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Protocols
OSTEOPOROSIS

This protocol details a comprehensive regimen of supplementation and therapies designed to stop and possibly reverse the effects of osteoporosis

Normal aging causes a decline in bone density that occurs to varying degrees in otherwise healthy people. This decline does not induce bone fractures. Osteoporosis on the other hand, is a progressive marked reduction in bone mineral density that often results in pathological fractures, particularly of the vertebrae of the spine. It occurs more frequently in women than in men.

Many factors may cause osteoporotic bone loss, which is not associated with aging. These include major surgery, glucocorticoid (anti-inflammatory steroid) drugs, liver cirrhosis, Crohn's disease, cystic fibrosis, and hormone deficiencies. This Life Extension Protocol confines itself to age-related osteoporosis.

Osteoporosis and hormone metabolism

The primary cause of osteoporosis is a hormonal imbalance that interferes with the bone-forming cells. The osteoblasts are specialized bone cells that function to pull calcium, magnesium and phosphorous from the blood in order to build bone mass. Osteoblasts require the hormone progesterone to maintain youthful bone-forming capability during and after menopause.

Provera is a drug frequently prescribed by conventional doctors that causes many side effects in women. Provera (medroxyprogesterone) is an artificial molecule that should not be confused with natural progesterone. Natural progesterone provides the benefits with none of the side effects of synthetic drugs. A stark example of the safety of natural progesterone compared to synthetic progestin drugs can be seen by the labeling. Provera carries a warning that its use in early pregnancy may increase the risk of early abortion or inflict congenital deformities on the fetus. Natural progesterone, on the other hand, is necessary for the survival and development of the embryo throughout the pregnancy. In response to pregnancy, ovarian secretion of progesterone increases significantly. As a general rule, pregnant women should not use any hormone replacement therapy without consulting their obstetrician.

Natural progesterone may be obtained in several different forms. The safest route of progesterone administration is via a topically-applied cream that absorbs directly through the skin into fat cells. It is important to apply natural progesterone cream to different parts of the body (face, breasts, abdomen, and thighs) so as not to over-saturate the fat cells under the skin that are required to assimilate the hormone into the body. The topical application of progesterone enables it to enter the body without first going through the digestive system. If progesterone were to be taken orally, it would have to first pass through the liver which degrades and excretes much of the hormone into the bile. Natural progesterone is available in topically-applied creams that contain between 900 mg and 1400 mg of natural progesterone per 2-oz jar.

In using progesterone cream, peri and postmenopausal women should start with 1/4 to 1/2 teaspoon per day. Those with severe osteoporosis should use 1/2 teaspoon morning and night for the first jar followed by 1/2 teaspoon a day for the second jar on. Premenopausal women over age 30 who suffer from premenstrual syndrome (PMS) may consider taking 1/4 to 1/2 teaspoon of progesterone on days 12 through 26 of their menstrual cycle.

It is advisable for women to ask their doctor to measure blood or saliva levels of hormones such as progesterone to best individualize the correct dosage, though natural progesterone has been safely used by millions of women by individually adjusting the dose to reflect alleviation of PMS or menopausal symptoms. In other words, if hot flashes, night sweats, headache and depression are alleviated by using 1/4 teaspoon of natural progesterone cream a day, then a woman may be able to safely stay at that dose. While it is prudent to consider physician supervised progesterone blood or saliva testing, the safety of natural progesterone is such that a pregnant woman will naturally secrete large amounts of progesterone without encountering toxicity. In an ideal setting, hormonal blood or saliva testing would be done routinely, but since most peri and postmenopausal women produce very little progesterone, these women have historically safely self-administered topical progesterone cream according to how well it corrects their menopausal symptoms. With the advent of lower cost saliva-and-blood testing, it should be possible for more women and their doctors to target their ideal progesterone level.

Some women who do not respond well to progesterone creams may do very well with hormone implants. These are little pellets about one-eighth inch in diameter that are implanted under the skin every six to 12 months. It is done in a physician's office taking only ten minutes.

In women whose doctors are prescribing excess amounts of supplemental estrogen, the administration of progesterone may enable the dose of estrogen to be reduced, since progesterone restores sensitivity to estrogen receptors on cell membranes. If the estrogen dose is not lowered, some women develop symptoms of "estrogen dominance" (such as water retention, headaches, weight gain, swollen breasts) when progesterone is first supplemented. The objective of the physician should be to gradually lower the dose of estrogen in relation to progesterone therapy. If estrogen is reduced too rapidly, hot flashes can occur.

