

### **Clinical risk factors and biochemical variables were not useful predictors of BMD**

#### **Evaluation of methods for prediction of bone mineral density by clinical and biochemical variables in perimenopausal women**

Vestergaard P, Hermann AP, Gram J, Jensen LB, Eiken P, Abrahamsen B, Brot C, Kolthoff N, Sorensen OH, Beck Nielsen H, Pors Nielsen S, Charles P, Mosekilde L, *Maturitas* 2001;40:211-220.

**Background:** Identification of women with low BMD in the perimenopausal period could result in therapy and prevention of osteoporotic fractures later in life. The gold standard for identification of low BMD is DXA, but clinical and biochemical variables might be useful for identification of subjects with low BMD when measurement with DXA is not practical.

**Study and Results:** Healthy perimenopausal women (n=2016; mean age 50 years) participating in the Danish Osteoporosis Prevention Study (DOPS) were evaluated with DXA to determine whether simple clinical variables and biochemical markers of bone turnover could predict BMD. Age, serum osteocalcin, serum bone-specific alkaline phosphatase, and maternal fracture history were significant risk factors for low BMD in several mathematical models, but when applied to a new population the models using these risk factors did not perform well. A large percentage of the predictive value was associated with age. Age, biochemical variables, and prior fracture history might be more predictive of low BMD in older women.

**Conclusion:** Simple clinical and biochemical variables were not useful predictors of low BMD in perimenopausal women.

### **Insulin-like growth factor shown to be an important influence on bone in postmenopausal women**

#### **The contribution of IGF-I to skeletal integrity in postmenopausal women**

Munoz-Torres M, Mezquita-Raya P, Lopez-Rodriguez, Torres-Vela E, de Dios Luna J, Escobar-Jimenez F, *Clin Endocrinol* 2001;55:759-766.

**Background:** Insulin-like growth factor I (IGF-I) and growth hormone (GH) are secreted maximally during puberty and are important contributors to maintenance of bone mass and determination of body composition in adulthood. Previous studies have shown a complex relationship among age, estrogen deficiency, and IGF-I. *In vitro* cell studies have shown IGF-I to be an important regulator of osteoblast function. Recent studies described a relationship between risk of vertebral fracture and IGF-I that was independent of BMD.

**Study and Results:** IGF-I, BMD at the spine and femur, quantitative ultrasound at the heel, and anthropometric variables were studied in otherwise healthy, ambulatory postmenopausal women (n=154) who were referred for osteoporosis screening. Half of the women were osteoporotic using WHO guidelines. Mean IGF-I levels were lower in osteoporotic women (95 µg/l) compared with non-osteoporotic women (120 µg/l). IGF-I, years since menopause, and body mass index explained 23% of the observed variance in spine BMD and 30% of the variance in femur neck BMD. IGF-I accounted for 8.5% of the variance in BMD at the spine, 4.6% at the femur neck, and 7.1% of the variance in heel BUA after adjustment for all other variables. IGF-I was significantly lower in women with prevalent vertebral fractures (91 µg/l vs. 114 µg/l) compared to those without vertebral fractures. Vertebral fractures were most strongly associated with BMD <-2.5 SD (Odds Ratio (OR) = 3.3), followed by IGF-I (OR = 3.0).

**Conclusion:** IGF-I is an important factor in influencing bone quantity and bone quality in postmenopausal women.

## **Moderate, but not severe, functional disability increased risk for hip fractures among stroke patients**

### **Long-term fracture risk following ischemic stroke: a population-based study**

Melton III LJ, Brown Jr RD, Achenbach SJ, O'Fallon WM, Wisnant JP, *Osteoporos Int* 2001;12:980-986.

**Background:** Immobilization following a stroke results in substantial bone loss, especially on the affected side. Increased tendency to fall elevates the risk of fracture among stroke patients. Few studies have quantified the risk of fracture following stroke.

**Study and Results:** Minnesota residents (179 women and 209 men) who survived for 90+ days following a stroke were examined retrospectively to determine their subsequent overall risk of fracture. Average survival was 7.4 years (range 91 days to 35 years). Cases were matched with controls of similar age and sex from the same population. There was no increased risk of fractures generally or hip fractures specifically in stroke patients compared with controls. Fracture risk was high among stroke patients, but advanced age also was an important determinant of fracture risk in patients and controls (71% were 65 years or older; 10% were over 85 years of age). Fracture risk increased with age, hospitalization, and with moderate functional impairment among stroke patients, but severe disability was not related to increased fracture risk, perhaps because of a reduced chance of falling.

**Conclusion:** Fracture risk related to falls increased among stroke patients who were independently mobile, but there was no overall increased risk among stroke patients compared with controls.

## **Osteoporotic fractures reduce the quality of life among Canadians**

### **The influence of osteoporotic fractures on health-related quality of life in community-dwelling men and women across Canada**

Adachi JD, Ioannidis G, Berger C, Joseph L, Papaioannou A, Pickard L, Papadimitropoulos EA, Hopman W, Poliquin S, Prior JC, Hanley DA, Olszynski WP, Anastassiades T, Brown JP, Murray T, Jackson SA, Tenenhouse A, and the Canadian Multicentre Osteoporosis Study (CaMos) Research Group, *Osteoporos Int* 2001;12:903-908.

**Background:** The effect of fracture on the quality of life of patients is often overlooked. Few studies have attempted to quantify the impact of fractures on health-related quality of life (HRQL).

