

Leptin Acts as a Growth Factor on the Chondrocytes of Skeletal Growth Centers

In order to examine the mechanism(s) by which obesity might lead to enhanced linear growth and advanced skeletal maturation relative to chronologic age, these investigators studied the effects of leptin, a 16-kDa protein product of adipocytes with anorexigenic properties, upon cartilage cell growth and function *in vitro*. They employed mandibular condyles from 6-day-old mice in organ culture for their model of endochondral ossification. Leptin-specific receptors were identified in chondrocytes in the cartilage growth plate; the molecular weight (148 kDa) of these receptors suggested that they were likely to be the intact, biologically active isoform of this class I cytokine receptor. Addition of leptin (0.5 and 1.0 $\mu\text{g}/\text{mL}$) to the organ culture stimulated chondrocyte division in a dose dependent manner, thereby increasing the width of the proliferative zone and the size of the mandibular condyle. Enhanced functional chondrocyte maturation was demonstrated by increased production of chondroitin sulfate and collagen type II after incubation with leptin. The authors also found that leptin increased expression of the IGF-I receptor in chondrocyte precursors and that immunoneutralization of IGF-I prevented the growth and functional effects of leptin, thus suggesting that leptin's actions are mediated by the IGF-I/IGF-I receptor unit. The authors concluded that leptin has direct effects upon cartilage growth and differentiated function.

Maor G, et al. *J Bone Miner Res*;17:1034-1043.

Editor's Comment: *It has been previously reported that leptin stimulates osteoblast differentiation and maturation. However, leptin levels do not correlate with bone mineral density, an index of bone strength that is more closely related to lean body mass than to body fat content or total body weight. Indeed, experimentally central administration of leptin actually reduces bone mass by an as yet unrecognized mechanism. Of concern and consideration in evaluating this study is the need to employ very high concentrations of leptin to demonstrate biological effects, levels far greater than those achieved in vivo even in the most obese subject. Furthermore, there was a biphasic effect of leptin in this system in that, when incubated with 1.5 $\mu\text{g}/\text{mL}$, most of the reported effects were attenuated. Nevertheless, the data are of interest in furthering our understanding of how obesity might mediate its effects on linear growth and cartilage maturation - particularly in the interesting patients who grow despite complete GH deficiency as after neurosurgical removal of a craniopharyngioma or those with septo-optic dysplasia.*

Root AW, Diamond FB Jr. *Pediatric Endocrinology* 2nd ed, Saunders, Philadelphia, 2002, p 65-95.

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Effect of Supplemental Zinc on the Growth and Serum Zinc Concentrations of Prepubertal Children: A Meta-Analysis of Randomized Controlled Trials

This study performed meta-analyses of all randomized controlled intervention trials that completed the assessment of the effects of zinc supplementation on the serum zinc concentrations and physical growth of pre-pubertal children. A total of 33 acceptable studies with appropriate data were identified by MEDLINE searches and other methods. Weighted mean effect sizes were calculated for changes in height, weight, weight-for-height, and serum zinc concentrations. The authors used random-effects models, extrapolated by meta-regression techniques.

Zinc supplementation produced highly significant, positive responses in height (+0.35 SDS) and weight (+0.39 SDS) increments. Zinc supplementation caused a large increase in the children's serum zinc concentrations (+0.82). Growth responses were greater in children with low initial weight-for-age z scores, and in those aged more than 6 months with low initial height-for-age z scores.

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