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NOT TO BE MISSED

Clinical and Basic Research Papers – June 2005 Selections

Ego Seeman, Clinical Editor
Gordon J. Strewler, Editor

Bone Modeling and Remodeling

Sugawara Y, Kamioka H, Honjo T, Tezuka K-i, Takano-Yamamoto T. Three-dimensional reconstruction of chick calvarial osteocytes and their cell processes using confocal microscopy. *Bone*. 2005 May;36(5):877-83. [Abstract]

> *This is a lovely study of morphology that lays to rest the notion that bone is somewhere between a rock and a hard place. The average of 10 osteocytes was 52.7 processes, and the point-to-point distance between the centers of the osteocytes was 24.1 µm. Each osteocyte spanned an average of 4180 µm^2 of bone volume. The average total length of the processes, average surface area, and average volume of one osteocyte were 1070 ± 145 µm, 1509 ± 113 µm^2, and 394 ± 49 µm^2, respectively. —ES*

Diagnosis

Kern LM, Powe NR, Levine MA, Fitzpatrick AL, Harris TB, Robbins J, Fried LP. Association between screening for osteoporosis and the incidence of hip fracture. *Ann Intern Med.* 2005 Feb 1;142(3):173-81. [Abstract]

> *This is an important paper because it implies that screening works. The problem is that the lower hip fracture rate in the two cities providing a screening service, compared with the two cities that did not, may not necessarily be the result of the densitometry service. This point is discussed in an incisive editorial by Cummings. (Cummings SR.* Ann Intern Med *2005;142[3]: 217-9) —ES*

Epidemiology

Lanou AJ, Berkow SE, Barnard ND. Calcium, dairy products, and bone health in children and young adults: a reevaluation of the evidence. *Pediatrics.* 2005 Mar;115(3):736-43. [Abstract]

> *This is one of the most intellectually honest and forthright reviews of this topic I have read. It was a refreshing pleasure to read an article in which the data were interpreted as is, not with the twists and turns spun by the advocates of calcium supplementation. In essence, in clinical, longitudinal, retrospective, and cross-sectional studies, neither increased consumption of dairy products nor total dietary calcium consumption show even a modestly consistent benefit for bone health in children or young adults. —ES*

Genetics

Morko J, Kiviranta R, Hurme S, Rantakokko J, Vuorio Differential turnover of cortical and trabecular bone in transgenic mice overexpressing cathepsin K. *Bone.* 2005; May;36(5)::854–65. [Abstract]

This study is a nice illustration of what seems to be adaptive modeling and remodeling. In the face of cathepsin K overexpression producing high turnover osteopenia of metaphyseal trabecular bone, mice homozygous for the transgene locus (UTU17$^{+/+}$) had increased cortical thickness and BMD,and increased porosity of diaphyseal cortical bone. The increased cortical thickness and BMD in diaphyses demonstrate the different nature and reactivity of trabecular and cortical bone in mice and suggest that the biomechanical properties of cortical bone are preserved through adaptation. —ES

Physiology and Metabolism

Khosla S, Melton III LJ, Robb RA, Camp JJ, Atkinson EJ, Oberg AL, Rouleau PA, Riggs BL. Relationship of volumetric BMD and structural parameters at different skeletal sites to sex steroid levels in men. *J Bone Miner Res.* 2005 May;20(5):730-40. [Abstract]

Advancing age is associated with a decline in everything, including sex steroids in men. The significance of this work, and other work by this group, is to drive home the importance of estrogen in men, as well as women, and that free estrogen is the most consistent predictor of volumetric density and several geometric variables. —ES

Revankar CM, Cimino DF, Sklar LA, Arterburn JB, Prossnitz ER. A transmembrane intracellular estrogen receptor mediates rapid cell signaling. *Science.* 2005 Mar 11;307(5715):1625-30. [Abstract] [Full Text]