**Study and Results:** Prevalent fractures were compared to HRQL in 4816 participants (1235 men and 3581 women) in the Canadian multicenter study (CaMos) who were age 50 years and older. The HRQL instrument assessed functional ability, well-being, and overall health. Subjects were divided into four groups based on fracture prevalence. Group I subjects had clinically recognized fractures attributed to osteoporosis (hip, vertebral, wrist/forearm, pelvis, and rib fractures). Subjects with subclinical vertebral fractures made up group II. Group III subjects had fractures not found in subjects from groups I and II. Group IV subjects had no prevalent fractures. Anthropometric data, medical histories, therapeutic drug use, spinal radiographs, and prevalent fractures were recorded for all participants. Fractures occurred in 41.4% of women and 37.7% of men. HRQL scores were lower for subjects from group I compared with subjects from group IV, particularly in the physical functioning and role-physical domains for women with hip and pelvis fractures and for men with hip fractures. Nearly 30% of hip fracture patients became dependent on others to carry out daily living activities. Subclinical vertebral fractures had a modest negative effect on HRQL, with no additional effect of multiple vertebral fractures. No differences in HRQL scores were found between group III and group IV subjects. Time since last fracture was not highly related to HRQL scores, indicating that impairment related to fracture persisted over time.

**Conclusion:** Fractures of the hip and pelvis in women and hip in men had the greatest negative effect on HRQL scores. Subclinical vertebral fractures were moderately related to HRQL score.

## **Several modifiable risk factors for hip fracture identified in men**

Tanaka T, Latorre MRDO, Jaime PC, Florindo AA, Pippa MGB Zerbini CAF, *Osteoporos Int* 2001;12:942-949

### **Risk factors for proximal femur osteoporosis in men aged 50 years or older**

**Background:** Osteoporotic fracture is a major health problem among men that will become greater with increased life expectancy. Hip fractures are the most costly fractures among both men and women and produce greater morbidity and mortality in men than women. Identification of men who will develop osteoporosis is important for prevention of future fractures. Evaluation of BMD with densitometry is the principal means of determining risk of osteoporosis and fracture, but clinical risk factors might also contribute to identification of susceptible individuals when densitometry is not available.

**Study and Results:** Male participants over 50 years of age (n = 325) were evaluated with DXA at the femoral neck, measured with anthropometric techniques, and questioned about medical history, maternal and paternal history of fracture after age 50 years, smoking habits, alcohol consumption, calcium intake and physical activity. Independent risk factors for osteoporosis included: a) low body mass index (BMI < 25; Odds Ratio (OR) = 13.3), b) low current leisure/physical activity (lowest tertile of the physical exercise/leisure activity score; OR 15.4), c) older age ( $\geq 70$  years; OR 3.5), d) current smoker (OR 6.4), e) former smoker of 20+ cigarettes/day (OR 4.3), f) no use of thiazide diuretics (OR 3.8), g) white race (OR 4.5), and h) maternal history of fracture after age 50 (OR 6.3). There was no association of femur fracture with calcium consumption or ingestion of alcohol, coffee or cola beverages.

**Conclusion:** Modification of several risk factors for proximal femur osteoporosis in men could have beneficial effects on male fracture risk, morbidity, and mortality.

### **Skin tensile properties could prompt BMD evaluation with DXA**

#### **Comparative effect of hormone replacement therapy on bone mass density and skin tensile properties**

Pierard GE, Vanderplaetsen S, Pierard-Franchimont C, *Maturitas* 2001;40:221-227.

**Background:** Bone and skin are collagen-rich structures affected by hormonal changes that occur at the menopause. Hormone replacement therapy (HRT) helps prevent postmenopausal bone loss and skin deterioration.

**Study and Results:** Healthy postmenopausal women (n=120) were evaluated with DXA at the spine, total hip and femoral neck. Skin tensile properties were measured with a computerized suction device (Cutometer 474) on the underside of the forearm to minimize effects of photoaging. Half of the women were receiving HRT and half were untreated. Skin elasticity was correlated with BMD in both groups of women. Women on HRT showed a reduced decline in skin elasticity compared with untreated women. There was no significant difference in BMD between the two groups of women, although a trend towards higher BMD in the HRT group was apparent.

**Conclusion:** Skin tensile properties indicated HRT efficacy in postmenopausal women. Authors noted that a decline in skin tensile properties should prompt BMD evaluation with DXA.

### **Ultrasound (Achilles) and DXA measurements depressed in patients with Rett Syndrome**

#### **Dual X-ray absorptiometry and bone ultrasonography in patients with Rett Syndrome**

Cepollaro C, Gonnelli S, Bruni D, Pacini S, Martini S, Franci MB, Gennari L, Rossi S, Hayek G, Zappella M, Gennari C, *Calcif Tissue Int* 2001;69:259-262.

**Background:** Rett Syndrome (RS), a progressive neurological disorder in girls, is caused most likely by a genetic mutation on the X-chromosome. RS results in severe or profound mental retardation, profound psychomotor retardation, absence of speech, inability to use hands, and reduced brain growth. RS patients also have skeletal abnormalities that include reduced BMD and increased fracture risk.

**Study and Results:** Patients with RS (n = 82; age 2 to 22 years) evaluated with DXA and quantitative ultrasonography (QUS) at the heel (Achilles) and phalanges were compared with 82 age-matched controls. Biochemical markers of bone turnover were also examined. DXA results at the ultradistal and distal radius and QUS results were lower in RS patients compared with controls and were lower in non-ambulatory RS patients compared with ambulatory patients. QUS Stiffness (% of young adults) was 74.5% in controls and 34.5% in RS patients. Stiffness among nonambulatory RS patients (22.1%) was about half (41.3%) that

seen in ambulatory RS patients. RS patients on anticonvulsants had lower skeletal values than other RS patients. Serum markers of bone turnover were significantly higher in RS patients compared with controls. **Conclusion:** Ambulatory status and anticonvulsive use were important contributors to altered bone status in RS patients.

