

examined from each individual for spontaneous aberrations. Two hundred cells from each person were examined for radiation-induced aberrations. In order to be certain that cells were examined at first mitotic division, the investigators used 5-bromo-2'-deoxyuridine (BrdUrd) and phytohemagglutinin (PHA).

No patient showed a significant increase in aberrant cells with treatment. However, the mean frequency of chromatid-type aberrations was significantly higher after treatment on a per cell basis. Because 2 patients contributed inordinately to this increase, they repeated the studies on these 2 patients. No remarkable changes occurred with time. There also was a low frequency of ring chromosomes in the 6-month samples.

Although these data are not totally comparable to other studies, no real cause for concern about the risk that GH therapy predisposes to leukemia was generated.

Slyper AH, et al. *Pediatr Res* 2000;47:634-639.

Judith G. Hall, OC, MD

Inhaled Corticosteroid Use and Bone Mineral Density in Patients With Asthma

The investigators report the results of a cross-sectional survey of bone mineral density (BMD) by dual-energy X-ray absorptiometry (DXA) in a basically healthy, young adult population (20 to 40 years of age; females 119, males 77) who because of mild asthma had received inhaled glucocorticoids (primarily beclomethasone, median dose=876 mg; few to no doses of oral, parenteral, or dermal preparations) for a median period of 6 years. An inverse relationship between the *cumulative* dose of glucocorticoids and the BMD of the lumbar spine (L2-L4), left femoral neck, trochanter, and Ward's triangle was found. No relationship was found between the *daily* dose of glucocorticoids and BMD at any site, nor did any subject have a vertebral fracture. Although mean BMD measurements were normal at all sites, doubling of the *cumulative* dose of inhaled agents resulted in a "decline" in BMD of approximately -0.03 SD at all sites (approximately -0.020 g/cm² at L2-L4). The *total duration* of inhaled corticosteroid intake also was inversely related to BMD at each site. The authors estimated that if a patient received a *cumulative* dose of 5,100 mg of inhaled corticosteroids over 7 years, the L2-L4 BMD would fall 1 SD; if continued over longer periods, the patient could be at substantial risk for osteopenia and fracture.

Wong CA, et al. *Lancet* 2000;355:1399-1403.

Editor's comment: Although these data were accumulated in young adults, they have clear implications for children, many of whom receive prolonged courses of inhaled glucocorticoids for treatment of asthma. Inhaled glucocorticoids have been associated with impairment of growth and adrenal function in children.¹ Glucocorticoids adversely affect chondrocyte proliferation and skeletal mineralization; they depress bone formation by suppressing osteoblastogenesis and hastening osteoblast apoptosis, enhance bone resorption, decrease intestinal absorption of calcium, and increase urinary excretion of calcium.^{2,3} Records quantitating the cumulative dose of inhaled glucocorticoids should be maintained on all subjects receiving them. It has been suggested that BMD be determined in the young adult after

Editor's comment: Clearly, if there is a risk from GH therapy, it needs to be identified so that it can be weighed against the benefits. The present study does not seem to suggest that there is a major risk. However, it suggests there may be a subpopulation of individuals who would be at risk or contribute to any increase in chromosomal aberrations. The unusual increase in observed leukemia in the Japanese population receiving rhGH certainly deserves further evaluation, and whether there are some subgroups receiving rhGH who might be at risk must be further evaluated.

Your attention is called to a previous paper by Dr. Slyper entitled "How Safe and Effective Is Human Growth Hormone at Pharmacologic Dosing?" (GGH 1998;14[1]:4-7) Dr. Slyper and his colleagues are providing recommendations and much-needed data to utilize in our considerations of rhGH as a therapeutic tool.

he/she has received 5,000 mg of these agents and consideration be given to administration of a bisphosphonate in order to prevent glucocorticoid-induced bone loss.⁴ Careful study of mineral metabolism and BMD in children receiving these medications is warranted and necessary. The readers may be interested in the lead article in GGH (2000;16[2]:21-26) entitled "Effects of Glucocorticosteroids on Growth," by Drs. O. Mehls and B. Tönshoff of Heidelberg.

Allen W. Root, MD

1. Allen DB. *Acta Paediatr* 1998;87:123-129.
2. Manelli F, Giustina A. *Trends Endocrinol Metab* 2000;11:79-85.
3. Manolagas SC, Weinstein RS. *J Bone Miner Res* 1999;14:1061-1066.
4. Sambrook PN. *Lancet* 2000;355:1385.

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