

Achilles – Useful for predicting foot fracture in osteoarthropathy

Calcaneal ultrasonometry in patients with Charcot osteoarthropathy and its relationship with densitometry in the lumbar spine and femoral neck and with markers of bone turnover

Jirkovska A, Kasalicky P, Boucek P, Hosova J, Skobova J. *Diabetic Medicine* 2001;495-500.

Background: Patients with diabetes suffer frequently from diabetic neuropathy, a disease of the peripheral nerves. Charcot osteoarthropathy (CO) is characterized by inflammatory conditions that lead to bone and joint destruction in the affected foot. Most patients with CO first present with a foot fracture.

Study and Results: Diabetic patients (n = 16) with CO and healthy controls (n = 16) were evaluated with quantitative ultrasonometry (Achilles) at the heel and by DXA at the lumbar spine and femoral neck. Patients with CO had significantly lower stiffness at the heel and significantly lower BMD at the hip, but not at the spine, than healthy controls. Stiffness T-score for CO patients was significantly lower than the T-scores for BMD at the spine and hip. Stiffness was strongly associated with a bone resorption marker (ICTP) (r = -0.73).

Conclusion: Lower calcaneal stiffness in the Charcot foot was associated with decreased femoral BMD and increased bone resorption markers. Authors state, "Calcaneal ultrasonometry may be useful for assessing foot osteoporosis and risk of foot fractures in patients with CO."

Ankylosing spondylitis – Risk factor for osteoporosis?

Changes in bone density in patients with ankylosing spondylitis: A two-year follow-up study

Maillefert JF, Aho LS, El Maghraoui A, Dougados M, Roux C. *Osteoporos Int* 2001;12:605-609

Background: Ankylosing spondylitis (AS) is a chronic inflammatory disease of unknown origin that affects mainly the spine and adjacent structures, with possible involvement of other major joints (hip, shoulder, neck, ribs, and jaw). Advanced cases may result in spinal fusion. Osteoporosis is common in AS patients.

Study and Results: Change of BMD over a 2-year period was measured by DXA in 54 consecutive outpatients. There was no significant change in spine BMD, but femoral neck BMD showed a small decline (1.6%) that was associated with measurement of systemic inflammatory processes. Disease processes that result in new, pathologic bone formation at the spine in some AS patients could have confounded results at the spine. About 20% of patients did show significant BMD losses at the spine.

Conclusion: Systemic inflammation may be responsible for BMD loss in AS.

Body composition -- Change in fat distribution with menopause

Prospective evaluation of body weight and body fat distribution in early postmenopausal women with and without hormone replacement therapy

Gambacciani M, Ciaponi M, Cappagli B, De Simone L, Orlandi R, Genazzani AR. *Maturitas* 2001;39:125-132

Background: The onset of menopause is accompanied by an increase in weight and a change in body fat towards a more central distribution that is recognized as an independent predictor of cardiovascular disease.

Study and Results: Women taking hormone replacement therapy (HRT) or calcium (controls) were followed prospectively for 36 months to study changes in body weight and fat distribution in the early postmenopausal period. Total body BMD (DPX) decreased and body weight, fat mass, %fat, and body mass index (BMI) increased in the control group. Women on HRT showed small increases in BMD and maintained BMI, fat mass, and weight at baseline levels. The greatest increase in abdominal fat following

menopause occurred in control women with the least amount of excess of abdominal fat prior to menopause.

Conclusion: Long-term HRT appeared to protect women from early postmenopausal loss of total body BMD and reduced fat distribution in the central, abdominal region.

Body composition – Characteristics associated with BMD in the elderly

Body composition characteristics are associated with the bone density of the proximal femur end in middle- and old-aged women and men

Kirchengast S, Peterson B, Hauser G, Knogler W. *Maturitas* 2001;39:133-145

Background: Men and women experience similar age-related changes in BMD, but women have additional changes related to the menopause. Body weight, one key influence on BMD in both men and women, acts presumably by altering the biomechanical forces applied to different parts of the skeleton.

Study and Results: Body composition and BMD at the proximal femur were evaluated in 77 healthy women and 62 healthy men ranging in age from about 60 to 90 years. Results showed a significant, positive association between BMD and higher weight, lean mass and fat mass in women, but increased BMD was associated only with higher lean mass in men. Increased lean mass may reflect a more active lifestyle and increased biomechanical forces on the skeleton.

Conclusion: Body composition characteristics were associated with BMD in a group of elderly men and women.

Depression – Osteoporosis risk factor?

