M005

35. Changes in Osteocyte Densities During Skeletal Organogenesis. J. G. Skedros, K. J. Hunt, D. Gingell.* Depart. of Orthopaedic Surgery, U. of Utah, Salt Lake City, UT, USA.

Recent advanced analytical models of bone organogenesis and adaptation suggest that osteocyte densities significantly influence remodeling rates [Mullender and Huiskes, 1995, J. Orthopaedic Res., 13:503-512]. However, the utility of these models is limited by a paucity of relevant quantitative data from developing mammalian limb bones. In this investigation we quantified ontogenetic changes in osteocyte population densities in artiodactyl calcanei, which are subject to a relatively simple loading regime. Calcanei from 26 mule deer were classified into four age groups: 1) young fawns, 2) older fawns, 3) subadults, and 4) adults. Two sections, obtained from mid-third diaphysis, were prepared for backscattered electron imaging. Osteocyte lacuna population densities (no./mm^2) were counted in two 100X images (1.15 X 0.75mm) obtained in periosteal, middle and endosteal regions of cranial (Cr.) and caudal (Cd.) cortices. Results (see Table: Means) show age-related regional variations in osteocyte density, with progressively greater numbers in the cranial cortex. Regression analysis of Cr/Cd ratio vs. diaphyseal length demonstrated a moderate positive correlation ($r = 0.621$, $p<0.001$). Combined data (Cr + Cd), however, showed no significant differences in young fawns, old fawns, and adults. Furthermore, cell density is relatively lower in caudal cortex of subadults and adults, even though remodeling rates in this region are known to be relatively greater. These data challenge the dictum that osteocyte densities are greatest in bones or regions with greater remodeling rates.

	Young	Old Fawn	Subadult	Adult
Cranial	1074	966	1339	1121
Caudal	1097	1001	1169	881
Cr./Cd.	0.99	0.97	1.15	1.29
Cr + Cd	877	993	1239	1000

M006

Possible Involvement of Increasing Plasma Homocysteine Level in the Age Dependent Bone Loss. M. K. Miyao,[1] T. Hosoi,[2] S. Inoue,[1] M. Shiraki,[3] Y. Ouchi.[1] [1]Department of Geriatrics, Graduate School of Medicine, University of Tokyo, Tokyo, Japan, [2]Endocrinology Section, Tokyo Metropolitan Geriatric Hospital, Tokyo, Japan, [3]Research Institute and Practice for Involutional Diseases, Nagano, Japan.

Accelerated bone loss during aging contributes largely to the pathogeneis of osteoporosis. However, mediators of the aging effects are not determined. Recent studies suggest that a mild increase in plasma homocysteine level is associated with higher incidences of atherosclerotic and thromboembolic diseases. In addition, homocysteine levels are known to rise progressively with age. These data suggest that homocysteine may play roles in the pathogenesis of aging-dependent diseases including osteoporosis. However there have been no studies which focused on the relationship between plasma homocysteine and bone loss during aging. In this study, we examined the plasma levels of homocysteine and their relationship with bone mineraldensity (BMD) and other biochemical parameters in healthy Japanese women. We enrolled 273 Japanese healthy volunteer women (mean age 61 years). Lumbar (L2-4) and total body bone mineral density(BMD) were measured by dual-energy X-ray absorptiometry (DXA). Plasma homocystein level and bone turnover markers were measured with the samples after overnighit fasting. In univariate analysis, homocystein was correlated with lumbar BMD ($r=0.012$; $p<0.01$), total body BMD ($r=0.013$; $p<0.0001$). In addition, plasma homocystein level was also correlated with serum intact osteocalcin ($r=0.46$; $p<0.0001$) and urinary deoxypyridinoline (($r=0.254$; $p<0.0001$). Lower level of serum vitamin B12 was associated with higher homocysteine levels but there were no correlation with folic acid or vitamin B6 levels. We performed multivariate analysis using the following variables; plasma homocystein, body mass index,1,25(OH)2 vitamin D3, parathyroid hormone, calcitonin. As a result, plasma homocystein, body mass index and 1,25(OH)2 vitamin D3 were correlated independently to L2-4 and total body BMD. Homocysteine level, parathyroid hormone, 1,25(OH)2 vitamin D3, BMI were significantly associated with age (for plasma homocysteine, $r=.097$, $p=0.0001$). These results suggest that the increase in plasma homocysteine level during aging may play important roles in the age-dependent bone loss in postmenopausal women. The measures to control plasma homocysteine level would be one of the options to prevent and treat osteoporosis.

