Dpd levels (5.02 ± 1.20 nMol / mol Cr, p<0 .01), increased levels of urinary FSH (38.6 ±3.84 m IU / mg Cr, p<0.0001) and IL6 (11.68±2.61 ng/ml, p<0.05) with osteopenic changes on BMD whereas E_1G, bone formation markers and BMD though low did not show any significant change. In the osteopenic menopausal women all the bone markers were significantly elevated indicating increased rate of bone remodeling. Of the three cytokines, IL6 increased significantly (15.85±3.5 ng/ml, p<0.0001) correlating well with increased bone turnover (CTx 1126 ± 362 µg /mol Cr and Dpd 8.49 ± 2.65 nM/ mol Cr) while there was marginal increase in TNFα levels (6.5 pg/ml; p < 0.0056) only in the osteoporotic women. A significant drop in E_1G (8.99 ng/mgCr; p<0.0001) and BMD measurements with rise in IL 6 was also observed in these women. The data suggests that elevated cytokines (IL 6 and TNFα) and bone resorption markers (CTx and Dpd) are associated with rapid of fall of estrogens in the first decade of menopause leading to postmenopausal osteoporosis. Combination of hormonal profiles, bone resorption markers and cytokines will thus aid in identifying women at risk for osteoporosis.

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M459

See Sunday Plenary Number S459

M460

Relationships Between Leptin, PTH, Vitamin D and Bone Metabolism Markers in Patients with Hip Fracture. A. A. Fisher*[1], E. K. Southcott*[1], S. L. Goh*[2], W. Srikusalanukul*[1], M. W. Davis*[1], P. N. Smith*[2]. [1]Department of Geriatric Medicine, The Canberra Hospital, Australian National University, The Canberra Hospital, Woden, ACT, Australia, [2]Department of Orthopaedic Surgery, The Canberra Hospital, Australian National University, The Canberra Hospital, Woden, ACT, Australia.

The relationship between leptin and bone metabolism is controversial. The study aim was to investigate leptin-skeletal interactions in older patients with hip fracture (HF), a population not previously studied.
In 207 consecutive patients (mean age 82.1 ± 7.9 years; 75.8% women) with low-energy trauma HF (119/88 cervical/trochanteric) serum concentrations of leptin, 25 hydroxy-vitamin D [25(OH)D], parathyroid hormone (PTH), calcium, phosphorus, magnesium, osteocalcin (OC), bone-specific alkaline phosphatase (BAP) and urine excretion (normalised for urinary creatinine) of free deoxypyridinoline (DPD) and N-terminal cross-linked telepeptide of type 1 collagen (NTx) were measured and clinical data collected prospectively.
Elevated PTH (> 6.5pmol/L) was present in 53%, 25(OH)D insufficiency (< 50nmol/L) in 81.6%, excessive bone resorption (increased DPD and/or NTx excretion) in 93.7% and low bone formation (low OC and/or BAP) in 59.2%. Leptin (log-transformed) was significantly and positively correlated with OC (r= 0.18; p= 0.006) and negatively with NTx (r= -0.17: p= 0.015) and DPD (r= - 0.14: p= 0.037). In both cervical and trochanteric HF groups, leptin was positively associated with OC, but the association with DPD was significant only in trochanteric HF (r= -0.30; p= 0.009). Trochanteric compared to cervical HF patients have higher levels of PTH (7.9 ± 6.0 vs 5.9 ± 3.8 pmol/L; p = 0.005), but the concentrations of leptin, 25(OH)D and bone turnover markers were similar. Only in cervical HF patients were leptin and PTH positively correlated (r= 0.26; p= 0.005) and 25(OH)D levels were negatively and significantly correlated with NTx (r= -0.25; p= 0.016), DPD (r= -0.31; p= 0.002) and BAP (r= -0.24; p= 0.012). Other bone metabolism parameters were not associated with leptin in neither group.
These findings suggest that in HF patients there exists a complex relationship between leptin and calciotropic factors, that serum leptin may independently contribute to bone remodelling and is likely to exert different effect on cortical and trabecular bone compartments.

Disclosures: A.A. Fisher, None.

M461

72. Do Periosteal and Intracortical Responses to Ulnar Fatigue Loading Differ Between Old and Young Rats? J. B. Jones*, R. T. Kitterman*, S. D. Mendenhall*, J. G. Skedros. Dept. of Orthop. Surgery, Univ. of Utah, SLC, UT, USA.