The association of bone mineral density and depression in an older population

Robbins J, Hirsch C, Whitmer R, Cauley J, Harris T, for the Cardiovascular Health Study. *J Am Geriatr Soc* 2001;49:732-736.

Background: Osteoporosis is increasing concurrently with increases in life expectancy. Many osteoporosis risk factors have been identified, but few studies have examined depression as a potential risk factor.

Study and Results: BMD was evaluated in 1566 randomly selected, older subjects (age 65 and older) participating in the Cardiovascular Health Study (CHS), a long-term, follow-up study. Results showed a significant inverse association between depression and BMD after adjustment for osteoporotic risk factors such as BMI, age, estrogen use, gender, race, smoking, and alcohol consumption. This association was stronger among Caucasian than women African Americans, and stronger for women than men. Authors suggested that some unmeasured factor, such as an endogenous steroid, might be responsible for the association between depression and BMD.

Conclusion: Depression was significantly associated with decreased BMD in elderly subjects.

Finger DXA – Low sensitivity at T-score < -2.5

A comparative study of computed digital absorptiometry and conventional dual-energy X-ray absorptiometry in postmenopausal women

Fiter J, Nolla JM, Gomez-Vawuero C, Martinez-Aguila D, Valverde J, Roig-Escofet D. *Osteoporos Int* 12:565-569

Background: DXA is the 'gold standard' for BMD assessment, but cost and lack of portability somewhat limit its availability. Less expensive, portable devices such as computed digital absorptiometry (CDA) of the hand could provide greater access.

Study and Results: Ambulatory, postmenopausal women (n = 230) were assessed by DXA at the spine and hip and by CDA (AccuDEXA) at the middle phalanx of the nondominant hand. The correlations of CDA versus spinal DXA (r = 0.66) and femoral neck DXA (r = 0.65) were similar to the correlation between spine and femoral neck DXA (r = 0.70). Thirty-three percent of women had osteoporosis at either spine or femur sites, according to WHO guidelines (T-score \leq -2.5), compared with 18% using CDA. ROC

curves showed that the best cut-off for osteoporosis according to CDA was T-score = -1.65. The ability of CDA to identify subjects osteoporotic by DXA (sensitivity) was 35.8% at the spine, 50% at the femoral neck, and 34.2% at either spine or femoral neck.

Conclusion: The CDA device showed moderate correlation with spine and femur DXA and low sensitivity for identifying patients with DXA-defined osteoporosis. A higher cut-off defining osteoporosis with this CDA device seems appropriate.

Male osteoporosis therapy – Effectiveness of calcitriol unproven

Effects of calcitriol or calcium on bone mineral density, bone turnover, and fractures in men with primary osteoporosis: A two-year randomized, double blind, placebo study

Ebeling PR, Wark JD, Yeung S, Poon C, Salehi N, Nicholson GC, Kotowicz. *J Clin Endocrinol Metab* 2001;86:4098-4103.

Background: Osteoporosis is a growing problem for men as well as women. Vertebral fractures occur earlier and nearly as frequently in men as in women and mortality after spine or hip fractures is higher for men than women. Despite an increased awareness of the seriousness of male osteoporosis, few studies have examined the effectiveness of specific drug therapies for male osteoporosis.

Study and Results: The effect of calcitriol or calcium was studied in a two-year prospective study of 41 men with primary osteoporosis and at least one fragility fracture at baseline. Treatment resulted in short-term increases in spine and femur BMD (DPX) and total body BMC, but there was no significant change in BMD from baseline after two years of treatment. There was no significant difference in fracture incidence between the two treatment groups, but there was a trend for an increased rate of vertebral fracture in the calcitriol group.

Conclusion: Calcitriol was not shown to be effective in treating men with primary osteoporosis.

Bisphosphonates prevent bone loss during therapy for prostate cancer

Pamidronate to prevent bone loss during androgen-deprivation therapy for prostate cancer

Smith MR, McGovern FJ, Zietman AL, Fallon MA, Hayden DL, Schoenfeld DA, Kantoff PW, Finkelstein JS, *New Engl J Med* 2001;345:948-955. (Lit Rev Oct 10, 2001)

Background: Androgen deprivation therapy (ADT) has become the standard of care for men with advanced prostate cancer, but ADT has substantial negative effects on bone health. Osteoporosis is found commonly in men undergoing ADT. Bisphosphonates such as pamidronate may lessen the negative effects of ADT on bone.

Study and Results: Intravenous pamidronate was given to half of 47 men taking ADT. Results showed that BMD decreased 2% to 3% at the spine, trochanter and total hip in patients taking ADT alone, but no loss occurred in men taking pamidronate in addition to ADT.