### **Alendronate prevents bone loss related to inhaled steroids**

#### **Alendronate for the prevention of bone loss of patients on inhaled steroid therapy**

Lau EMC, Woo J, Chan YH, Li M, *Bone* 2001;29:506-510.

**Background:** Oral glucocorticoids are recognized as a major cause of osteoporosis among treated patients. High doses of inhaled glucocorticoids are somewhat less deleterious for bone and even low-dose inhaled corticosteroid therapy may have some negative bone effect. Alendronate therapy may limit bone loss associated with inhaled glucocorticoid therapy.

**Study and Results:** Women (n = 100) taking inhaled steroid therapy (800 to  $\geq 1600$   $\mu\text{g}/\text{day}$ ) were randomized to either 10 mg of oral alendronate or placebo and measured with DXA at baseline, 6 months, and 12 months. Spine BMD increased about 3% in the alendronate group and decreased by about 1% in the placebo group over a 12-month period. Femoral neck BMD increased by about 1% in the alendronate group and decreased by about 0.5% in the placebo group.

**Conclusion:** Bone loss among women on inhaled glucocorticoid therapy was prevented by a daily dose of alendronate.

### **Bone turnover regulated by low circulating levels of estrogen in elderly postmenopausal women**

#### **Role of low levels of endogenous estrogen in regulation of bone resorption in late postmenopausal women**

Heshmati HM, Khosla S, Robins SP, O'Fallon MO, Melton III LJ, Riggs BL, *J Bone Miner Res* 2002;17:172-178.

**Background:** Estrogen acts directly on bone cells to regulate bone turnover. Postmenopausal bone loss results from cessation of ovarian function that leads to a rapid decline in estrogen levels beginning at the menopause and extending for up to 10 years. A gradual decline in estrogen then continues indefinitely. Estrogen in postmenopausal women is produced mainly through conversion (aromatization) of testosterone and adrenal androgens to estrogen by a process that utilizes the aromatase enzyme. There is little information on whether these low levels of estrogen regulate bone turnover in elderly postmenopausal women. If low serum estrogen levels exert some control over bone turnover in the very elderly, then variations in these levels could explain differences in the rate of bone loss among postmenopausal women.

**Study and Results:** A potent aromatase inhibitor (letrozole) was used to test the hypothesis that even low levels of estrogen synthesis in elderly postmenopausal women have a restraining effect on bone turnover. Bone turnover markers were evaluated in 42 normal women (mean age 69 years) receiving either the aromatase inhibitor or placebo for a 6-month period. Bone resorption markers increased (~14%) in the letrozole-treated group compared with the placebo group. No changes were seen in bone formation markers.

**Conclusion:** Experimental reduction of low levels of serum estrogen increased bone turnover in elderly postmenopausal women. Individual variability in low circulating estrogen levels might be an important factor in the development of osteoporosis in elderly postmenopausal women.

### **DXA recommended for all children with HIV infection treated with highly active antiretroviral therapy**

**Highly active antiretroviral-treated HIV-infected children show fat distribution changes even in absence of lipodystrophy**

Brambilla P, Bricalli D, Sala N, Renzetti F, Manzoni P, Vanzulli A, Chiumello G, di Natale B, Viganò A, *AIDS* 2001;15:2415-2422

**Background:** Adult patients with human immunodeficiency virus (HIV) infection receiving antiretroviral therapy often have lipodystrophy syndrome (LD), a variable condition often characterized by redistribution of fat from peripheral areas to central body areas, and other abnormalities of lipid and glucose metabolism. Children with HIV are now treated increasingly with highly active antiretroviral therapy (HAART), but few studies have documented the development of LD in childhood. Precise measurement of regional body composition is necessary to distinguish LD from other forms of obesity. DXA is the current gold standard for *in vivo* measures of body composition in children. Magnetic resonance imaging (MRI) provides accurate measurement of intra-abdominal fat tissue.

**Study and Results:** DXA (DPX) and MRI were used to document changes in fat distribution and possible adverse metabolic changes in 34 HIV-infected children aged 6.5 to 16.9 years receiving HAART and an equal number of healthy, matched controls. Children with HIV were divided into those with lipodystrophy (LD+; n = 6) and those without lipodystrophy (LD-; n=28). Fat mass and fat distribution were significantly different in HIV patients vs. controls, but lean mass was the same. All treated patients showed that reduced total fat resulted from moderately reduced truncal fat (~ -10%), and markedly reduced limb fat mass (~ -40%) compared with healthy controls. This discordant fat loss resulted in a marked change in limb/trunk fat ratio (23.5 to 28.2) compared with healthy controls (31.2 to 41.7). This fat redistribution was especially apparent in LD+ children. Intra-abdominal adipose tissue (IAT) was higher in LD+ children than LD- children and healthy controls and was even higher than levels reported for childhood obesity, even though LD+ children generally were not obese or overweight.

**Conclusion:** Atrophy of peripheral fat stores and true central obesity was present in HAART-treated children with lipodystrophy. Peripheral fat wasting and pseudotruncal obesity was evident in treated children in the absence of clinical signs of LD. Authors recommended "...a need for body composition analysis with DXA in all HAART-treated children and intra-abdominal fat depot estimation by MRI in children with LD+... Therefore an intensive monitoring of body composition in all HAART-treated children is highly recommended in order to add pharmacological, diet and lifestyle suggestions."

### **Exercise effect on BMD related to skeletal loading**

#### **Exercise may induce reversible low bone mass in unloaded and high bone mass in weight-loaded skeletal regions**

Magnusson H, Linden C, Karlsson C, Obrant KJ, Karlsson MK, *Osteoporos Int* 2001;12:950-955.

