OSTEOPOROSIS

Osteoporosis is a disease whereby bones of the body are weakened. They do not have enough calcium mineral content to withstand the normal stresses and wear on them, resulting in unexpected bone fractures. These fractures typically occur in the spinal vertebrae, hip, and wrist, but they can occur elsewhere as well. Osteoporosis is a major health issue, as it is estimated to affect 1/3 of women over the age of 65. When hip fractures occur, about 15% are ultimately fatal, and another 40% precipitate nursing home placement. There are two general types of osteoporosis: Type I, postmenopausal osteoporosis, occurs in women with the start of menopause, and results in accelerated bone calcium loss for the next 10 or more years. Type II, senile osteoporosis, occurs in all adults, and progresses very slowly for the remainder of life, beginning about the age of 30 to 35. Both kinds of osteoporosis appear to be related to decreased ability to absorb calcium from the intestine and decreased production by the kidney of a vitamin D hormone. But in Type I osteoporosis, there is also accelerated bone calcium loss and decreased parathyroid hormone, a hormone that stimulates vitamin D production. There may be many other factors involved in producing osteoporosis. Certain medical problems will also predispose to osteoporosis. Some of these are excess alcohol intake, anticonvulsant drugs, chronic lung disease, corticosteroid drugs, diabetes, prior stroke, overactive thyroid, partial stomach removal, immobilization and removal of gonads (castration). This risk is higher in elderly white thin females who do not consume much calcium in the diet. Menopause for most women begins around age 49 to 53, with the last menstrual period. The ovaries can only produce small amounts of estrogen, in spite of strong stimulatory signals from the brain. The ability to reproduce is lost, and blood estrogen levels fall quite low. A number of symptoms can occur, such as vaginal and genital dryness and itching, irritation of the urinary opening, skin dryness, breast softening and shrinkage, osteoporosis and hot flushes. Hot flushes can continue to occur for as long as 10 years, and are characterized by upper chest, neck and face flushing, warmth, and perspiration accompanied by a quickened pulse for several minutes. Night sweats can occur that interrupt sleep. These symptoms can be effectively treated with estrogens in the form of tablets or skin patches. However, when estrogens are used alone to treat menopausal symptoms, they increase the risk of cancer of the uterus, possibly high blood pressure, possibly blood clotting and gallstones. However, if used in small doses (less than or equal to the equivalent of Premarin .625 mg/day), and in proper combination with progestins (ovarian hormones that can and sometimes do induce vaginal monthly bleeding), there is NO increased risk of cancer of the uterus, and less increased risk of high blood pressure or blood clots. From concerns about the lack of data on the usefulness of estrogens in postmenopausal women as well as safety issues regarding the use of estrogens the Women's Health Initiative (WHI) was designed in the early 1990s. The WHI was launched in 1991 and consisted of a set of clinical trials and an observational study, which together involved 161,808 generally healthy postmenopausal women. The clinical trials were designed to test the effects of postmenopausal hormone therapy, diet modification and calcium and vitamin D supplements on heart disease, fractures, and breast and colorectal cancer. The hormone trial had two studies: the estrogen-plus-progesterone study of women with a uterus and the estrogen-alone study of women without a uterus. (Women with a uterus were given progestin in combination with estrogen, a practice known to prevent endometrial cancer.) In both hormone therapy

studies, women were randomly assigned to either the hormone medication being studied or to placebo. Those studies have now ended. The women in these studies were followed until 2010. The results of these studies are as follows:

Compared with placebo, estrogen plus progestin resulted in:

- Increased risk of heart attack
- Increased risk of stroke
- Increased risk of blood clots
- Increased risk of breast cancer
- Reduced risk of colorectal cancer
- Fewer fractures
- No protection against mild cognitive impairment and increased risk of dementia (study included only women 65 and older)
- Overall health risks exceeded potential benefits

Compared with the placebo, estrogen alone resulted in:

- No difference in risk for heart attack
- Increased risk of stroke
- Increased risk of blood clots
- Uncertain effect for breast cancer
- No difference in risk for colorectal cancer
- Reduced risk of hip fracture
- No overall benefit compared with placebo.

The implications of these studies on the use of estrogens in postmenopausal women is profound, and is summarized under treatment options for osteoporosis found below.

There are a number of screening tests to look for osteoporosis. Most of them are not sufficiently accurate or reproducible to be of use in a given individual. Routine X-rays only detect osteoporosis after about 30% of bone calcium is already gone. Another technique, called Single Photon Absorbtiometry, is a good test, but isn't able to check the bones (hip and back) that are most likely to fracture. There are two good techniques, called Dual Photon Absorbtiometry and Quantitative Computed Tomography, to measure bone mineral calcium. Both of these are accurate and reproducible, but tend to be expensive, costing $75 to $300. Careful clinical trials have shown that estrogen supplementation alone can maintain bone mineral calcium in menopausal women and can increase bone calcium in menopausal women with osteoporosis. Estrogens appear to work by helping to increase vitamin D availability, increase gut absorption of calcium, and decrease bone breakdown. Studies have not clearly shown that calcium supplementation alone can maintain bone mineral calcium in menopausal women, although there is a suggestion that calcium MAY be helpful. There is evidence that estrogen combined with calcium is better than either one alone. Although the U.S. R.D.A. (recommended daily amount) for calcium is 800 mg for non-pregnant adults, studies suggest that larger amounts, up to 1500 mg/day, may benefit postmenopausal women. In fact, some data suggests that calcium supplementation may be more helpful if it is begun in young adulthood. Calcium supplementation however should be used cautiously in people with a history of kidney stones. Dietary calcium is most readily obtained from milk, cheese and other dairy products.

For the treatment of osteoporosis, there are several categories of medications available. These include estrogen preparations and selective estrogen-receptor modulators

(SERMS). Calcium and vitamin D supplements is a second group. Calcitonin (a hormone derived from the thyroid gland) is a group by itself. Bisphosphonates such as alendronate, risedronate, ibandronate and zolendronate is another group. Injectable parathyroid hormone (Forteo) is another group. A newer agent, denosumab (Prolia) represents another group. Denosumab is given by injection twice yearly, and is used primarily in people at high risk for fracture or who have been on bisphosphonates for 10 years or more. Estrogens are no longer recommended for the prevention or treatment of osteoporosis (Their use should generally be limited to a single indication: treatment of post-menopausal hot flashes). SERMS do help to maintain bone mineral calcium in the spine but have not been shown to be effective in maintaining bone mineral content in the hips or elsewhere. Calcitonin is used by injection or by a nasal spray. It has been shown to increase bone mineral calcium content by small amounts, but there have been no long term studies showing that it actually will lead to a decrease in the number of future fractures. Calcitonin can lead to serious allergic reactions, and is expensive ($1500 to $3000 per year). Bisphosphonates are derivatives of detergents, and act by binding with bone and inhibiting bone resorbing cells from acting. These drugs can have serious side effects (inflammation of the esophagus, abdominal and muscle pain) and the brand names are expensive. But now generic Fosamax is available and works just as well as the brand name medication does. Several bisphosphonates are now available as an IV injection. Used this way they can be given much less frequently (once every 3 months or once every year), but the IV preparations are expensive and may be associated with side effects such as osteonecrosis of the jaw. Forteo, a synthetic analogue of parathyroid hormone, is expensive, has to be taken as a daily injection for 18 to 24 months, and usually is reserved for severe osteoporosis unresponsive to other medications. If you have further questions about osteoporosis or its treatment, feel free to ask about it the next time you visit our office.

Revised 3/2019