Conclusions: Pamidronate prevented BMD loss in men with advanced prostate cancer taking ADT.

Body composition -- Daughters resemble parental body composition

Familial resemblance of body composition in prepubertal girls and their biological parents.

Trueth MS, Butte NF, Ellis KJ, Martin LJ, Comuzzie AG, *Am J Clin Nutr* 2001;74:529-533 (Oct 10, 2001)

Background: Biological characteristics are influenced during growth and development by both environmental and genetic factors. Studies of twins and other family relationships allow researchers to estimate the degree to which certain traits are inherited. These studies refer to the *heritability* of a particular trait. For example, studies have shown that body mass index (BMI) has a heritability of 50% to 70%. BMI is an overall index of body size, but, unlike DXA, does not differentiate between regions and between fat and lean tissue.

Study and Results: Body composition of 101 normal weight girls (mean age 8.5 years) was compared with body composition of their biological parents. Fat mass, fat free mass, and %body fat (%BF) showed

low-to-moderate similarities between girls and their parents. Heritability estimates were significant for BMI and %BF measured with DXA.

Conclusions: Body composition of prepubertal girls was significantly related to body composition of their parents.

Bone density evaluation recommended for patients undergoing blood or marrow transplantation

Decreased bone mineral density is common after autologous blood or marrow transplantation

Schimmer AD, Mah K, Bordeleau L, Cheung A, Ali V, Falconer M, Trus M, Keating A, *Bone Marrow Transpl* 2001;28:387-391. (Lit Rev Oct 10, 2001)

Background: Autologous (patient receiving a transplant of his/her own tissue) blood or marrow transplantation (ABMT) is a life-saving procedure for cancer patients. Concerns about potential increased risk for osteoporosis associated with ABMT seem inconsequential initially, but in the long term osteoporosis carries a considerable burden of morbidity and mortality. High doses of chemotherapy, total body irradiation, and hypogonadism that accompany ABMT contribute to a dramatically increased bone turnover and decreased BMD. The long-term effects of ABMT on BMD are not known.

Study and Results: BMD was measured in 64 of 68 consecutive patients (mean age 49.6 years) about 4 years after ABMT treatment. Twenty-six percent of patients had osteopenia and one had osteoporosis at the lumbar spine. A larger proportion (46%) was osteopenic at the femoral neck and 8% were osteoporotic. The frequency of patients with reduced BMD at either spine or hip (61%) was about twice the expected frequency for subjects of similar age (46 to 54 years). A high percentage (86%) of subjects with reduced BMD either stabilized or showed improved BMD after one year of osteoporosis treatment.

Conclusions: Most men and women showed reduced BMD after ABMT. Authors recommended BMD measurements for ABMT patients. "Since early recognition and aggressive treatment of bone loss can prevent bone fracture, we recommend that measurement of BMD and aggressive preventive therapy be an integral component to the follow-up of ABMT patients."

Bone density evaluation recommended for patients using inhaled glucocorticoids for asthma

Effects of inhaled glucocorticoids on bone density in premenopausal women

Israel E, Banerjee TR, Fitzmaurice GM, Kotlov TV, LaHive K, Leboff MS, *New Engl J Med* 2001;345:941-947. (Lit Rev Oct 10, 2001)

Background: Oral glucocorticoids are known to accelerate bone loss and increase risk of osteoporotic fractures, but studies about the effect of inhaled glucocorticoids on bone density have been less conclusive. Inhaled glucocorticoid therapy is now the treatment of choice for patients with asthma.

Study and Results: Premenopausal women (n = 109) with asthma treated with inhaled glucocorticoid (triamcinolone acetonide, 100µg per puff) were evaluated with densitometry over a three-year period. There was a small dose-related decline in BMD at the trochanter and total hip, but not at the femoral neck or spine. Each additional puff was associated with a small decline in total hip and trochanteric BMD. Although the yearly loss of BMD was small, projected over 20 years of treatment, the loss would be nearly equivalent to 1 T-score, or a doubling of fracture risk. Biochemical bone markers were not predictive of BMD loss.

Conclusions: Inhaled glucocorticoids were associated with small yearly declines in BMD at the trochanter and total hip in premenopausal women with asthma. Biochemical markers of bone resorption did not predict BMD loss. Authors suggested that "patients using high doses of inhaled glucocorticoids may benefit from periodic assessment of bone density and, when necessary, prophylactic measures to protect the skeleton."

