

## Oestrogen Treatment of Constitutionally Tall Girls with 0.1 mg/day Ethinyl Oestradiol

Thirty-five constitutionally tall girls (mean age, 12.5 years) were treated with ethinyl estradiol, in a dosage of only 0.1 mg/day. Their ultimate heights were compared with those of 23 untreated girls of similar initial ages, bone ages (BAs), and predicted adult heights, and with those of five girls treated with ethinyl estradiol, 0.3 mg/day. Treatment lasted more than 2 years for the girls whose BA was > 12.5. Final heights were defined

as heights measured at the end of a year during which growth was < 0.7 cm.

The Bayley-Pinneau predictions underestimated by an average of 0.7 cm the heights of controls whose BA was <12.5 years, and overestimated by 0.6 cm the heights of controls with a BA > 12.5 years. Making allowance for these discrepancies, the investigators calculated that the reductions in predicted adult height achieved by estrogen treatment averaged 7.4 cm in girls with BA values > 12.5 years. The authors concluded that the higher dosage of estrogen offers little, if any ad-

vantage over the dosage of 0.1 mg/day.

Bartsch O, Weschke B, Weber B. *Eur J Pediatr* 1988;147:59.

**Editor's comment**—*The authors admit that it is difficult to compare their results with those in the literature because of methodological differences in determining BA and predicting height. Nonetheless, it certainly seems that the lower, and hence more desirable, dosage of estrogen produces much the same results as the higher one. The authors' review of results in the literature is also a valuable one.*

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## Changes in Serum Insulin Concentration During Puberty and Their Relationship to Growth Hormone

Hindmarsh and colleagues investigated the relationship between insulin concentration and growth hormone (GH) secretion during puberty in a cohort of 40 tall or short children. Oral glucose tolerance tests were performed in 34 children during puberty and in six adolescents who had reached their final height. The pubertal children were growing at a normal velocity for their stage of development and had no family history of insulin-dependent diabetes. Following glucose ingestion, blood samples were drawn at time 0, and at 30-minute intervals for 3 hours. In addition, 24-hour GH profiles were determined in 16 tall girls (four prepubertal, six in early puberty at breast stages II and III, and six in late puberty, at breast stages IV and V). Twenty-four-hour GH (sampled every 20 minutes) and insulin profiles were obtained in 13 of the 40 children (five short prepubertal, four tall prepubertal, and four tall pubertal). GH pulses were identified, and incremental areas under the glucose and insulin curves were calculated.

The 34 children and six young adults demonstrated no significant increase in fasting blood glucose or in incremental area under the glucose curve. In

both tall and short pubertal children there was a significant increase in fasting insulin concentration during puberty; this increase was related to pubertal status rather than stature. The incremental area under the insulin curve increased almost twofold. Age played no part in these changes. Among the six young adults, the glucose and insulin parameters resembled those of prepubertal children. Among individuals in whom GH secretion was studied, increases in fasting insulin were seen at breast stages II and III, and declines were seen at breast stages IV and V. The changes in GH pulse amplitude were coincident with the changes in fasting insulin concentration. There was a threefold increase in the mean sum of GH pulse amplitudes between prepubertal children and girls at breast stages II and III.

The authors concluded that they have demonstrated a threefold increase in serum insulin concentration during puberty and that this increase is coincident with the rise in GH associated with breast development stages II and III. They suggested that during pubertal growth in children with diabetes, the standard dose of insulin should

be doubled and possibly tripled to maintain good metabolic control and maximize pubertal growth. As further evidence that the changes in insulin secretion are due to GH, they cited the increase in fasting insulin concentrations in 14 prepubertal children during the first year of exogenous GH therapy.

Hindmarsh P, Di Silvio L, Pringle PJ, et al. *Clin Endocrinol (Oxf)* 1988;28:381-388.

**Editor's comment**—*Amiel and colleagues (N Engl J Med 1986;315:215) have previously demonstrated impaired insulin action in pubertal children with diabetes and in their nondiabetic siblings. As Hindmarsh et al point out, the comparison with siblings of children with diabetes may not be appropriate, and clamp studies such as those performed by Amiel et al may not be as physiologically meaningful as the oral glucose loads given in this most recent study. Although this investigation studied children at a variety of prepubertal and pubertal phases, including differences of stature, its findings are significant and suggest one of the reasons for poor glucose control in adolescents with diabetes. Longitudinal studies are needed to corroborate these findings.*

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