"New Advancements in Treating Osteoporosis"

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Last month (June 19-22, 2003), at the Annual Meeting of the Endocrine Society in Philadelphia, endocrinologists from around the world gathered to present and attend sessions on the latest research in the field. One topic in particular - the Women's Heath Initiative early study findings (WHI) – caused passionate discussion and debate in just about every session. Released last year, the WHI revealed the increased risks associated with long-term use of hormone replacement therapy (HRT) in menopausal and post-menopausal women. These findings startled physicians and patients who had long assumed that HRT provided successful management of menopausal symptoms including night-sweats, vaginal dryness, heart disease and osteoporosis. As a result, many are seeking alternative therapies.

This trend was quite notable at the Endocrine Society meeting's sessions on osteoporosis. The discussions often centered on the WHI and the quest for alternatives to HRT. Experts presented cutting edge data and theories about new treatments for the disease. Furthermore, two other events in the past year, besides the WHI, elevated these sessions to among the most popular at the meeting. First, the Surgeon General's Workshop on Osteoporosis and Bone Health met as the first step towards a report and broad education campaign about osteoporosis for physicians and the public due for 2004. Second, in November, the U.S. Food and Drug Administration (USFDA) approved the first anabolic bone forming treatment for osteoporosis – parathyroid hormone (PTH).

Along with Medicare's coverage of osteoporosis screenings since 1998, the increased attention in the area of osteoporosis indicates a growing appreciation for the rising prevalence of the disease and for the need for early intervention to prevent the rapid deterioration associated with it after an initial fracture occurs.

How serious is osteoporosis for our aging society? Consider a few facts: individuals over

50 years old are 29% of our population. Their numbers are increasing at a rate of 2.5% per year and 55% of these individuals are at risk for osteoporosis.

These older Americans are more active and healthier than previous generations. However, they increasingly face osteoporosis, a silent illness that robs people of their mobility and can lead to permanent dependence and even death. Osteoporosis causes 1.5 million fractures each year in the United States, and 300,000 of these individuals die from fracture-related complications. Only a small percentage of the estimated 10 million who suffer from osteoporosis, and the 34 million who are at risk, even realize that they have these conditions.

Further, once a woman has had a single osteoporotic fracture, without treatment her risk of additional fractures is estimated to increase 50 - 100% above women with similar bone density who have not had a fracture.

Even without causing fractures, osteoporosis can dramatically alter an older person's life. A Gallop survey in May 2000 for the National Osteoporosis Foundation found that 73% of women with osteoporosis are concerned about losing their independence and 67% are concerned about having to reduce activities with family and friends – both very real possibilities. This same survey found that only 31% of women had taken steps to prevent osteoporosis before diagnosis.

In light of the WHI and as evidenced by the discussions at the Endocrine Society meeting, physicians and patients alike are asking for more choices and improved alternative therapies to treat the disease. Traditionally, there have been three options, in addition to a diet rich in vitamin D and calcium, for treating osteoporosis. With the approval last year of PTH, there are now four.

The Selective Estrogen Receptor Modulators (raloxifene) act by selectively targeting a subset of the body's estrogen receptors – activating some and blocking others. Specific to osteoporosis, it activates estrogen receptors in the bones to reduce resorbtion and has

been found to reduce the rate of vertebral factures by 30-50% after 3 years.[1] Conversely, it appears to block estrogen receptors in the uterus and breast and thus in one study of postmenopausal women with osteoporosis showed a reduction in the rate of estrogen-receptor positive breast cancer.

The bisphosphonate class of medicines, (alendronate and risedronate) act by increasing the strength of new bone by physically integrating themselves into the mineral matrix of the bone. These oral medicines have been found to reduce the risk of fractures by 30-50% over a 3-4 year period.

Calcitonin has been available as a nasal spray since 1984, and more recently as a subcutaneous injection. It acts by reducing the number of osteoclasts and their bone resorbing activity, and has been found to reduce vertebral fractures by 36%.

The newest treatment option – and one that received a great deal of attention at the meeting - is teriparatide. As the first bone growth promoting medicine, it encourages physicians to shift the way they think about treating osteoporosis. Teriparatide is a portion of naturally occurring human parathyroid hormone (PTH) that acts by stimulating osteoblasts. This contrasts with the other treatments for osteoporosis that act by reducing the activity of osteoclasts to slow bone resorbtion. Teriparatide is administered as a subcutaneous injection with an auto-injecting pen device, and it has been found to increase BMD in over 90% of men and women. In women, it has been shown to lower the risk of vertebral factures by 65% and other fractures by 53% when used for an average of 19 months.[2]

Adding to the utility of teriparatide treatment are new reports from the recent meetings of the European Calcified Tissue Society (Rome, May 8-12, 2003) and the Endocrine Society. The first of these directly demonstrated the effectiveness of teriparatide in

[1] Raloxifene also appears to activate estrogen receptors related to lipid metabolism and thus lowers LDL cholesterol levels.

[2] These results were in a clinical trial comparing teriparatide, plus vitamin D and calcium versus vitamin D and calcium plus placebo. As an anabolic agent adequate vitamin D and calcium intake should support its bone forming properties.

forming new trabecular and endosteal bone using bone biopsies. The second showed that the effectiveness of teriparatide treatment could be evaluated by monitoring changes in patients' bone specific alkaline phosphatase - a marker of bone formation - as early as one month after initiating treatment. Thus, in the future, it may be possible to assess the progress of patients' bone using blood tests rather than the more expensive and time consuming dual x-ray absorptiometry (DXA) scans.

Future treatment options for osteoporosis fall into two categories. The first uses currently available medications (in addition to vitamin D and calcium), either concurrently or sequentially. Now that we have medicines that act via several mechanisms of action, these combinations provide very exciting opportunities for improving treatment regimens. The second category encompasses a range of innovative experimental compounds being developed to treat osteoporosis. As these experimental medicines prove both safe and effective, physicians will have additional and possibly more effective options for individualizing their patients' treatment plans towards the goal of actually ending osteoporosis.

A number of factors put osteoporosis at the forefront of national health concerns. Our aging population continues a trend of remaining active later in the life. The WHI raises troubling questions about the benefit/risk ratio of HRT, once considered the primary treatment for osteoporosis. The Surgeon General plans to launch an educational campaign about osteoporosis for both physicians and patients in the next year. All these factors not only create demand for improved treatment options but also provide opportunities for new ways of thinking about osteoporosis. As Dr. Henry Kronenberg, of the Endocrine Unit at Massachusetts General Hospital, Boston, explained at a plenary session at the Endocrine Society Meeting, "It's not enough to prevent and treat, we want to end the disease of osteoporosis."

***** Sidebar or separate box of text?*******

The most prevalent risk factor for osteoporosis is age. As we age, the rate of bone resorbed by osteoclasts remains the same, but less new bone is formed by osteoblasts to replace the resorbed bone. In osteoporosis, the imbalance between these two processes is so great over a long enough period of time that the bones lose their mass and strength putting patients at greater risk for fractures, even from normal stresses. Inherent risk factors for osteoporosis include female gender, postmenopausal, low testosterone levels in men, and family history of osteoporosis. Additional risk factors that can cause osteoporosis at an early age are diverse and include hypogonadism in both men and women, hyperthyroidism, some anti-seizure medications, long-term systemic steroid use, Cushing's syndrome, conditions that affect calcium absorbtion – including alcoholism.

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