Forearm BMD – A particularly sensitive site for assessing fracture risk in kidney transplant patients

Prevalence and causes of low bone density and fractures in kidney transplant patients

Pate S, Kwan JTC, McCloskey E, McGee G, Thomas G, Johnson D, Wills R, Ogunremi L, Barron J, *J Bone Miner Res* 2001;16:1863-1870. (Lit Rev Oct 10, 2001)

Background: Kidney transplantation is the treatment of choice for patients with end-stage renal failure. Kidney transplantation, however, does not result in reversal of the bone loss that occurred prior to transplantation, in part because immunosuppressive drugs that accompany transplantation continue to adversely affect BMD.

Study and Results: Osteoporosis evaluation with DXA was performed on 165 men and women patients with kidney transplants. BMD (DPX) was reduced at the radius (Z-score -1.5) and femoral neck (Z-score -0.7), but was normal at the spine. Males showed less bone loss than women at all skeletal sites. Osteoporosis was found in 35% to 50% of women, depending on skeletal site. Fracture prevalence following transplantation, 37% for men and 63% for women, was related to age, duration of renal disease, hemodialysis, time since transplantation, and cumulative dose of steroids. Postmenopausal women were particularly susceptible to fracture.

Conclusions: Kidney transplantation was associated with reduced BMD and increased risk of fracture, particularly in postmenopausal women. The forearm appeared to represent be the most sensitive site for fracture assessment in kidney transplant patients.

QUS (Sahara) – Precision inadequate to justify monitoring antiresorptive therapy

Changes in QUS and BMD measurements with antiresorptive therapy: a two-year longitudinal study
Frost ML, Blake GM, Fogelman I. *Calcif Tissue Int* 2001;69:138-146. (Lit Rev Oct 10, 2001)

Background: Quantitative ultrasonometry (QUS) is a portable, relatively inexpensive, radiation-free method for assessing skeletal status. Results vary among different QUS devices vary, but most experts agree that QUS can predict the risk of fracture, with some devices as successfully as DXA measurements at central measurement sites. There is considerably less agreement on whether QUS can be used to monitor therapy.

Study and Results: Bone mineral density (BMD) and QUS were measured in 195 women over a two-year period. Postmenopausal women who began antiresorptive therapy at the beginning of the study were compared with control women who had never been on therapy. A third group of women who had been on therapy for at least two years prior to the study continued therapy during the study. Measurements were made at the spine, hip, and total hip by DXA and at the heel with QUS (Sahara). BMD and QUS changes were compared to the least significant change (LSC) required to be accepted as a biological change, based on the precision error of the different techniques. Over 90% of the women who began therapy for the first time showed spine BMD changes that exceeded the LSC, but only 50% exceeded the LSC at the total hip and only 6% exceeded the LSC at the femoral neck and heel (QUS) site.

Conclusion: Heel QUS measurements showed a highly significant response to antiresorptive therapy, but were not sufficiently precise to allow QUS results to be useful for monitoring skeletal response to therapy.

Kidney stones – Risk factor for osteoporosis in patients with low milk consumption

Bone mineral density and fracture among prevalent kidney stone cases in the Third National Health and Nutrition Examination Survey

Lauderdale DS, Thisted RA, Wen M, Favus MJ, *J Bone Miner Res* 2001;16:1893-1898. (Lit Rev Oct 10, 2001)

Background: The formation of kidney stones in some cases is associated with abnormally high urinary calcium excretion, a risk factor for decreased BMD and fracture. The association of kidney stone formation and BMD, however, has been inconsistent regarding which skeletal sites are affected, whether women are affected predominantly, and whether only patients with increased calcium excretion develop the disorder.

Study and Results: The Third National Health and Nutrition Examination Survey (NHANES), a nationally representative sample of over 14,000 men and women, was used to examine associations among femoral neck BMD, gender, history of kidney stones, and spine or wrist fracture. Results showed that men

with kidney stones had lower femur BMD and were more likely to have suffered spine or wrist fractures than men without kidney stones. The association of BMD and kidney stones was weaker in women. Increased milk consumption was associated with a weakening of the BMD and kidney stone relationship in both men and women.

Conclusions: The association of BMD and kidney stones in both men and women was seen only in subjects with low levels of milk consumption.

Exercise (soccer) beneficial for BMD in adolescent and young adult males

High femoral bone mineral content and density in male football (soccer) players

Calbet JAL, Dorado C, Diaz-Herrera P, Rodriguez-Rodriguez LP. *Med Sci Sports Exerc* 33,1682-1687.

Background: Soccer playing involves intermittent high intensity exercise that should stimulate increased bone formation and density. Previous studies of marathon runners, however, have found lower spine BMC and BMD compared with inactive controls. The purpose of the current study was to determine whether recreational soccer players had increased BMD at spine and femur sites.

