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Height correlations between parents and mature offspring in normal subjects and in subjects with Turner, Klinefelter and Down syndromes, idiopathic precocious puberty and congenital adrenal hyperplasia.

| Group | Number | Mid-parent/offspring correlation coefficient | Corrected heritability |
|------------------------|--------|--|------------------------|
| Normal males | 90 | 0.57 | 0.85 |
| Normal females | 116 | 0.66 | 0.74 |
| Klinefelter males | 27 | 0.62 | 1.12 |
| Turner females | 33 | 0.61 | 0.71 |
| Down males | 48 | 0.21 | 0.25 |
| Down females | 27 | 0.29 | 0.40 |
| Id. prec. pub. males | 11 | -0.09 | -0.17 |
| Id. prec. pub. females | 27 | 0.68 | 1.17 |
| CAH untreated females | 10 | 0.29 | 0.33 |

Heritability of stature was slightly higher in males than in females and the findings in patients with sex chromosome disorders were very similar. The genetic pattern was largely lost in Down syndrome which implicates the autosomes in the determination of normal adult stature.

The findings in idiopathic precocious puberty and CAH indicate a loss of genetic determination except in girls with idiopathic precocious puberty. This may be a reflection of the fact that idiopathic precocious puberty in boys and CAH are pathological conditions; most girls with precocious puberty are extreme variant of normal.

59 WETTENHALL, H.N.B.* (Introduced by H.K.A. Visser). LONG-TERM FOLLOW-UP OF TREATED TALL GIRLS.

Since 1959, 657 girls have been seen because of tall stature. 213 have received oestrogen therapy to control growth rate. In December 1975 letters were sent to 79 girls whose treatment had been completed for at least 2 years, inquiring re marital status, contraceptive measures, and any problems since oestrogen therapy. In 56 replies received, 34 are married. 13 were married in 1971 or earlier, and of these 9 have children, 2 have used contraceptive measures continuously, 1 is separated, and the husband of 1 has oligospermia. 21 were married in 1972 or later, and of these 2 have had children and 1 is pregnant. 29 of the 34 married have used contraceptive measures; 4 of the remaining 5 have had children, and 1 is married only 8 months. There is no evidence of infertility as a result of treatment. The mean height of the treated girls is 176.5 cm; the mean height of their husbands is 181.0 cm. 5 of 34 girls married men shorter than themselves. 22 were not married; 12 admit using contraceptive measures, 10 did not answer the question. Problems mentioned were acne (2), oligomenorrhoea (2), obesity (5), underweight (1), ovarian cyst (1), diabetes (1). 2 of the obese girls had a familial tendency, and 2 were associated with psychiatric problems. Most girls were very happy they had been treated.

Ref. Tall Girls: A Survey of 15 Years Management and Treatment. J. Ped. 86:602 (1975).

60 J. VIDNES* (Intr. by M. Seip) Pediatric Research Institute, Rikshospitalet, Oslo, Norway.

Persistent hereditary neonatal hypoglycaemia caused by glucagon deficiency. A Pakistani boy with a family history of infant deaths from hypoglycaemia, was transferred to our clinic shortly after birth because of hypoglycaemic seizures. After some initial improvement, his condition became critical, with up to 15 seizures daily. His insulin values, triglycerides, FFA, and ketones were normal, but his gluconeogenesis from ¹⁴C-alanine was severely impaired, and despite severe hypoglycaemia, glucagon values were at the lower detection limit of our assay. Stimulation with alanine i.v. resulted in no rise. Therapy was started with glucagon i.m. 6 times daily, then after 5 days with zink-protamine-glucagon s.c. twice daily. This therapy resulted in immediate cessation of the seizures, while blood glucose started rising at day 3. Gluconeogenesis increased three times. After one week he had improved dramatically, and his blood glucose values were within normal limits. After three weeks the EEG had normalized, and he was deemed psychomotorically normal. Discontinuation of glucagon therapy resulted in a relapse, and it had to be resumed. After two months the amount of glucagon had to be gradually increased, possibly because of antibody production. A similar case of hypoglycaemia because of glucagon deficiency, verified with glucagon determination, has not previously been described.

