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Spinal Osteoporosis

Charles H. Chesnut III, MD*

Osteoporosis remains the most common of the metabolic bone diseases. Nevertheless, it is only in the past two decades that the academic community, the practicing physician, the patient, and the media have recognized the morbidity and economic health care costs of this disease, particularly to the aging population. An example of the evolution of osteoporosis' recognition in the academic sphere is the relative time and space allotment for previous Henry Ford Hospital International Symposia. In the first (1972) International Symposium, "Clinical Aspects of Metabolic Bone Disease," a three-hour afternoon session with eight presented papers was devoted to osteoporosis; the subsequent publications occupied 62 pages of the 694-page volume of the Proceedings. At the second (1983) International Symposium, "Clinical Disorders of Bone and Mineral Metabolism," osteoporosis occupied four hours of the program, with 11 presented papers encompassing 59 pages of the 552-page Proceedings. For the current 1988 International Symposium, an entire day was directed toward information on osteoporosis, with a morning session devoted to spinal osteoporosis, and an afternoon session to metabolic bone disease of the hip. A total of 17 presented papers comprised the osteoporosis presentations; undoubtedly a major portion of the Proceedings will be devoted to this disease. In 1988, it would appear that appropriate recognition of osteoporosis and its complications has occurred.

Osteoporosis: 1988 and Beyond

Peck (1) provided a timely introduction to the session on spinal osteoporosis, timely in that this session corresponded to the beginnings of National Osteoporosis Week. He gave an informative overview of progress in the field during the 1980s, noting particular advances in understanding the regulation of bone remodeling, in developing techniques for quantitating bone mass (particularly the new x-ray based procedures), and in devising preventive therapeutic programs. He noted that prevention is currently the most important therapeutic strategy in osteoporosis; estrogen therapy remains the major prophylactic modality but cannot and should not be utilized by all women. Alternative antiresorptive strategies are available, such as calcitonin and possibly the diphosphonates; in addition, on the horizon are numerous other antiresorptive and even bone-reconstructive approaches. The 1980s have been a most productive time for osteoporosis research, but obviously much remains to be accomplished.

Further Characterization of the Heterogeneity of the Osteoporotic Syndromes

Melton and Riggs (2) offered an innovative epidemiological approach in support of their hypothesis of two heterogeneous osteoporosis syndromes: type I, and type II. They noted the similarity of the type II osteoporosis to a Gompertzian disease model; ie, a degenerative disease with an exponentially increasing incidence rate with aging, an early-onset and insidious progression and later symptomatic threshold, a multifactorial etiology, a common occurrence in the population at large, and a lack of response to treatment. Type I osteoporosis, on the other hand, resembles a non-Gompertzian disease model: a lack of an exponential increase with age, an acute onset after the menopause, a less common occurrence in the population at large, a specific pathophysiology or pathogenesis—estrogen deficiency, and a greater potential response to treatment. While currently available data do not definitively prove the heterogeneity of osteoporosis and the presence of type I and type II osteoporosis syndromes, such an obviously thoughtful and intellectually challenging approach to the epidemiological pathogenesis of osteoporosis was stimulating and led to an invigorating discussion.

Appropriate Use of Bone Densitometry

Genant et al (3) reviewed the current status of bone densitometry, noting the technical capabilities of the three noninvasive techniques for quantitating bone mass: single and dual photon absorptiometry, computed tomography, and the new x-ray dual energy technique. They discussed the controversy regarding bone mass quantity as a primary determinant of fracture risk, noting that while the areas of controversy are under clinical and epidemiological investigation, critical management decisions must be made for the current female population at risk for, or already affected with, osteoporosis. In this regard, the authors noted, as Wasnich et al have indicated, that bone mass is a continuous variable with fracture the primary outcome. Individuals with low bone density may not have yet had a fracture, but this does not mean that they are free of osteoporosis; the probability of fracture is increased, and fractures display a probabilistic nature. Genant et al noted that most investigators accept usage of bone mass quantitation to detect low bone mass (and presumably an increased risk for fracture) in individuals with secondary osteoporosis (athletic amenorrhea, chronic steroid therapy, etc), but that there is no consensus regarding their use in assessing the need for estrogen therapy and in assessing the presence and severity of osteoporosis generally. In terms of screening for osteopenia (either "mass screening" or "selective screening"), a definitive recommendation could not be made;

*Osteoporosis Research Center, University Hospital, University of Washington, Seattle. Address correspondence to Dr. Chesnut, Osteoporosis Research Center, University Hospital, University of Washington, 1959 NE Pacific Street, Seattle, WA 98195.
this remains an area of considerable medical, political, and financial controversy. Even "selective screening" of individuals with a suggestive history of osteopenia and the presence of multiple risk factors is not universally accepted as a reasonable clinical tool, due to some evidence suggesting that historically based risk factors, alone or in combination, have limited predictive value for fracture risk in the individual patient. Genant et al noted appropriately that the progress in improving precision with rectilinear single photon absorptiometry scanning, x-ray based dual photon absorptiometry, and automatic image analysis quantitative computed tomography have enabled the clinician to monitor efficacy of treatment intervention with a higher degree of certainty than was possible in the past.