Study and Results: Young (mean age 23 years) males (n = 33) with a history of at least 12 years of recreational soccer were evaluated with DXA and compared with sedentary controls. Football players showed an 8% increase in lean mass, 10% greater total body BMC, 10% higher spine, and 21% higher femur neck BMD than controls. Leg BMC and BMD were increased by 16% and 10%, respectively. Approximately one-third of this increase in BMC was related to increased bone size, as indicated by increased bone area. No difference was seen between dominant and non-dominant kicking legs. There were no differences in arm BMD and BMC between players and non-players.

Conclusion: Marked increases in BMC and BMD at the spine and femur neck were found in young males who had participated in soccer since preadolescence.

Intense exercise may not always be good for bones

The influence of intense ballet training on trabecular bone mass, hormone status, and gonadotropin structure in young women

Valentino R, Savastano S, Tommaselli AP, D'Amore G, Dorato M, Lombardi G. *J Clin Endocrinol Metab* 2001;86:4674-4678.

Background: Moderate weight-bearing physical exercise is beneficial for bones, but intense training during adolescence, associated with weight loss, undernutrition, and menstrual abnormalities can result in diminished BMD and failure to attain peak bone mass.

Study and Results: Ballet dancers were studied to determine the effects of intense exercise on BMD and hormonal factors related to menstrual function. Results showed that intense ballet training during puberty was associated with low body weight, reduced body mass index, reduced BMD, delayed menarche, and menstrual dysfunction. These effects on BMD were still evident in exdancers, despite current normal reproductive function.

Conclusion: Intense physical exercise may have adverse effects on BMD in adolescent ballet dancers.

Fracture risk related to age, family history, and BMD

Risk factors for osteoporosis related to their outcomes: fractures

Van der Voort DJM, Geusens PP, Dinarnt,GJ. *Osteoporos Int* 12:630-638

Background: Osteoporotic fractures are a major concern of health care workers who treat the elderly. Nearly half of all Caucasian women will sustain a fracture in their lifetime. Besides BMD, many other risk factors have been suggested as potential indicators of fracture risk.

Study and Results: This cross-sectional, epidemiological study focused on the prevalence of osteoporosis and 'easily obtainable' risk factors related to BMD and fracture in 4725 postmenopausal women between ages 50 and 80 years. The most important variables associated with a) lifetime fracture risk, b) fracture risk after age 50, and c) fractures during the past five years, were older age, family history of fractures, and low

BMD. Other factors associated with fractures were hysterectomy, history of long-term (> 35 years) smoking, early menopause, and decreased body mass index. Obese women were less likely to be osteoporotic and had a markedly lower fracture risk than women of normal weight.

Conclusion: Decreased BMD, fracture history, and age were the most important predictors of fracture. Decreased BMI increased fracture risk among elderly subjects. Lean women with low BMD should be included in fracture prevention programs.

Growth hormone replacement may provide benefits to deficient adults

A prospective study of 5 years of GH replacement therapy in GH-deficient adults: sustained effects on body composition, bone mass, and metabolic indices.

Gotherstrom G, Svensson J, Koranyi J, Alpsten M, Bosaeus I, Bengtsson B-A, Johannsson G. *J Clin Endocrinol Metab* 2001;86:4657-4665.

Background: Growth hormone (GH) replacement therapy has been shown to reduce fat, increase lean mass, and, in long-term studies (6 to 30 months), increase BMC. Few studies have determined the long-term effects of GH on body composition and BMD.

Study and Results: Men and women (n = 118) with adult-onset GH deficiency treated with GH for five years showed a sustained increase in lean body mass, a decrease in fat mass, and a progressive increase in lumbar spine and femur neck BMD (DPX). T-scores for spine BMD increased from -0.49 at baseline to 0.04 after 5 years of treatment. Similarly, T-scores for femur neck BMD increased from -0.72 at baseline to -0.47 after 5 years. Changes in total body BMD and BMC were not significant.

Conclusion: Five-years of GH treatment was well tolerated and resulted in beneficial effects on body composition and spine and femur BMD, especially in men.

Haptoglobin genotype – Possible risk factor for osteoporosis

Haptoglobin genotype as a risk factor for postmenopausal osteoporosis

Pescarmona GP, D'Amelio P, Morra E, Isaia GC. *J Med Genet* 2001;38:636-638

Background: Iron deficiency affects bone metabolism and can lead to bone loss. Nutritional studies have shown that iron may be more important than calcium in predicting BMD at the femoral neck. One of the major sources of iron in the body is the breakdown of hemoglobin in red blood cells. Haptoglobin, one of three proteins required for hemoglobin turnover, occurs in several genetic forms (polymorphism). Sixteen percent of Europeans have the haptoglobin 1.1 genotype, 48% have the 2.1 genotype, and 36% have the 2.2 genotype.