**Background:** Increasing peak bone mass and reducing age-related bone loss through exercise might reduce the risk of osteoporosis and fracture later in life. Numerous studies have shown bone gain in weight-loaded skeletal regions, but few studies have examined BMD changes in unloaded skeletal sites of subjects who exercise.

**Study and Results:** Active soccer players (n = 67; mean age 22.7 years), former soccer players (n = 128, mean age 50.6 years), and controls (n = 138, mean age 50.6 years) were evaluated by DXA at the upper part of the skull (unloaded skeletal region), arms (partly loaded region), and femoral neck (fully loaded region). BMD (DPX) in active players was reduced 10.4% in the unloaded upper skull region, not increased significantly in the partly loaded arm region, and increased by 12.7% in the fully loaded femoral neck region compared with controls. Former soccer players had reduced BMD in the skull until age 70 years and increased BMD in the femoral neck until age 50 years compared with controls. No differences in BMD between soccer players and controls were seen for subjects 70 years of age or older.

**Conclusion:** Unloaded and weight-loaded regions of the skeleton respond differently to increases and decreases in activity level.

### **Non-vertebral fracture coupled with low BMD should trigger osteoporosis prevention strategies**

**Secondary prevention of osteoporosis: when should non-vertebral fracture be a trigger for action?**

Eastell R, Reid DM, Compston J, Cooper C, Fogelman I, Francis RM, Hay SM, Hosking DJ, Purdie DW, Ralston SH, Reeve J, Russell RGG, Stevenson JC, *Q J Med* 2001;94:575-597.

**Review:** This article provides an extensive review conducted by a UK Consensus Group of all relevant English-language articles on non-vertebral osteoporosis-related fractures. Several recent reports have provided evidence that orthopedic surgeons often do not do DXA measurements or treat osteoporosis in patients who present with a hip fracture. The aim of the review was to outline risk factors for non-vertebral fractures and to provide recommendations for when these fractures should signal the need for beginning osteoporosis prevention measures. About 39% of all osteoporotic fractures are hip fractures, 14% are symptomatic vertebral fractures, and 23% are wrist fractures in the UK. Decreased BMD at various skeletal sites is the most important predictor of hip, spine, and vertebral fractures. Prior low-impact fractures dramatically increase fracture risk. Increases in longevity are responsible, at least partly, for the trend towards increased incidence of hip, limb and spine fractures. The incidence of hip fractures increases exponentially for men and women over age 75 years. Guidelines were presented for identifying and treating patients at risk for non-vertebral fractures, based on an algorithm recently published by the Royal College of Physicians and the Bone and Tooth Society. DXA measurements figure prominently in initial diagnosis and follow-up after initiation of therapy.

### **Site specific densitometry best predictor of bone strength**

#### **Bone strength at clinically relevant sites displays substantial heterogeneity and is best predicted from site-specific bone densitometry**

Eckstein F, Lochmuller E-M, Lill CA, Kuhn V, Schneider E, Delling G, Muller R, *J Bone Miner Res* 2002;17:162-171.

**Background:** Bone mineral status is the best predictor of fracture risk, and DXA is accepted widely as the gold standard for bone densitometry. There is considerable discordance of BMD at different skeletal sites, despite the belief that osteoporosis is a systemic disease. Many experts believe that site-specific BMD measurement best predicts fracture at that site, although DXA measurements at the spine appear to be less predictive of spine fractures than DXA measurements at the femur are for hip fracture.

**Study and Results:** Cadavers (n = 110) of elderly subjects were used to determine experimentally the mechanical load required to break a bone at specific skeletal sites. Mechanical failure loads only were correlated moderately among different skeletal sites, suggesting considerable regional variation in bone strength in the elderly. Authors suggested this finding argued against osteoporosis being strictly a systemic disease. Site-specific DXA measurements at the spine, femur, and radius were associated more highly with failure loads at these sites than non-site-specific measurements. Site-specific DXA measurements predicted 50% to 60% of the variance in failure loads in identical or closely adjacent sites, while non-site-specific measurements predicted only 20% to 35% of the variance. Non-site-specific measurements generally added a small, but significant, independent prediction of bone strength. The exception was the proximal femur, where non-site-specific data provided no increased predictability of bone strength. Total body BMD provided the most balanced estimate of overall bone strength, but was not better statistically than site-specific measurements in estimating bone strength at all sites. No single site was substantially better than others were at predicting failure loads throughout all sites.

**Conclusion:** Site-specific measurements of BMD were superior to non-site-specific measurements in predicting bone strength. Total body BMD did not estimate global bone strength better than regional measurements. Bone strength and fracture risk in the elderly were influenced by substantial regional variation that suggested that osteoporosis might not be entirely a systemic disease.

### **Wrist radiographs unsatisfactory for diagnosing osteoporosis**

#### **Assessment of osteoporosis using standard radiographs of the wrist**

Olschewski E, Murray P, Buckley R, Fennell C, Powell JN, *J Trauma* 2001;51:912-916

**Background:** Osteoporosis awareness in the general population is at an all time high, but there are concerns about the availability and accessibility of equipment to measure all subjects who might benefit from a bone density measurement. Low BMD measured with DXA is the best predictor of fracture risk, but

some experienced clinicians believe that a review of a patient's radiograph of the wrist is accurate enough to allow patient management without the more expensive DXA test.

**Study and Results:** This study determined whether experienced orthopedic clinicians could predict accurately whether a patient is osteoporotic by viewing standard radiographs of the wrist. Radiographs of injured and non-injured wrists and DXA of the radius were performed on patients who sustained a low-energy impact wrist fracture (n = 38) within the past 12 months. Radiographs were viewed in a blinded, randomized fashion by three orthopedic surgeons who were asked whether the patient needed treatment for osteoporosis. Intraobserver agreement varied from 93% to 69% for the fractured wrist, and from 81% to 73% for the unfractured wrist. DXA showed that 17 patients had radius BMD levels that required treatment according to WHO guidelines, and 11 of these had osteoporosis. If patient management were based on clinician assessment of standard x-rays of normal or fractured wrists, 40% to 56% of patients with normal BMD would be treated incorrectly. Patients with fractured wrists requiring treatment by DXA would not be treated 24% of the time based on x-ray assessment. This percentage increased to 32% when patients without fracture requiring treatment with DXA were included.

