

Osteopenia in Growth Hormone-Deficient Adult Males and Men With Constitutional Delayed Puberty

Finkelstein et al determined bone mineral density in a cohort of 23 men (age 26 ± 2 years) who had a history of delayed pubertal development and who had presented to the Pediatric Endocrine Clinic of Massachusetts General Hospital between 1974 and 1980. Each had a history of the onset of puberty after age 15 years and also a history of height at or below the 5th percentile for chronologic age before the pubertal growth spurt. The findings were compared with those determined in a control group of 21 men (age 24 ± 3 years) who had a history of puberty beginning before 14 years of age. Control subjects at the time of the study were 2 years younger than those in the study group in order to match the groups for duration of exposure to adult levels of gonadal steroids. Forearm bone mineral density was determined by single-photon absorptiometry, and spinal bone density was determined by dual energy X-ray absorptiometry of the first through fourth lumbar vertebrae.

Bone mineral density was significantly lower in the men who had experienced delayed puberty. Multivariate analysis of variance demonstrated that the timing of puberty remained a significant determinant of bone density after accounting for the effects of age, body mass index, exercise, alcohol intake, calcium intake, and serum testosterone. The authors conclude that their data are consistent with the hypothesis that the timing of puberty is an important determinant of peak bone mineral density in male.

Kaufman et al measured bone mineral content by photon absorptiometry in 30 men (age 26.5 ± 1.2 years) with growth hormone deficiency (GHD) (8 with isolated GHD and 22 with multiple pituitary deficiencies) and compared the results with those from 30 male controls of similar age, weight, and body mass index. Bone mineral content was measured at the distal third of the nondominant forearm (proximal site) and close to the carpal joint (distal site) of the same forearm by single photon absorptiometry. Bone mineral content of the lumbar spine (L2 to L4) was determined with dual-photon absorptiometry. All subjects with GHD had received growth hormone (GH) replacement therapy and had reached adult bone age. GH treatment had been interrupted for at least 6 months, but other hormonal replacement was continued. Bone mineral content was significantly lower at both the forearm and the lumbar spine in the subjects with pituitary hormone deficiencies. This was true regardless of whether there were single

or multiple hormonal deficiencies. A 6- to 28-month prospective evaluation of 19 subjects showed no subsequent bone loss. The authors conclude that adult men with childhood GHD have a significant bone mineral deficit as compared with age- and weight-matched controls.

Finkelstein JS, Neer RM, Beverly MK, et al. Osteopenia in men with a history of delayed puberty. *N Engl J Med* 1992;326:600-604.

Kaufman JM, Taelman P, Vermeulen A, Vandeweghe M. Bone mineral status in growth hormone-deficient males with isolated and multiple pituitary deficiencies of childhood onset. *J Clin Endocrinol Metab* 1992;74:118-123.

Editor's comment: *These 2 papers should be read together. The methodology for each is similar as are the findings. Kaufman et al show that individuals with GHD have lower bone mineral density at adulthood than controls, but they do not exclude the possibility that some of the deficit observed is due to an associated androgen deficiency. Indeed, the majority of their subjects have gonadotropin deficiency. Finkelstein et al conclude that since the only known physiologic abnormality in their subjects is a delay in the onset of puberty, this transient delay in gonadal steroid secretion is important to achieving peak bone mineral density during adolescence. However, Finkelstein's subjects had both delayed puberty and constitutional delay of growth. These patients were at or below the 5th percentile for age and their height before the pubertal growth spurt was at least 3 standard deviations below the mean. Since it is known that gonadal steroids increase GH pulse amplitude during puberty, it is possible that the decrease in bone mineral content associated with pubertal delay is secondary to a relative GH insufficiency during early adolescence. Neither study reported an increased incidence of bone fractures in adults with either GHD or delay of puberty. Such data would be exceedingly important in demonstrating the significance in the findings of either paper. Both authors suggest that their data support a role for early therapy with either androgen supplementation in boys with delayed puberty or GH treatment of males with hypopituitarism.*

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