Study and Results: The genotypes of women with postmenopausal osteoporosis (n = 135) and controls (n = 65) were determined along with BMD evaluated with DXA. Subjects with the haptoglobin 1.1 genotype had a significantly higher risk of osteoporosis than subjects with either 1.2 or 2.2 genotypes. The functional basis for this increased risk could be a greater hemoglobin carrying ability and greater elimination rate of iron in subjects with haptoglobin 1.1 genotype.

Conclusion: Certain haptoglobin genotypes could be important risk factors for osteoporosis.

Hip fracture -- Predicted by maternal height and rate of childhood growth

Maternal height, childhood growth and risk of hip fracture in later life: a longitudinal study

Cooper C, Eriksson JG, Forsein T, Osmond C, Tuomilehto J, Barker DJP. *Osteoporos Int* 2001;12:623-629

Background: Factors that affect growth and development in infants and children are believed to be very important for fracture risk in later life, but few studies have actually examined the association of growth rates in childhood with future risk of hip fracture. The present study linked a unique set of birth and childhood growth data with hospital discharge records in later life to assess fracture risk.

Study and Results: An epidemiological study of men (n = 3639) and women (n = 3447) born in Helsinki University Central Hospital between 1924 and 1933 and still living in Finland in 1971 found that tall maternal height and a low rate of childhood growth were the two most important determinants of hip

fracture in later life. Men and women with mothers taller than 1.61 meters were more than twice as likely to sustain a hip fracture than those with mothers shorter than 1.54 meters. Similarly, subjects with childhood growth falling into the lowest quartile between the ages of 7 and 15 years were nearly twice as likely to fracture a hip in later life. Paternal height was not available for these subjects.

Conclusion: A low rate of childhood growth and tall mothers were independently predictive of a higher risk of hip fracture in adulthood. Results offer support for childhood interventions designed to increase growth and bone size during childhood.

PTH improves cortical bone and trabecular microarchitecture

Effects of daily treatment with parathyroid hormone on bone microarchitecture and turnover in patients with osteoporosis: a paired biopsy study

Dempster DW, Cosman F, Kurland ES, Zhou H, Nieves J, Woelfert L, Shane E, Plavetic K, Muller R, Bilezikian J, Lindsay R. *J Bone Miner Res* 2001;16:1846-1853

Background: Human parathyroid hormone (PTH) will probably be the first FDA-approved osteoporosis drug that works by increasing bone formation rather than by inhibiting bone resorption. Recent clinical trials showed that PTH significantly decreased fracture risk in postmenopausal women with osteoporosis. The present article provides a structural basis for the anti-fracture efficacy of PTH.

Study and Results: Iliac crest biopsies were examined for microarchitectural changes before and after 18 months of PTH treatment in 8 men (age 49 years) and following 36 months of treatment in 8 postmenopausal women (age 54 years). Women had been taking hormone replacement and continued during the study. Women showed significant increases in cortical width with PTH, with no increased cortical porosity, refuting the suggestion that PTH might be deleterious to cortical bone. Men maintained baseline levels of both cortical and cancellous (trabecular) bone. Micro-CT analysis showed an increase in connectivity density, a histomorphometric index indicating improved microarchitecture in cancellous bone.

Conclusion: Daily PTH treatment increased cortical bone in patients with osteoporosis and improved trabecular microstructure.

Transplantation -- Risk factor for osteoporosis

Bone disease after liver transplantation: A long-term prospective study of bone mass changes, hormonal status and histomorphometric characteristics

Monegal A, Navasa M, Guanabens N, Peris P, Pons F, Martinez de Osaba MJ, Ordi J, Rimola A, Rodes J, Munoz-Gomez J. *Osteoporos Int* 2001;484-492.

Background: Rapid bone loss and fractures occur frequently in the first few months following liver transplantation. Less is known about changes in bone mass and the incidence of fracture over a longer time period.

Study and Results: Forty-five patients participated in a three-year prospective study of BMD (DPX), bone turnover, and hormones following liver transplantation. Fractures, mostly vertebral, occurred in 33% of patients, with the highest risk occurring in older patients who had low BMD prior to transplantation. Following transplantation, a rapid, short-term (3 to 6 months) decline in BMD was totally reversed at the lumbar spine after two years, but femoral neck BMD did not return completely to baseline levels after 36 months. Immunosuppressive drugs (cyclosporin, glucocorticoids) presumably contribute to the rapid bone loss immediately following transplantation. Although bone formation markers increased 6 months after transplantation, corresponding to the time of BMD recovery, bone markers were not predictive of fracture following transplantation.