**Conclusion:** Assessment of wrist radiographs should not be used as a method to determine presence or absence of osteoporosis. Authors recommended that, "All orthopaedic surgeons treating a patient with a wrist fracture, secondary to low-energy mechanism of injury, should recommend further evaluation of the patient's bone mineral density with DXA."

### **BMD is the best indicator of heightened fracture risk among patients with inflammatory bowel disease.**

#### **Osteoporosis in patients with inflammatory bowel disease**

Arden NK, Cooper C, *Gut* 2002;50:9-10.

A recent paper by Bernstein C et al., (*Ann Intern Med* 2000;133:795-799) reported that fracture among patients with inflammatory bowel disease (IBD) was 40% higher than among the general population. Other recent papers have disagreed on whether fracture risk increased for both Crohn's disease (CD) and ulcerative colitis (UC) in men and women. A large study from Denmark found a 250% increase in fracture risk among women with CD, but no increased fracture risk among women with UC. The same study showed no increased fracture risk for men with either disease. Risk factors for fracture among IBD patients include oral corticosteroid use, vitamin D deficiency, hypogonadism, malabsorption, malnutrition, and systemic inflammation. BMD measured by axial densitometry is the most important predictor for future fracture. Authors recommended that clinicians use DXA to identify IBD patients with low BMD and high fracture risk. A history of fracture or continuous corticosteroid therapy also should be included in treatment decisions. Treatment with estrogen replacement therapy or bisphosphonates (alendronate) reduced bone loss and/or increased BMD among IBD patients.

### **BMD evaluation essential for patients with liver disease prior to transplantation**

#### **High prevalence of osteoporosis in patients with chronic liver disease prior to liver transplantation**

Ninkovic M, Love SA, Tom B, Alexander GJM, Compston JE, *Calcif Tissue Int* 2001;69:321-326.

**Background:** Liver transplantation is associated frequently with osteoporosis. The frequency of osteoporotic fracture post transplantation can be as high as 35%. The extent to which post-transplant fractures relate to preexisting bone disease prior to transplantation is unclear.

**Study and Results:** The prevalence of osteoporosis prior to transplantation was evaluated prospectively by DXA in 243 consecutive adult patients (age 51.1 years) with chronic liver disease who were undergoing assessment for liver transplantation. Sixty-five percent of patients were classified with the most severe liver disease, as assessed by Child-Pugh status (Child-Pugh C). Osteoporosis and osteopenia were found in 37% and 48% of all patients, respectively, using WHO guidelines. Osteoporosis occurs in less than 5% of subjects of similar age in a normal population. Osteoporosis and osteopenia were somewhat more prevalent at the femoral neck than at the lumbar spine. Osteoporosis was present at either the spine or femur sites in 34.4% of males and 39.1% of females. Older women were more likely to be osteoporotic than younger women, but there was no age effect among men. Severity of liver disease was not associated with

prevalence of osteoporosis. Increasing age and lower weight were associated with osteoporosis in women, but not men. Weight was not associated with severity of liver disease.

**Conclusions:** Patients with chronic liver disease had a high prevalence of osteoporosis prior to transplantation. The lack of independent risk factors for osteoporosis other than increasing age and lower body weight led the authors to emphasize the need to evaluate BMD in patients with serious liver disease.

### **Body composition quantifies body fat deficits in girls with anorexia**

#### **Body composition in adolescents with anorexia nervosa**

Kerruish KP, O'Connor J, Humphries IRJ, Kohn MR, Clarke SD, Briody JN, Thomson EJ, Wright KA, Gaskin KJ, Baur LA, *Am J Clin Nutr* 2002;75:31-37.

**Background:** Anorexia nervosa affects about one in every 200 adolescent girls in Western societies. This chronic disorder is particularly detrimental for adolescents because it disturbs important adolescent growth and developmental events. Few studies of anorexia have focused exclusively on the adolescent female, and no studies of adolescents have measured body composition using DXA.

**Study and Results:** Body composition measurements by DXA (DPX) and by anthropometry were evaluated in 23 adolescent girls aged 13-18 years with anorexia and 25 healthy girls of similar ages. Anorexic girls were significantly lower than controls in body fat (13.8% vs. 26.3%), fat free mass (34.5kg vs. 41.2 kg), trunk fat (2.1 kg vs. 6.6 kg), leg fat (2.6 kg vs. 7.1 kg) and trunk-to-leg ratio (0.79 vs. 0.93). Triceps skinfold thickness was correlated highly with percentage body fat among anorexics ( $r = 0.83$ ) and among controls ( $r = 0.79$ ). Body mass index (BMI) also correlated significantly with percentage body fat in anorexic ( $r = 0.46$ ) and control ( $r = 0.79$ ) subjects. Weight was a significant predictor of total body nitrogen, an indicator of protein nutritional status.

**Conclusions:** Adolescent patients with anorexia nervosa were depleted in both total body protein and body fat. Measurements of triceps skinfold thickness, BMI, and body weight can be used to assess body composition among anorexic patients when DXA is not available.

### **Chemotherapy effects on BMD reduced by clodronate therapy**

#### **Chemotherapy-induced ovarian failure has long-term effect on bone mineral density (BMD) in premenopausal breast cancer patients. The effect of adjuvant clodronate treatment**

Vehmanen L, Saarto T, Elomaa I, Makela P, Valimaki M, Blomqvist C, *Eur J Cancer* 2001;37:2373-2378.