**Developing Strong Bones: The Teenage Female**

The presentations and discussions then shifted to a consideration of female populations not usually thought of in the context of osteoporosis (i.e., the teenager, the young adult, and the premenopausal and perimenopausal female) and the determinants of bone mass within these premenopausal populations. Matkovic and Dekanic (4) reiterated the hypothesis that peak bone mass at skeletal maturity (age 10 to 20) is a major determinant of postmenopausal bone mass; a low bone mass at skeletal maturity presumably contributes to low postmenopausal bone mass and presumably increases the risk for subsequent fracture. In addition, data were presented from multiple sources noting that the demands for skeletal calcium are highest during the adolescent growth spurt (the time of peak bone mass attainment), that calcium deficiency at this time can decrease the degree of positive calcium balance and presumably the amount of bone mass, and that calcium intake is deficient (below the RDA) in many American adolescent females. While such observations are validated by current data, it was noted in subsequent discussion that no definitive data currently exist demonstrating that increasing and/or repleting calcium intake in adolescent females increases bone mass over control groups. Nevertheless, the concept of developing maximal peak bone mass in adolescence to protect against further osteoporosis appears most reasonable.

**Preserving Strong Bones: The Young Adult Female**

From a consideration of factors contributing to the development of adequate bone mass, the session then turned to factors for preserving peak bone mass. Drinkwater (5) agreed that failure to achieve one's maximal potential bone mass during the young adult years is a risk factor for subsequent osteoporotic fracture, but she also noted that a genetic component to maximal attainable bone mass precludes all women being equally successful in reaching bone mass levels presumed to be protective. She did, however, point out that all women can make changes in their life-styles to maximize their potential bone mass gain and minimize their bone mass loss. Alcohol, caffeine, and tobacco are three possible negative risk factors for preserving bone mass in the premenopausal years. More importantly, three variables known to have a positive effect on premenopausal bone mass include the maintenance of a normal menstrual cycle, adequate calcium intake, and adequate physical activity. In terms of the menstrual cycle, normal levels of estrogen (as determined by normal menstrual cycles) are necessary for maintenance of bone mass during a woman's young adult years. The role of calcium in preserving bone mass remains controversial, as do the overall effects of increasing physical activity, although current data support physical activity increases to be effective in increasing bone mass in women across a wide range of ages. However, Drinkwater's studies in amenorrheic athletes raise questions about the abilities of exercise to preserve bone if estrogen levels are inadequate. Obviously, normal menses, adequate calcium intake, and adequate exercise are important in preserving bone mass; it also appears that the lack of any single factor cannot be completely compensated for by increasing the other two factors. Preserving bone mass prior to the menopause is an area that will receive much attention in the future.

**Optimizing Bone Mass in the Perimenopause: Calcium**

The session then considered perimenopausal and immediate postmenopausal bone loss. Heaney (6) noted four components of perimenopausal bone loss, including age-related bone loss, bone loss associated with estrogen deficiency, bone loss associated with calcium deficiency, and bone loss associated with other factors, such as alcoholism, etc. A hypothetical model incorporating the first three of these factors was presented. Heaney concluded from the model that while estrogen deficiency is a major contributor to bone loss immediately after the menopause (in the "young elderly"), it is a less prominent contributor later on (10 to 20 years postmenopausal, the "old elderly"). In the later years, calcium intake may be a more important contributor to bone loss than estrogen deficiency. Indeed, when evaluated in the Heaney model (assuming a 20 mg/day calcium loss), calcium deficiency accounts for 50% more bone loss than does estrogen deficiency 20 to 30 years after the menopause. Heaney also reiterated current concerns regarding the absorbability of calcium from various calcium sources, noting that most food sources have readily absorbable calcium, but that a number of calcium supplements and pills may have difficulties with dissolution and resultant absorbability.