Conclusion: Rapid bone loss and high rate of fracture are common during the first months following liver transplantation. Osteoporosis treatment, especially in patients with low BMD prior to transplantation, could reduce fracture rates in transplant patients.

BMD helpful in assessing progression of primary biliary cirrhosis

Bone disease in primary biliary cirrhosis: independent indicators and rate of progression

Menon KVN, Angulo P, Weston S, Dickson ER, Lindor KD, *J Hepatol* 2001;316-323

Background: Bone loss is a frequent consequence of primary biliary cirrhosis (PBS), a disease characterized by obstruction of bile ducts leading to inflammation and degenerative changes of the liver. Bone loss and a dramatically elevated fracture risk are common among liver transplant patients during the first 6 to 12 months post-transplantation, especially among those with osteopenia prior to transplantation.

Study and Results: Patients (n = 176) with PBS were studied over 7 years of follow-up. Osteoporosis was found in 20% of PBS patients, a > 30-fold higher prevalence than would be expected in a 'healthy' population of similar age. Severity and progression of PBS were associated with severity of osteoporosis and risk of fracture. Evaluation of BMD is now accepted as 'standard of care' for patients with PBS.

Authors concluded that patients with advanced PBS should be offered annual BMD measurements, treatment for osteoporosis, and enrollment in clinical trials designed to determine the best treatments for preventing and treating PBS-related bone loss.

Conclusion: Progression and severity of PBS was associated with progression and severity of bone disease, especially in older and thinner women.

Celiac disease – Frequently undiagnosed risk factor for osteoporosis

A prospective, longitudinal study of the long-term effect of treatment on bone density in children with celiac disease

Mora S, Barera G, Beccio S, Menni L, Proverbio MC, Bianchi C, Chiumello G, *Pediatrics* 2001;139:516-521.

Background: Patients with celiac disease are affected adversely by exposure to an antigen present in wheat, rye, and barley. Dietary exposure results in a gradual loss of villus cells of the small intestine that are essential for normal absorption of nutrients. Normal functioning of intestinal mucosa is compromised and malabsorption of nutrients such as vitamin D and calcium results in secondary hyperparathyroidism, osteomalacia, and bone loss. Early diagnosis and adherence to a gluten-free diet (GFD) prevents or partially reverses disease complications. Celiac disease is relatively common, affecting 1 in 100 to 300 people of European descent, but the disorder is frequently undiagnosed in adults living in non-European countries.

Study and Results: The BMD (DPX) of celiac patients (n = 19, mean age 14.2 years) was evaluated at diagnosis, after one year, and after 4.3 years on a GFD diet. BMC, BMD, and bone area were significantly lower than controls at diagnosis, but returned to normal values after adherence to the GFD.

Conclusion: Compliance with a gluten-free diet for one year resulted in a complete recovery of BMD in children and adolescents with celiac disease. BMD was maintained at normal levels with the GFD.

Celiac disease – undiagnosed risk factor for osteoporosis in elderly women

Prevalence of undiagnosed coeliac syndrome in osteoporotic women

Nuti R, Martini G, Valenti R, Giovani S, Salvadori S, Avanzati A, *J Intern Med* 2001;250:361-366

Background: Celiac disease is characterized by an adverse reaction of small intestinal cells to an antigen present in wheat, rye, and barley. Normal functioning of intestinal mucosa is compromised and malabsorption of nutrients such as vitamin D and calcium results frequently in secondary hyperparathyroidism, osteomalacia, and bone loss. Celiac disease usually is diagnosed in young patients with clinically evident signs of malabsorption, but recent studies have shown that the disease also is quite prevalent (1 in 100 – 300) in adult populations of European descent. Celiac disease often is unrecognized clinically in adults, with bone loss preceding overt gastrointestinal symptoms.

Study and Results: The prevalence of undiagnosed celiac disease in 255 osteoporotic women (T-score < -2.5) was determined. None of the subjects had diarrhea, malabsorption, weight loss, or anemia, the common symptoms of celiac disease. Nearly 10% women were found to have antibodies that demonstrated the presence of celiac disease. These women also had reduced vitamin D and increased parathyroid hormone levels. The prevalence of celiac disease determined from intestinal biopsies was 2.3%, but only 10 of the 24 affected women were studied histologically.

Conclusion: Undiagnosed celiac disease occurs far more frequently than expected in women with osteoporosis. Malabsorption of calcium and vitamin D and resulting increased parathyroid hormone secretion may contribute to osteoporosis in women with undiagnosed celiac disease.

