

Growth in Turner's Syndrome: Long-Term Treatment With Low-Dose Ethinyl Estradiol

The use of low-dose estradiol (100 ng/kg/day) was previously reported by Ross et al (*N Engl J Med* 1983;309:1104) to increase the growth rate of patients with Turner's syndrome after six months of treatment. In this study, Martinez et al attempted to reproduce and extend the studies of Ross et al.

Nine patients with Turner's syndrome between the ages of 8.6 and 13.3 years were treated with ethinyl estradiol, 100 ng/kg/day, for 18 months. The growth rates increased in all nine patients during the first six months of treatment ($3.09 \text{ cm/yr} \pm 1.05$ v $7.09 \text{ cm/yr} \pm 1.47$), but fell progressively during

the 6th to 12th months ($6.08 \text{ cm} \pm 1.78$) and the 12th to 18th months ($4.03 \text{ cm} \pm 1.65$). The bone ages increased by more than two years in six of the nine patients during the 18 months of treatment (from 9.23 ± 1.60 to 11.63 ± 1.27), and the predicted heights did not change.

The integrated concentrations and the number of peaks of GH observed during a seven-hour period (07:30 to 14:30) did not change, as was the case for IGF-I levels as determined by both bioassay and radioimmunoassay. The predicted heights also did not change.

Sexual development was noted during the first six months of treatment in all patients, but regression occurred in seven patients over the next 12 months.

The authors conclude that growth velocity is increased with this regimen but ultimate height is

probably not affected.

Martinez A et al. *J Clin Endocrinol Metab* 1987;65:253.

Editor's comment—*The patients in this study have been treated with estrogen longer than those in any other study reported to date. The effect of oxandrolone alone, growth hormone (GH) alone, and both together also has resulted in increased growth over a 12-month period (J Pediatr 1986;109:936-943). My personal observations using oxandrolone over the years are that growth rates return to their low levels by the third year of treatment. Will oxandrolone or GH or both increase ultimate height when used over an extended period? The answer to this question will not be known for several years.*

RMB

Testosterone Treatment of Constitutional Delay of Growth and Development: Effect of Dose on Predicted Versus Definitive Height

Boys with constitutional delay of growth and adolescent development (CDGAD) are treated with different hormones or anabolic steroids or testosterone or a combination of the three. In adolescents, testosterone is favored, since it stimulates both growth and sexual development. While there is no doubt about the short-term success of such treatment, opinion regarding the long-term effects is divided, particularly with respect to ultimate height.

Martin et al carried out a large longitudinal study on 44 adolescents with CDGAD who received different doses of testosterone enanthate. A group of 14 untreated boys with CDGAD served as controls. The inclusion criteria for the study were pretreatment growth

velocity less than 4.0 cm/year, height less than the 5th percentile, retarded puberty (P_1 or P_2), and a delay in bone age corresponding to that in height. Treatment was started when the boys were 14 or 15 years of age. Group I received 200 mg testosterone enanthate monthly, group II received 100 mg, and group III, 50 mg. During a year of continuous treatment, the growth velocity advanced considerably in all treated groups ($10.9 \text{ cm} \pm 0.5 \text{ cm}$ in group I, $11.0 \text{ cm} \pm 0.6 \text{ cm}$ in group II, $10.7 \text{ cm} \pm 0.4 \text{ cm}$ in group III). The $\Delta\text{BA}/\Delta\text{HA}$ ratio was 2.0:1.8 in group I, 1.8:1.7 in group II, and 1.5:1.5 in group III. In the year after the discontinuation of therapy, the growth rates dropped—most markedly in group I (4.6 cm/year), less in group II (5.0 cm/year), and least in group III (7.0 cm/year). This led to a statistically significant loss of ultimate height in group I. Measured adult height in these patients was 167.8 cm, or 3.3 cm less than the predicted ultimate heights that were calculated at the start of treatment ac-

ording to RWT. No significant differences were seen between predicted and measured adult height in groups II and III.

Martin MM, Martin ALA, Mossman KL. *Acta Endocrinol* 1986; 279(suppl):147-153.

Editor's comment—*This study of a fairly large number of patients brings about important, statistically ascertained results. With testosterone treatment, the desired and expected growth spurt occurs in all three treatment groups. However, in the year after treatment, a rebound phenomenon occurs, which depresses the gain in height age to 0.7 years/year and leads to a significant loss of ultimate height. In light of these results, long-term therapy with 200 mg testosterone per month is certainly contraindicated. On the other hand, treatment with 50 mg testosterone per month provides satisfactory results and is free of undesired side effects as well.*

JRB