**Background:** Circulating estrogen stimulates some forms of breast cancer in premenopausal women. Chemotherapy can induce ovarian failure, early menopause, and rapid bone loss, particularly during the first few years of treatment. Bisphosphonates are effective in preventing bone loss in women with osteoporosis and might be useful in preventing bone loss among women undergoing chemotherapy for breast cancer.

**Study and Results:** Premenopausal women ( $n = 148$ ) diagnosed with breast cancer and treated with chemotherapy were randomized for daily treatment with the oral bisphosphonate clodronate (1600 mg) for three years or no treatment. Lumbar spine BMD decreased 3.0% in the treated group compared with 7.4% in the controls. The loss of femoral neck BMD was not different statistically between the treated (1.7%) and control (2.8%) groups. Patients were divided after five years of follow-up into those with menstrual periods and those menopausal. Roughly half of the original 148 women were excluded at the five-year follow-up because their cancer had spread to other regions of the body. Seventy-four percent of the remaining 73 women were no longer menstruating five years after chemotherapy. Spine and femoral neck BMD decreased 1.3% and 0.3%, respectively, in women who continued their menses, and 10.4% and 5.8%, respectively, in women with amenorrhea. There was no difference in BMD loss between women with an early onset of menopause and those with a later onset. Clodronate treatment reduced loss of BMD of the spine in both menstruating and amenorrheic women, but had no discernable effect on femur neck BMD.

**Conclusions:** Chemotherapy-induced ovarian failure in premenopausal women with breast cancer led to increased bone loss of the spine and hip. Clodronate therapy significantly reduced bone loss at the spine, but not the hip. This reduction in bone loss at the spine continued to be evident two years after the end of clodronate therapy.

## **Effectiveness of ERT on BMD depends on treatment regimen**

### ***Effect of continuous and sequential oral estrogen-progestogen replacement regimens on postmenopausal bone loss: a 2-year prospective study***

Figueras F, Castelo-Branco C, Pons F, Sanjuan A, Vanrell JA, *Obstet Gynecol* 2001;99:261-265.

**Background:** Hormone replacement therapy (HRT) increases bone mass and reduces the incidence of low-impact fractures in postmenopausal women. The risk of endometrial hyperplasia and cancer, however, are increased by long-term exposure to estrogen alone. The addition of a progestin is necessary to prevent this risk. Side effects such as edema, abdominal cramping, breast tenderness, and, most troublesome of all, withdrawal bleeding, however, result in poor compliance for sequential HRT regimens. In recent years, HRT has been offered as a continuous, combined hormone regimen that produces only minimal endometrial hyperplasia, infrequent bleeding, and favorable changes in plasma lipids. Few studies have compared the effects of sequential versus combined continuous HRT on bone density.

**Study and Results:** Postmenopausal women (n = 104) received either continuous estrogen (0.625 mg conjugated equine estrogen) and progestin (2.5 mg medroxyprogesterone acetate) daily for 24 months or sequential estrogen (0.625 mg) on days 1-25 and progestin (2.5 mg) on days 14-25 for 24 months. Lumbar spine BMD was evaluated by DXA (DPX) at baseline, 12 months, and 24 months. Women who completed the study showed no significant differences in spine BMD (DPX) at 24 months between continuous (+6.6%) and sequential (+6.3%) regimens. There was a significant difference in BMD between the continuous (+5.5%) and sequential (+4.6%) groups when all women who started the study were examined at the end of the study (intention-to-treat analysis). Women in the sequential treatment group dropped out of the study at a higher rate than women in the continuous combined treatment group (23% versus 11.3%).

**Conclusions:** ERT resulted in significant increases in spine BMD in both treatment groups. Combined continuous estrogen therapy resulted in significantly higher BMD than sequential therapy in the intention-to-treat analysis, suggesting that the combined continuous regimen would be the most effective for women requiring long-term ERT.

## **Male BMD appears to be unaffected by lupus (systemic lupus erythematosus)**

### **Bone mineral density, biochemical markers of bone turnover, and hormonal status in men with systemic lupus erythematosus**

Bhattoa HP, Kiss E, Bettembuk P, Balogh A, *Rheumatol Int* 2001;21:97-102.

**Background:** Systemic lupus erythematosus (SLE) is a chronic, inflammatory disease that affects joints, muscles, skin, blood vessels, and membranes surrounding the lungs and heart. Most studies of SLE and bone health have involved women, due to the rarity of the disorder among men. Reduced physical activity, avoidance of sunlight, renal involvement, hypogonadism, corticosteroid therapy, and elevated levels of cytokines known to affect bone turnover have all been implicated in bone loss among affected women. Few studies have examined BMD loss among males with SLE.

**Study and Results:** Spine, femur, and radius BMD (DPX) and biochemical markers of bone turnover were evaluated in 23 men with SLE (mean age 45.6 years; mean disease duration 11.9 years) and a control group. There were no differences in BMD at any measurement site between men with SLE and controls. There also were no significant correlations between BMD and disease activity, disease duration, and cumulative corticosteroid dose. Markers of bone turnover and BMD were not correlated significantly. These somewhat surprising results may have resulted from a relatively small sample size and large variation among the variables studied.

**Conclusion:** Males with SLE showed no loss of BMD, even when treated with corticosteroid therapy.

## **Response to ERT associated with age and baseline BMD in postmenopausal Japanese women**

### **Clinical features affecting the results of estrogen replacement therapy on bone density in Japanese postmenopausal women**

Morishige K, Matsumoto K, Ohmichi M, Nishio Y, Adachi K, Hayakawa J, Nukui K, Tasaka K, Kurachi H, Murata Y, *Gynecol Obstet Invest* 2001;52:223-226.