M007

Long-term Osseointegration of Titanium Nitride-coated Implants i Rat Femur. A. Weiss,[1] G. Sovak,*[1] I. Gotman,*[2] E. Gotmanas.*[2] [1]Faculty of Mec Technion, Haifa, Israel, [2]Faculty of Mechanical Engineering, Technion, Haifa, Israel.

Hard TiN-coatings may improve the relatively poor wear-resistance and increa life-span of titanium-based orthopaedic implants. The aim of the present research v evaluate the long-term osseointegration of Ti-6Al-4V alloy implants coated with Tit nitride (TiN) by a new technique. Pins 1mm x 2cm, were inserted into the distal fem six-month-old female Wistar rats. Animals were killed 2 and 6 months after surge rays were taken immediately after surgery and before sacrificed. In order to demon bone mineralization, animals were given 50 mg/kg body weight of oxytetracycline, 3 before sacrificed. Femurs were embedded undecalcified in LKB Historesin an microns thick crosssections were cut with a low-speed diamond saw, coated with gol examined by scanning electron microscopy (SEM). SEM revealed that both TiN-c and uncoated implants were surrounded by a collar of trabecular bone. Strong fluore tetracyclin label, indicating ongoing mineralization, was observed 2 month after imp tion, and diminished after 6 months. Frozen sections of decalcified specimens were ined for the activity of alkaline phosphatase (ALP) as a marker of osteoblasts, tar resistant acid phosphatase (TRAP) as a marker of osteoclasts and non-specific es (NSE) for macrophages. Of these enzymes, a strong ALP activity was observed in the collar around implants. TRAP and NSE activities in the implant area were weak, sim to their activities in the regions distant from the implants.

In conclusion, the finding of the present research indicate excellent long-term bio patibility and osteointegration of TiN-coatings. No adverse tissue reaction to to Ti observed. Hence, TiN may be considered as a novel wear-resistant coating for titan based prostheses, and may increase durability, reduce wear debris formation and pr aseptic loosening of prosthesis.

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M008

Identifying Young Women at High Risk for Osteoporosis. G. A. Hawk Ridout, L. J. Fielding,* C. C. Chase.* Osteoporosis Clinical Research, Women's Co Campus of Sunnybrook and Women's College Health Sciences Centre, Toronto, Canada.

In older women, low values for bone mass by *both* quantitative heel ultrasound ((*and* dual energy x-ray absorptiometry (DEXA) are associated with greatest fracture ris a cohort of healthy pre-menopausal women, we examined predictors of 'low bone mas DEXA and QUS.

We recruited 668 healthy Caucasian women ages 18 to 35 years to participate in a examining determinants of peak bone mass. Clinical determinants of bone mass assessed using a detailed, standardized interview. Bone mass was measured using D (femoral neck, lumbar spine) and QUS of the heel (stiffness, SOS, BUA). Bone mas considered low if the corresponding z score was < -1.00 (DEXA, stiffness) or if v were in the lowest quintile (BUA, SOS). Using multivariate logistic regression model we examined the predictors of low bone mass based on QUS, DEXA, or both.

The mean age of the cohort was 27.3 yrs (18-35 yrs). Depending on the site, up to of individuals were considered to have low bone mass at any one site, and up to 30% least one site. In multivariable regression analysis, predictors of having low BMD base *both* DEXA and QUS were: lower body weight, menarche at age 15 or later, and less p ical activity as an adolescent. Individuals with all 3 of these risk factors had an 85% ch of having low bone mass using *both* techniques.

Simple assessment by history of three risk factors for low bone mass can identify viduals at presumably very high risk for osteoporosis. Interventions, such as dietary lifestyle modification, may help to reduce risk for osteoporosis later in life and shoul considered.