Children treated for HIV infection have increased risk for bone loss

Bone mineral loss through increased bone turnover in HIV-infected children treated with highly active antiretroviral therapy

Mora S, Sala N, Bricalli D, Zuin G, Chiumello G, Viganò A, *AIDS* 2001;15:1823-1829

Background: Reports of some negative changes in bone mass of adult HIV patients treated with highly active antiretroviral therapy (HAART) have prompted interest in determining the effects of this treatment on children.

Study and Results: Lumbar spine and total body BMD (DPX) values of thirty-five children infected with HIV and treated with HAART were compared to five children with HIV and no antiretroviral treatment and 314 healthy controls. Children treated with HAART had lower spine and total body BMD (~3.8%) values than untreated HIV children or healthy controls. BMD values were also significantly lower in untreated children with HIV compared with healthy children. Bone markers showed that the BMD decrease in children treated with HAART was associated with increased bone formation and resorption.

Conclusion: HAART was associated with osteopenia in children infected with HIV.

Contraception -- Effects on BMD

A prospective, controlled study of the effects of hormonal contraception on bone mineral density

Berenson AB, Radecki CM, Grady JJ, Rickert VI, and Thomas A, *Am Coll Obstet Gynecol* 2001;98:576-582.

Background: Oral contraceptives have been shown to be beneficial for BMD by some studies and to have no effect on BMD by others. Studies of depot medroxyprogesterone acetate (DMPA) have generally shown reduced BMD, but a carefully controlled, prospective study comparing DMPA users with women using no hormonal contraception has not been reported.

Study and Results: Women assigned to DMPA (n = 33), oral contraceptives (n = 63), or no contraceptives (n = 28) were evaluated by DXA at the lumbar spine at baseline and 12 months later. DMPA users lost 2.7% of spine BMD over 12 months compared with controls. Women on contraceptive pills containing norethindrone showed a 2.3% gain in spine BMD; those on pills containing desogesterel showed only small, non-significant increases in BMD.

Conclusion: DMPA had a negative effect on BMD when compared with oral contraceptives or no contraceptives.

Exercise increases BMD in early adolescence

A school-based exercise intervention augments bone mineral accrual in early pubertal girls

Mackelvie KJ, McKay HA, Khan KM, Crocker PRE, *Pediatrics* 2001;139:501-508

Background: Experts believe that prevention of osteoporosis in the elderly begins in childhood and adolescence, during periods of maximal increase of bone mass. Good nutrition and exercise lead to improvement in peak bone mass and reduction in fracture risk later on in life.

Study and Results: School girls between 8.7 and 11.7 years were assigned to a control group or an intervention group that participated in ten minutes of jumping activity thrice weekly for seven months. Girls were divided into prepubertal and early pubertal sub-groups based on Tanner maturity stages. BMC, BMD and estimated volumetric BMD were measured with DXA. Lumbar spine and femur volumetric BMD after 7 months were 1.5% and 3.1% higher in exercising early pubertal girls compared with control girls of similar maturity. This amount of change in elderly women would translate into a 20% reduction of fracture risk. Significant differences also were found for BMC and areal BMD at the lumbar spine in early

pubertal girls. There were no differences in BMC, areal BMD and volumetric BMD between prepubertal girls in the two groups and no differences in total body values among any of the groups.

Conclusion: Seven months of participation in an exercise program had a beneficial effect on spine and femoral BMD in early pubertal, but not prepubertal, girls.

Forearm fractures in children are related to body composition

Bone mineral density and body composition in boys with distal forearm fractures: a dual x-ray absorptiometry study

Goulding A, Jones IE, Taylor RW, Williams SM, Manning PJ, *Pediatrics* 2001;139:509-515.

Background: Nearly one quarter of all childhood fractures occur at the forearm. Risk of forearm fracture is increased by low BMD in adulthood, but less is known about the relationship of fracture risk and BMD in children.

Study and Results: Bone mineral density (BMD) and body composition (DPX) of one hundred boys (age 3 to 19 years) with forearm fractures were compared to 100 matched controls. Fractures were associated with low BMD and BMC. Patients with forearm fracture also had less lean mass, more fat mass, and were three times more likely to be overweight than controls. Results for boys were similar to results from a previous study of forearm fractures in girls. Adults with forearm fractures tended to be more slender than fracture-free controls, but the reverse was found for children. Overweight children had lower BMD relative to their body size, a combination of factors that increased fracture risk.

Conclusion: Boys who sustain forearm fractures tended to have lower BMD, lower muscle mass, and were more likely to be overweight than controls.