Estrogen is used to prevent bone loss because it regulates the action of osteoclasts, which remove dead portions of demineralized bone. DHEA* and/or soy extracts may provide enough estrogen to maintain youthful osteoclast activity. Based upon records of dietary soy consumption in Japan, the typical daily phytoestrogen intake from soy has been estimated at 50 mg per person. By contrast, the typical Western diet has been estimated to provide only 2-3 mg a day of the phytoestrogen genistein. Not only are certain cancer levels lower in those who consume soy, but menopausal symptoms and the incidence of osteoporosis are reduced. New studies are showing that soy isoflavones promote an anabolic effect on bone density in postmenopausal women by binding to an estrogen receptor in bone. The protective effect of genistein seems to depend on stimulation of bone formation rather than estrogen's effect of suppressing bone resorption. Although both estrogen and genistein protect against bone loss after cessation of ovarian function, genistein has been shown to reduce both trabecular and compact bone loss.

A six month study on 66 postmenopausal women was conducted at the University of Illinois at Urbana-Champaign to investigate bone density and bone mineral content in response to soy therapy. In this study, postmenopausal women received, on a daily basis, either phytoestrogens derived from soy protein or milk-derived protein (that contained no phytoestrogens). The results showed significant increases in bone density and bone mineral content for the lumbar spine in the women receiving the phytoestrogens derived from soy protein diets compared to the control diet. Increases in other skeletal areas also were noted in the women on the soy diets. Dr. Erdman, the lead scientist, concluded that soy isoflavones show real potential for maintaining bone health. Kenneth D. Setchell, Ph.D. of Children's Hospital and Medical Center in Cincinnati, Ohio confirmed the estrogenic activity of the principle soy isoflavones daidzein, genistein, and glycitein. Dr. Setchell conducted research on the chemical structure and metabolism of soy phytoestrogens, and concluded that consuming modest amounts of soy protein results in relatively high blood concentrations of phyto-estrogens and that this could have a significant hormonal effect in many individuals.

There are enough phytoestrogens in the newer soy extracts for many women to derive effective estrogen replacement therapy. A soy supplement called Mega Soy Extract provides 110 mg of soy phytoestrogens in just two capsules. This is more than twice the amount in the typical Japanese diet. Since the phytoestrogen genistein is water-soluble, it is suggested that one capsule of Mega Soy Extract be taken in the morning and one in the evening. While all women should benefit from Mega Soy Extract, some women may need to consider direct, natural hormone replacement as well depending upon family history, severity of osteoporosis if already present, and other considerations.

Estrogen is a general name for a group of similar compounds (estradiol, estrone, estriol and their metabolites) with slightly different effects on the various tissues in a woman's body. A commonly prescribed drug is called Premarin because the estrogens it contains are an extraction from a pregnant mare's urine. As you might guess, the ratio of the various types of estrogens found in horse urine is different from those found in human females. So, Premarin works fine if you are a horse. Women, however, should get their estrogens from another source. A popular estrogen compound prescribed by alternative physicians is called TriEst (80% estriol, 10% estradiol, 10% estrone). Estriol is considered the safest form of estrogen, yet small amounts of the more potent estradiol and estrone are needed by some women. Europeans use estriol as an estrogen replacement therapy because of evidence it may help to prevent breast cancer, whereas high doses of estradiol and estrone have been shown to increase the risk of breast and ovarian cancer. For women not responding well to TriEst, compounding pharmacies are able to prepare custom estrogen formulas that may only contain estriol, or different percentages of the three estrogens (estriol, estradiol and estrone). Women seeking these prescription estrogen compounds should see a physician familiar with natural hormone replacement.

Additionally, it is important for peri and postmenopausal women to consider testosterone. Women have less than men do, but it is just as important to them as it is to men. Why? Testosterone contributes to stamina, proper female muscle mass, sex drive, and prevention and treatment of osteoporosis.

