4) the concept of the hypothalamic-pituitary analogy applies to a small fraction of hPL secretion.

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GLUCONEOGENESIS IN HUMAN PLACENTA: EFFECTS OF INSULIN AND HYPOXIA IN VITRO

The placenta as fetal tissue is subjected to alterations of gluconeogenesis like the newborn itself. We studied tissue of term placentae incubated in amino acid solution with 14.0 mmol glucose /l under gasing with either oxigen or nitrogen. As specific inhibitor of gluconeogenesis 2 mM of 2,5-anhydro-D-mannitol (AM) was used, human insulin was administered at a final concentration of 180 µU/ml. The glucose utilization (U(gluc)), L-lactate (P(lac)) and pyruvate production (P(pyr)) were calculated after tracing with (U-^{14}C)glucose and separation by HPLC technique.- RESULTS: 1. U(gluc) was 24.8 % (±1.3 S.D.)(n=9) per g tissue in 120 min. After AM, the glucose consumption was elevated up to 33.3 % (±4.1) ($p<0.01$)(n=6). Insulin did not significant influence the elevated U(gluc) in AM conditions.-2. P(lac) was lowered by AM from 18.2 % (±2.4) to 12.9 % (±2.3)($p < 0.02$)(n=6). Insulin abolished this effect (P(lac) up to 19.8 % (±5.7)).-3. P(pyr) remained unaltered by AM and insulin.-4. In hypoxic conditions with inhibited gluconeogenesis, elevation of U(gluc) from 38.2 %(±2.2) to 44.5 % (±6.7) was observed. Also P(lac) increased to 39.1 % (±6.6).- CONCLUSIONS: 1. Blocking of gluconeogenesis elevates the glucose utilization by one third. 2. The lactate production is reduced without gluconeogenesis, but is counteracted by insulin. 3. In hypoxia, the gluconeogenesis continues to function in placenta.

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THYROTROPIN AND CATECHOLAMINE INDUCED LIPOLYSIS DURING THE FIRST MONTHS OF AGE.

Thyrotropin (TSH), Noradrenaline (NA), Adrenaline (A) and isoprenaline (ISNA) induced lipolysis in isolated subcutaneous adipocytes was investigated in vitro. Fat cells were obtained from 16 infants aging 2 weeks-2 months and 10 adults during inguinal hernia operations. Glycerol release was measured as an index of lipolysis. NA increased lipolysis by 80% and A by 100% over the basal values in the infant group and in the adult group 300% and 200% respectively. With the addition of the alpha-2-blocking agent Yohimbine the differences between the doseresponse curves of the infants and adults disappeared. The effect of the beta agonist ISNA was almost identical in infants and adults (600% stimulation, ED50 10^{-9} M). In the infant group TSH caused a 600% stimulation of lipolysis with ED50 5×10^{-4} IU/ml. The TSH induced lipolysis was inhibted by preincubation of the medium with TSH antibodies but not influenced by the presence of propranolol in the medium. In the adult group TSH had no lipolytic effect below 1 unit/ml. With this concentration the mean increase was 80%. In conclusion, the lipolytic effect of catecholamines was poor during the first two months of age owing to an increased alpha-2-adrenoceptor mediated inhibition. TSH was during infancy a hormone with higher lipolytic capacity than catecholamines, the only hormones with pronounced lipolytic effect in adults. It is possible that TSH is of importance for the rise of lipolysis which is seen immediately after birth.