**Background:** Estrogen replacement therapy (ERT) is associated with maintenance of bone mass and a decreased fracture risk. Long-term ERT is not a popular therapy for preventing osteoporosis in postmenopausal Japanese women, at least in part due to the potential for adverse side effects. A study determining which women would most likely benefit from ERT could provide some guidelines for use.

**Study and Results:** Women (n = 93; median age 53 years) who were from 6 months to 10 years postmenopausal were evaluated at the lumbar spine by DXA (DPX) at baseline and at regular follow-up intervals. Estrogen-treated women increased BMD by about 2%/year during the first two years of treatment. Age and years-since-menopause (YSM) correlated positively with rate of BMD change. Baseline BMD was correlated negatively with BMD change. Age and baseline BMD accounted for 34.4% of the change in vertebral BMD. Approximately 19% of subjects continued to lose bone and therefore appeared to be non-responders to estrogen. Nearly all non-responders had normal BMD. Nearly all osteoporotic and osteopenic women were characterized as estrogen responders, based on BMD change.

**Conclusions:** Age and initial BMD were the main predictors of BMD change in Japanese postmenopausal women.

### **Total Body BMD useful for growth studies on pigs**

#### **Total body and regional measurements of bone mineral content and bone mineral density in pigs by dual energy X-ray absorptiometry**

Mitchell AD, Scholz AM, Pursel VG, *J Anim Sci* 2001;79:2594-2604.

**Background:** Pig production provides important economic and nutritional value to human populations throughout the world. Growth patterns of pigs vary according to age, sex, and breed. Animal scientists study pig growth extensively, usually following methods that involve slaughter at different life stages and dissection and examination of bones. DXA overcomes disadvantages of subject death and allows sequential measurement of growth in live animals.

**Study and Results:** Multiple DXA (DPX-L) scans were performed on 587 pigs at life-stage intervals of about 30 kg of body weight. Pediatric scan mode was used for 3 to 29 kg pigs, adult medium mode for 30-69 kg pigs, and adult slow mode for 70 to 138 kg pigs. BMD was evaluated in three major regions (front legs, back legs, and trunk). BMD and bone area were evaluated in the total body and seven skeletal regions. Results showed that bone was deposited most rapidly in the trunk region during the initial period of growth (3 to 30 kg). Growth was concentrated in leg regions, especially in the back legs, during growth from 30 to 138 kg.

**Conclusions:** DXA proved to be an efficient way of studying growth in pigs. Authors concluded "These procedures could be quite useful for the development of optimal nutritional and genetic strategies to ensure adequate bone growth in pigs, using standards based on DXA for normal bone mineral content and density within age, weight, sex, and breed classifications."

### **Exercise overrides negative effects of menstrual irregularities in elite gymnasts**

#### **Bone density in female elite gymnasts: impact of muscle strength and sex hormones**

Helge EW, Kanstrup I-L, *Med Sci Sports Exerc* 2002;34:174-180.

**Background:** Female athletes, even those undergoing intense weight-bearing exercise, are affected often by eating disorders, menstrual irregularities, and low BMD, well known features of the so-called 'female athletic triad'. Potential bone benefits of intense weight-bearing exercise might be limited by the negative effect of lowered estrogen levels associated with amenorrhea in female athletes. Estrogen appears to be a controlling factor in determining when mechanical strain brought on by exercise results in increased bone formation. Menstrual disturbances are particularly frequent among female gymnasts, but the impact forces encountered during gymnastic training are so large that bone might not be compromised significantly.

**Study and Results:** Six artistic and five rhythmic elite gymnasts recruited from Danish national teams were evaluated with DXA (DPX-L and EXPERT) at the spine, femur, radius, and total body sites. Three of the artistic gymnasts had amenorrhea, defined as a menstrual cycle of more than 90 days. Two artistic and one rhythmic gymnast had oligomenorrhea, defined as a menstrual cycle of 36 to 90 days. Body weight was similar for all three groups, but body fat for artistic gymnasts was 36% lower than that for rhythmic gymnasts and 53% less than controls. Ground reaction forces and bone stress were estimated to be equivalent to 11 times body weight for artistic gymnasts and possibly 5 times body weight for rhythmic gymnasts. BMD was strongly correlated with muscle strength and was higher in gymnasts than controls. BMD of artistic and rhythmic gymnasts was not different significantly, except at the radius site, where high impact occurs regularly during artistic, but not in rhythmic, gymnastic routines. BMD appeared to be unrelated to menstrual status among all gymnasts, but positive correlations of progesterone with BMD in rhythmic gymnasts and estrogen with BMD in artistic gymnasts suggested that sex hormones might have some effect on BMD in the subgroup of gymnasts with abnormal menstrual function.

**Conclusions:** BMD levels at both appendicular and axial sites were elevated in elite gymnasts, despite the presence of menstrual irregularities. Positive correlations ( $r = 0.6$  to  $0.9$ ) between maximal muscle strength and axial and appendicular BMD appeared to override any negative effects on bone associated with menstrual irregularities, particularly among the artistic gymnasts.

### **Exercise and vitamin D receptor genotype associated with BMD in active elderly women**

#### **Association of physical activity and bone: influence of vitamin D receptor genotype**

Blanchet C, Giguere Y, Prud'Homme D, Dumong M, Rousseau F, Dodin S, *Med Sci Sports Exerc* 2002;34:24-31.