Thomas P, Pang Y, Filardo EJ, Dong J. Identity of an estrogen membrane receptor coupled to a G protein in human breast cancer cells. *Endocrinology.* 2005 Feb;146(2):624-32. [Abstract] [Full Text]

Hewitt SC, Deroo BJ, Korach KS. Signal transduction. A new mediator for an old hormone? *Science.* 2005 Mar 11;307(5715):1572-3. [Full Text]

Estrogen may prevent bone loss through nongenomic events. These two papers provide convincing evidence that the G protein-coupled transmembrane receptor GPC30 is a nongenomic estrogen receptor that activates different downstream signaling pathways than nuclear estrogen receptor α. Revankar et al. *identify the plasma membrane as the home of GPC30; Thomas* et al. *find it in the endoplasmic reticulum. Both groups report the presence of endogenous GPC30 mainly in cancer cells. What role does GPC30 play in estrogen signaling in bone and other normal tissues? —GJS*

Reviews, Perspectives, and Editorials

Brown MA. Genetic studies of osteoporosis--a rethink required. *Calcif Tissue Int*. 2005 May;76(5):319-25. [Info]

Cranney A, Adachi JD. Benefit-risk assessment of raloxifene in postmenopausal osteoporosis. *Drug Saf.* 2005;28(8):721-30. [Abstract]

Dang ZC, Lowik C. Dose-dependent effects of phytoestrogens on bone. *Trends Endocrinol Metab.* 2005 Jul;16(5):207-13. [Abstract]

Davies JH, Evans BA, Gregory JW. Bone mass acquisition in healthy children. *Arch Dis Child.* 2005 Apr;90(4):373-8. [Abstract]

Ebeling PR. Defective osteoblast function may be responsible for bone loss from the proximal femur despite pamidronate therapy. *J Clin Endocrinol Metab.* 2005 Jul;90(7):4414-6. [Full Text]

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Jarvinen TL, Sievanen H, Jokihaara J, Einhorn TA. Revival of bone strength: the bottom line. *J Bone Miner Res.* 2005 May;20(5):717-20. [Info]

Kobayashi T, Kronenberg H. Minireview: transcriptional regulation in development of bone. *Endocrinology.* 2005 Mar;146(3):1012-7. [Abstract] [Full Text]

Kobayashi T, Soegiarto DW, Yang Y, Lanske B, Schipani E, McMahon AP, Kronenberg HM. Indian hedgehog stimulates periarticular chondrocyte differentiation to regulate growth plate length independently of PTHrP. *J Clin Invest.* 2005 Jul;115(7):1734-42. [Abstract] [Full Text]

Kuehn BM. Evidence-based guidelines needed for osteoporosis screening and treatment. *JAMA.* 2005 Jul 6;294(1):34. [Info]

Mystakidou K, Katsouda E, Stathopoulou E, Vlahos L. Approaches to managing bone metastases from breast cancer: The role of bisphosphonates. *Cancer Treat Rev.* 2005 Jun;31(4):303-11. [Abstract]

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Steddon SJ, Cunningham J. Calcimimetics and calcilytics--fooling the calcium receptor. *Lancet.* 2005 Jun 25;365(9478):2237-9. [Abstract]

Other Studies of Potential Interests

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Brachvogel B, Moch H, Pausch F, Schlotzer-Schrehardt U, Hofmann C, Hallmann R, von der Mark K, Winkler T, Poschl E. Perivascular cells expressing annexin A5 define a novel mesenchymal stem cell-like population with the capacity to differentiate into multiple mesenchymal lineages. *Development.* 2005 Jun;132(11):2657-68. [Abstract]

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Egusa H, Schweizer FE, Wang CC, Matsuka Y, Nishimura I. Neuronal differentiation of bone marrow-derived stromal stem cells involves suppression of discordant phenotypes through gene silencing. *J Biol Chem.* 2005 Jun 24;280(25):23691-7. [Abstract] [Full Text]

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