**NOT TO BE MISSED**

Clinical and Basic Research Papers – August 2004 Selections

Ego Seeman, Clinical Editor  
Gordon J. Strewler, Editor

**Bone Modeling and Remodeling**


Wnt genes, including Wnt4, Wnt14, and Wnt16, are expressed in developing synovial joints, where beta-catenin and transcription activity is upregulated. Ectopic expression of an activated form of beta-catenin or Wnt14 in differentiating chondrocytes induces ectopic joint formation, whereas removal of beta-catenin in chondrocytes leads to joint fusion. The Wnt/beta-catenin signaling pathway induces synovial joint formation. —ES


Osteoblast precursors induce formation of osteoclasts. Osteoclast precursors modulate osteoblast activity, too. Mononuclear cells attach to osteoblasts, which retract forming cell-free areas invaded by the mononuclear cells that fuse forming osteoclast-like cells. Inhibition of matrix metalloproteinase activity reduced retraction of the osteoblasts. —ES


Bone remodeling rates doubled from 0.13/year to 0.24/year across menopause and strangely tripled 13 years after menopause and remained elevated. Values were not higher in patients with osteoporosis than in controls. The continued increase in remodeling rate surprised me, but the lack of difference in remodeling rate between fracture cases and controls was not surprising. To consider patients with fragility caused by excessive bone loss as a homogenous group is not wise. —ES

**Physiology and Metabolism**

Harvey KB, Donahue SW. Bending properties, porosity, and ash fraction of black bear (Ursus americanus) cortical bone are not compromised with aging despite annual periods of disuse. *J Biomech*. 2004 Oct;37(10):1513-20.

Black bears maintain bone formation during hibernation, although bone resorption is increased. Cortical bending strength, bending modulus, fracture energy, porosity, and ash fraction are not compromised with age, despite annual disuse. A fascinating model. How does this occur? —ES
Treatment and Drug Effects


Antitumor effects of bisphosphonates have been previously reported, but this study describes a novel mechanism of bisphosphonate action. The bisphosphonate zoledronic acid inhibits cervical cancer progression in a mouse model of papilloma virus oncogene-induced carcinogenesis. The matrix metalloprotease MMP-9 is implicated in the pathway of zoledronate effects by experiments showing that macrophage numbers, macrophage expression of MMP-9, and recruitment of vascular endothelial growth factor are reduced by zoledronate and that effects of zoledronate resemble those of MMP-9 removal. —GJS


Cases and controls differed in the proportion of males, females, and hospital populations, by race and sex. Even small imbalances in these covariates may influence the data, independent of corticosteroids, because growth is so rapid. These design issues warrant a randomized trial before the inference that corticosteroids are safe in children can be made with confidence. Statistical “adjustments” can’t do everything. —ES


This is an important issue. There must be strength in 30,601 fracture cases and 120,819 controls. Fracture risk reduction was 23% for current beta-blocker use, 20% for current thiazide use, and 19% for combined current use, all statistically significant. Several studies support these findings, others don’t. Seems odd that the fractures were mostly not the type conventionally regarded as fragility fractures (12,837 hand/lower arm and 4627 foot). Nothing like a randomized trial to settle the issue. —ES


Disruptions in hypothalamic-gonadal function related to energy deficits are associated with low leptin. Recombinant leptin treatment increased mean luteinizing hormone (LH), LH pulse frequency, follicular number and diameter, ovarian volume, estradiol levels, and ovulatory cycles in some women. —ES

Reviews, Editorials, and Perspectives


Other Studies of Potential Interest