**Background:** Twin studies suggest that from 60 to 80% of BMD variability between individuals is related to genetic factors. Studies of genetic polymorphisms of the vitamin D receptor (VDR) genes have shown associations with BMD. A study of Australian twins examined the *BsmI* VDR polymorphism and found that postmenopausal women with two copies of the b allele (bb) had higher BMD than women with two copies of the B allele (BB). Attempts to replicate this association in other populations have had mixed results.

**Study and Results:** The aim of the current study was to evaluate the association between leisure-time activity, the *BsmI* polymorphism, and BMD (DPX-L) among postmenopausal women ( $n = 575$ ; mean age 63.3 years). Lifestyle exercise was determined by questionnaire. There were no associations overall among leisure physical activity, VDR genotypes, and BMD. However, among active women who exercised at least 3 times a week, women with the bb genotype had lower BMD than women with the BB genotype. Spine BMD was 4% higher in women with the BB genotype compared with women with the bb genotype. There were no associations between BMD, leisure time physical activity, and VDR genotypes among low and moderate exercise groups.

**Conclusions:** Leisure time physical activity and VDR genotype might be involved in preservation of BMD in active, elderly women.

### **High intensity exercise beneficial to bone in the elderly**

#### **Resistance exercise and bone turnover in elderly men and women**

Vincent KR, Braith RW, *Med Sci Sports Exerc* 2002;34:17-23.

**Background:** Exercise produces a strain on bones that stimulates bone formation. There are conflicting opinions on whether resistance exercise increases BMD. High resistance exercise might be more effective than low-resistance exercise in increasing BMD. The American College of Sports Medicine (ACSM) recommended that men and women over age 50 engage in resistance exercise to help prevent bone loss. No prior study has looked at the effect of the ACSM exercise regimen on BMD in elderly men and women.

**Study and Results:** Men and women ( $n = 62$ ) aged 60 to 83 years not involved in a regular resistance training program were assigned to either a control, low intensity, or high intensity resistance exercise group. Each participant participated in a progressive resistance-training regimen for six months. The one

repetition maximum, a measure of strength, increased for both low and high resistance exercise groups. Total strength increased by about 17% in both groups. BMD increased significantly (~2%) at the femoral neck in the high resistance group, but was not different significantly at the lumbar spine or total body for either of the exercise groups. Biochemical markers of bone formation increased in both exercise groups. **Conclusions:** High intensity exercise increased regional BMD (femur neck) in elderly men and women. Biochemical markers indicated increased bone turnover, with an emphasis on bone formation. Longer exercise periods might be necessary to show increases in BMD at all measured sites.

### **Peripheral densitometry was not ideal assessment for osteoporosis risk in women with forearm fracture.**

#### **Bone densitometry in the management of Colles' fractures: which site to measure?**

Ryan PJ, *Br J Radiol* 2001;74:1137-1141.

**Background:** Colles' fracture is common in patients with osteoporosis, but not all fracture patients have BMD in the osteoporotic range. Patients with Colles' fracture should be offered further assessment to determine whether osteoporosis therapy is warranted. Numerous devices are now available to measure BMD at peripheral sites, but peripheral measurements often do not correlate well with BMD measured at more established central densitometry sites (e.g., spine and femur).

**Study and Results:** DXA was used to determine whether peripheral measurements were adequate to detect osteoporosis at axial sites in 122 patients with recent Colles' fracture. Forty-three patients had a T-score  $\leq -2.5$  at one or more of the radius, lumbar spine, or femur neck sites. Sixty-three subjects had a T-score  $\leq -2.0$ , and 86 subjects had a T-score  $\leq -1.5$  when considering all three sites. Eleven of 43 osteoporotic subjects would be missed if spine and hip measurements were used, and 14 of 43 would be missed if only forearm measurements were evaluated. If forearm measurements were done only on patients with a spine or hip T-score between  $-2.5$  and  $-1$ , only 6 patients with T-score of  $< -2.5$  at the forearm would have been missed. Only four osteoporotic subjects would have been missed if patients with forearm T-scores between  $-1.5$  and  $-2.5$  also were evaluated with DXA at the spine and hip.

**Conclusions:** Assessment of patients with Colles' fracture using forearm densitometry alone will miss a substantial number of subjects with osteoporosis at the spine or hip. Clinical facilities that rely exclusively on BMD measurements with peripheral devices should send a portion of their patients on for axial densitometry.

### **Premenopausal fractures signal higher risk for postmenopausal fracture**

#### **Fractures between the ages of 20 and 50 years increase women's risk of subsequent fractures**

Wu F, Mason B, Horne A, Ames R, Clearwater J, Liu M, Evans MC, Gamble GD, Reid IR, *Arch Intern Med* 2002;162:33-36.

**Background:** The relationship between low BMD and fracture risk is well known, but studies of perimenopausal and postmenopausal women have found strong associations between fracture and subsequent fractures independent of bone density. The question of whether fractures in premenopausal women increase the risk of subsequent fractures has been largely ignored.

**Study and Results:** A cross-sectional study of 1284 postmenopausal women determined the presence of fracture prior to age 50 years using a standardized questionnaire. Fractures occurred in 9% of women prior to age 20 and 7% between age 20 and 50 years. There was no increased risk of fracture for women with fractures prior to age 20 years. Women with fractures between age 20 and 50 years had a 74% increase in fracture risk after age 50 years. This risk increased to 83% after adjustment for BMD, age, maternal history of hip fracture, history of HRT, and history of smoking and alcohol consumptions. The magnitude of this increased fracture risk was similar to the increased risk associated with low BMD, maternal history of hip fracture, low body weight, or previous osteoporotic fracture.

**Conclusions:** Fractures that occur between the ages of 20 and 50 years should be viewed as an indicator of increased fracture risk after age 50 years. Women with fractures between age 20 and 50 years represent a small (7%) group at increased fracture risk. These patients should be offered further testing with bone densitometry and possibly treatment.