Heaney pointed out that despite the current controversies regarding the importance of calcium in the prevention of immediately postmenopausal bone loss, an intake of 1,000 mg/day of calcium for estrogen-replete perimenopausal women and 1,500 mg/day for estrogen-deprived postmenopausal women is "safe and prudent." He also reiterated the fundamentally sound observation that while not all postmenopausal bone loss is due to calcium deficiency, such a deficiency does contribute to some bone loss. Since there is no way to distinguish individuals whose bone loss is due to calcium deficiency from those whose loss is due to other contributing factors, it is reasonable to ensure a calcium intake at the NIH recommendations noted above. Calcium deficiency, then, does appear to be a significant contributor to bone loss, with, however, its greatest effects later in the postmenopausal period.
Optimizing Bone Mass in the Perimenopause: Estrogen

Undoubtedly, estrogen deficiency is the main contributor to significant bone loss immediately (one to ten years) after the menopause, and this was again reinforced by Christiansen and Riis (7), who in reviewing laboratory data designated estrogen deficiency as the most important variable in immediately postmenopausal bone loss. They reinforced the now well-documented conclusions that estrogen and/or progesterone replacement therapy can prevent the progression of bone mass loss after the menopause, at all skeletal sites studied to date. However, defining the woman’s individual risk for subsequent bone loss, as well as her need for estrogen replacement therapy, remains difficult; definitive identification of at-risk women by various blood and urine parameters and bone mass quantitating techniques has not yet been possible. Nevertheless, current data certainly support estrogen replacement therapy as the primary therapeutic modality for the prophylaxis of osteoporosis.

Optimizing Bone Mass in the Perimenopause: Calcitonin and Diphosphonates

Alternatives to calcium and estrogen for optimizing bone mass in the perimenopausal woman were then discussed (8). Calcitonin and the diphosphonates (biphosphonates) are additional therapeutic agents for preventing bone loss, primarily by inhibition of bone resorption. Synthetic salmon calcitonin is safe and has proven efficacy in osteoporotic individuals; in addition, one study by Stevenson et al has shown it to be equivalent to estrogen in prevention of bone loss in immediately postmenopausal women without osteoporosis. However, the drug is currently available in most countries only as an injectable agent, which is unsuitable for prophylactic use; a nasal spray is available, and results of some, but not all, preliminary studies with this preparation appear promising. Expense of the calcitonin preparations currently available remains a problem. The bisphosphonates (such as etidronate) are reasonable candidates for prophylactic usage in that they are relatively safe when given intermittently, are relatively inexpensive, and are orally administered; their therapeutic efficacy, however, remains unproved. Studies in osteoporotic females are inconclusive with these agents, and there are no studies currently available in the immediately postmenopausal women in whom the bisphosphonates are utilized for prophylaxis. Nevertheless, these two potential prophylactic therapies, biphosphonates and calcitonin, have the attribute of safety; such safety is a significant asset when compared to estrogen. Estrogens can prevent bone loss over an extended period of time but occasionally at a high cost in terms of side effects.

Use of Vitamin D Metabolites in Osteoporosis

Presentations on the treatment of the osteoporotic woman were confined to a discussion of vitamin D therapy. Gallagher (9) noted a therapeutic rationale for the vitamin D congeners: a correction of the calcium malabsorption present in many osteoporotic patients, subsequent improvement of calcium balance, and, possibly, in high dosage, stimulation of bone formation. He reviewed the currently somewhat disparate data regarding usage of 1,α(OH)D₃ and 1,25(OH)₂D₃ in the osteoporotic individual, concluding that the vitamin D metabolites may have a beneficial effect on bone mass, but unfortunately at dosage levels frequently associated with significant renal toxicity. The role of the D metabolites in the therapy of osteoporosis remains undefined.

Steroids and Osteoporosis: An Unsolvable Problem?

The session concluded with consideration of a somewhat different topic: corticosteroid-induced osteopenia. Raisz (10) confronted this difficult problem, noting that this clinical entity is not “an unsolvable problem” as was intimated in his title, but, on the other hand, was currently unsolved at present. He reviewed the current understandings regarding the mechanism of corticosteroid action on bone and considered the therapeutic dilemma confronting the clinician in treating steroid-induced osteopenia, including the major problem of reversing the inhibitory effects of glucocorticoids on bone formation. The dilemma is compounded by the inability to predict accurately which steroid-treated patients will develop osteoporosis and fractures. As Raisz noted, however, progress is being made in the laboratory in learning more about the pathogenesis of corticosteroid-induced osteopenia, including regulation of bone cells, and about new classes of factors stimulating bone growth. Nevertheless, at the present time, it is unfortunately necessary to consider alternatives to corticosteroids when possible or to utilize the lowest possible dosage of cortisone both to treat the underlying problem and to spare the skeleton.

Final Note

The session closed with a final discussion of the topics considered; the new and innovative data presented, particularly by Melton and Riggs (2), Drinkwater (5), and Heaney (6), received much attention. Again, the obvious increased interest developing in osteoporosis over the past two decades was much in evidence throughout the session.

References