Age-related skeletal deterioration results not only in decreased bone mass but also bone quality. Inadequate modeling responses and/or incomplete infilling of resorption cavities following bone fatigue contribute to this decline in bone mechanical properties. Using the rat ulna fatigue model, we hypothesized that older adult rats would show less periosteal woven bone apposition and resorption space infilling when compared with younger adult rats following mechanical loading. With IACUC approval, 28 male F344 rats (14, 5 month-old, 14, 15 month-old) were obtained from the National Institute on Aging (Bethesda, MD). Eight rats of each age formed the experimental groups and the remaining were used for load/strain calibration. Right forearms were cyclically loaded [Uthgenannt & Silva, J Biomech, 2006] and the contralateral ulnae served as controls. Tetracycline was injected 13 and 3 days prior to sacrifice at 18 days post-loading. Ten transverse sections were then cut from mid-third ulnar diaphyses and mounted on slides. Resorption space areas (Rs.Ar/Ct.Ar), infilling areas (Rs.Inf.Ar/Ct.Ar), and periosteal woven bone area (PWb.Ar/Ct.Ar) were quantified. Kruskal-Wallis ANOVA was employed with significance set at p<0.05. Contrary to our hypothesis that older rats would exhibit less periosteal bone apposition, a larger amount was observed when compared to younger rats (see Table). Additionally, total resorption area was twice as large in older rats. However, when resorption space infilling area was considered, the older rats showed significantly less infilling than younger rats (33% vs. 55%, see Table). These data suggest that older rats show an imbalance between intracortical resorption and bone formation which leads to net bone loss--a similar phenomenon experienced by aging humans. The finding that older rats exhibit more periosteal woven bone than younger rats implies the possibility of a compensatory mechanism that counteracts the increased cortical porosity. Although a similar interaction between remodeling and modeling has been suggested in humans, the modeling response is relatively subtle [Ural & Vashishth: J Orthop Res 2006]. This demonstrates a limitation when attempting to extrapolate the capacity of bone modeling in 15-month old rats to that in aging humans.

Table: Periosteal modeling, intracortical resorption, and intracortical infilling by age in the rat

	5 month old rats (mean ± SD)	15 month old rats (mean ± SD)	
PWb.Ar/Ct.Ar	0.0630 ± 0.0875	0.1578 ± 0.1380	p < 0.001
Rs.Ar/Ct.Ar	0.0063 ± 0.0235	0.0129 ± 0.0225	p = 0.008
Rs.Inf.Ar/Ct.Ar	0.0035 ± 0.0118	0.0043 ± 0.0065	p = 0.030

PWb.Ar/Ct.Ar - periosteal woven bone area / cortical area (mm^2/mm^2)
Rs.Ar/Ct.Ar - total resorption space area / cortical area (mm^2/mm^2)
Rs.Inf.Ar/Ct.Ar - resorption space infilling area / cortical area (mm^2/mm^2)

Disclosures: J.B. Jones, None.
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M462

Increased Active Osteoclasts Are Associated with Acute Cancellous Bone Loss in Adult Mice Exposed to Ionizing Radiation and Musculoskeletal Disuse. H. Kondo[1], R. Mojarrab*[1], A. Wang*[1], J. Phillips*[1], E. A. C. Almeida*[1], D. J. Loftus*[1], E. Morey-Holton*[1], R. K. Globus*[1], W. Vercoutere*[1], C. Limoli*[2], N. D. Searby*[1]. [1]Bone and Signaling Lab, NASA Ames Research Center, Moffett Field, CA, USA, [2]Radiation oncology, University of California Irvine, Irvine, CA, USA.

Spaceflight challenges the skeletal health of astronauts by exposure to radiation in microgravity. Hamilton et al. (JAP (2006) 101:789) showed that irradiation alone decreases bone mass in growing mice 4 mo after exposure to 2 Gy vs. controls, as does musculoskeletal disuse. We hypothesize that radiation and disuse share cellular and molecular mechanisms to cause rapid bone loss in the adult. To define dose (1-2 Gy) and time dependence (3 or 10 d) of skeletal responses to radiation, 4 mo old C57/Bl6 mice were Cs^{137} gamma-irradiated (IR), then marrow cells analyzed for viability by FACS and bones for structure by microCT. In a second study, mice were hindlimb unloaded (HU) or normally loaded (NL) for 7 d; half the mice from each group were IR with 2 Gy 4 d into the unloading period. Bones were analyzed for structure (microCT), osteoclast surface (histomorphometry) and oxidative damage to lipids (peroxidation by malondialdehyde assay). As expected, HU for 7 d decreased cancellous bone compared to NL. Surprisingly, only 3 d after exposure, IR (2 Gy) caused a loss in cancellous BV/TV(~20%), trabecular number, and connectivity similar to 7 d HU. By 10 d after IR, BV/TV was 25% lower than controls at 1 Gy and 35% lower at 2 Gy, showing both dose and time-dependent effects of IR. Cancellous bone loss was similar in mice exposed to IR during HU, compared to mice treated with either IR or HU alone. IR transiently reduced (by 65% at 3 d) numbers of viable marrow cells due to increased apoptosis. IR elevated (by 36%) lipid peroxidation in bone. Osteoclast surface per bone surface increased 113% due to IR, 100% due to HU, and 153% due to both IR and HU compared to NL, indicating stimulated resorption. Hydrogen peroxide treatment of cultured bone marrow cells caused a dose-dependent increase in TRAP+ cells, inhibited by the anti-oxidant, alpha-lipoic acid. Together, these results showed that IR and HU caused similar detrimental effects on cancellous bone structure of adult mice, and shared the cellular mechanism of increasing active osteoclasts. In the short-term, continuous HU did not alter the structural changes caused by radiation, possibly due to depletion of osteoclast precursors by unloading or irradiation alone. Finally, radiation caused oxidative stress in bone tissue that may contribute to increased resorption leading to rapid bone loss. These results have potential clinical relevance to astronauts as well as to cancer patients treated therapeutically with radiation.

Disclosures: H. Kondo, None.
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