61 L. DAVID*, A. RUITTON-UGLIENGO*, and R. FRANCOIS. Service de Pédiatrie, S.bis, Hôpital Edouard Herriot, Lyon.

Contribution to the pathogenesis of pseudotype I glyco-genosis (P.type I G): prolonged hyperinsulinism induced by glucagon administration.

P.type I G and type I glyco-genosis (type I G) have identical clinical and biological features although the hepatic content of glucose 6 phosphatase is normal in P.type I G. Recently Hers et al showed that in this latter affection a shortening of the half life of glucose and an increase in the recycling of glucose were present (Biochem. Soc. Trans. 1975 p. 1051). Venous blood glucose, lactate, NEFA, pH, and plasma insulin levels were studied on several occasions before, 1, 2, 3, and 4 h after feeding in one case of type I G and one case of pseudo type I G, on basal conditions and after prolonged glucagon administration (1 to 2 mgIM every 8h. for several days to months). Both cases were severe forms with a fasting tolerance not exceeding 4 h. On basal condition the biological data were similar in both patients with low insulin levels (<7,5 to 40 µu/ml). Glucagon did not induce any significant changes in type I G and insulin levels were not modified (<7,5 to 48 µu/ml). By contrast glucagon induced important increases in plasma insulin in P.type I G with post-feeding values >200 µu/ml reaching on several occasions values >1 000 µu/ml; parallel blood glucose levels varied from low to high normal (20 to 145 mg/100ml) This hyperinsulinism was still present (120 to 335 µu/ml) 2 months after discontinuation of 6 months glucagon injections. This finding suggest that in spite of normal basal insulin levels, an abnormal insulin/glucagon secretion ratio is present in P.type I G which may be involved in the abnormal glucose kinetics.

62 J.L. CHAUSSAIN, P. GEORGES*, G. OLIVE* and J.C. JOB. Hosp. St-Vincent de Paul, Paris, France. Effect of fast in normal children: Influence of age.

A 24 hour fast was performed with consent of parents, in 85 normal children (55 boys and 30 girls) aged 1 to 18 years. After fast, blood glucose (BG) was measured and additionally in 27 children blood was drawn for plasma alanine (Ala) and free fatty acids (FFA) measurement. The mean BG value after fast was 52 ± 16 mg % in children aged less than 10 years, and 62 ± 7 mg % in children more than 10 years. Individual values in each group were distributed according to a Gaussian curve. The difference between the 2 groups was highly significant ($p < 0.001$). Fasting values of Ala ranged from 11 to 34 µM % and were highly significantly correlated with age ($r = 0.72$, $p < 0.001$). FFA values ranged from 0.5 to 8 mMq/l and were negatively correlated with age ($r = 0.59$, $p < 0.01$). These data demonstrate that the carbohydrate regulation during fast improves with age in normal children, correlating with a higher degree of proteic neoglycogenesis and a lower rate of lipolysis. This age dependent improvement of proteic neoglycogenesis is to be related to the fact that in children the accesses of ketotic hypoglycemia disappear spontaneously with age.

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Mechanism of fructose-induced hyperuricemia. To investigate the mechanism whereby fructose provokes a loss of total adenine nucleotides, the kinetics of purified rat liver AMP-aminohydrolase was studied with a new method based on the separation by column chromatography of radioactive IMP formed from [¹⁴C]AMP. The sensitivity of this method greatly facilitated the study of the enzyme in the presence of physiological concentrations of its substrate (0.2mM) and effectors (3mM for ATP, 0.5mM for GTP, 5mM for Pi). ATP 3mM increased the enzyme activity 200-fold due to a change of the kinetics from sigmoidal to hyperbolic. The inhibitory effect of Pi on the ATP-activated enzyme became only apparent at ATP concentrations below 1mM or if 0.3 to 0.5mM of the inhibitor GTP was also present. At physiological concentrations of substrate and effectors, the combined inhibitory effects reached 95%. Within 10 sec. after the administration of fructose (2.5 mg/g I.V.) to mice, the concentration of Pi decreased abruptly, reaching 50% of its control value at 30 sec. A similar decrease of the level of GTP was found. The concentration of ATP declined progressively, down to 1/2-1/3 of its normal value at 2 min. These findings may explain the transient purine catabolism observed in these conditions since the decrease of the inhibitors becomes offset by the depletion of the activator.