Postmenopausal women should consider dosing of all the sex hormones in a way that mimics the normal menstrual cycle of the woman of childbearing age. One must bear in mind that while progesterone is protective in the sense that it protects against cancer, estrogens, when taken without progesterone, may increase a woman's risk of cancer of the breast and potentially the uterus. This is very easy to understand. Estrogens stimulate breast tissue and the lining of the uterus. During the menstrual cycle progesterone production rapidly falls resulting in the shedding of the uterine lining and menstrual flow. If estrogen is taken continually, building up the uterine lining without opposing progesterone, there is a theoretical increased cancer risk. This is why you must discuss this with a physician knowledgeable about the subject. The risk is minimized in a postmenopausal woman if hormone replacement results in monthly menstruation or she undergoes yearly uterine tissue sampling or biopsy which is a simple procedure done in your doctor's office.

Women over 30, particularly those with a family history of osteoporosis, should consider hormone level analysis in consultation with a physician to see if hormone supplementation should be undertaken prior to menopause. Other hormones to consider are DHEA* and melatonin. DHEA has been shown to stimulate osteoblast activity to help prevent bone loss. Most women take about 25-50 mg a day of DHEA.

Women over the age of 35 or 40 should consider taking melatonin, in the range of 500 micrograms to 3 mg every night, to help prevent osteoporosis and reduce the carcinogenic risks associated with estrogen-replacement therapy.

Nutrient & Supplement Considerations

A number of women take calcium tablets, but calcium is a strong binding agent that often is difficult to break down in the digestive tract. Calcium capsules, on the other hand, burst open in the stomach within five minutes for quick absorption into the bloodstream. Calcium supplementation is only one part of an osteoporosis prevention and treatment program.

For bone mineral maintenance and replacement, women should take between 1,000 and 2,000 mg of elemental calcium along with 600 to 1,000 mg of elemental magnesium every day. The addition of between 400 IU and 1,000 IU of vitamin D3 is mandatory to ensure optimal calcium absorption. The inability to absorb calcium is a major reason that calcium therapy fails to prevent or slow the progression of osteoporosis. Vitamin D3 taken with calcium will normally promote absorption and assimilation of calcium into the bone matrix. Vitamin D3 also has been shown to promote the production of IGF-I and other growth factors in osteoporotic patients, which improves osteoblast (bone-building) function. Other minerals that are important for healthy bone metabolism include at least 30 mg a day of elemental zinc, 3 mg a day of elemental manganese, and 2 mg a day of elemental boron and 1.5 mg of copper.

There are dietary supplements designed to prevent and treat osteoporosis. A product called Bone Assure provides a complete combination of nutrients for the prevention and treatment of osteoporosis. The recommended dose for women is six capsules a day. Healthy men should take four capsules a day. It is best to take calcium supplements with meals. While certain fibers such as wheat bran, psyllium, guar gum and pectin can interfere with mineral absorption, calcium absorbs better with meals. The recommended dosage of a product like Bone Assure would be two capsules at lunch, dinner and at bedtime for women.

Recent investigations and clinical studies suggest that essential fatty acids and antioxidant nutrients influence bone formation. In animals, bone modeling appears to be optimal when omega-3 and omega-6 fatty acids are supplied in the diet. These studies support the role that dietary fatty acids and antioxidants play in reducing the severity of diseases involving bone-density loss. Vitamin E was reported to increase bone formation rate and to restore collagen synthesis. Daily supplementation with six 1000 mg capsules of perilla oil, or one tablespoon of flax-seed oil a day, will provide omega-3 fatty acids. Omega-6 can be obtained from borage or black-current seed oils.

The Importance of Exercise

Exercise is an effective therapy for preventing and treating osteoporosis. Its importance cannot be overstated. A study was performed to evaluate the effectiveness of the exercises for the treatment of postmenopausal osteoporosis. Both back extension and posture exercises lasting for one hour were undertaken twice a week, as well as fast walking exercises for one hour three times a week. At the end of the study, women who added exercise to their medical therapy increased spinal bone density by 4.4 percent, while women receiving only bone-restoring medicines showed an increase in spinal bone density of just 1.6 percent.

Severe Osteoporosis and Conventional Treatment

Calcitriol and calcitonin are FDA-approved drugs that can facilitate calcium absorption if vitamin D3 is not effective. One study showed that the addition of calcitonin (administered intra-muscularly) to calcium supplementation not only inhibited bone loss but significantly increased bone mass in fractured forearm bones. Another study showed that the drug calcitriol corrects the malabsorption of calcium. Higher amounts of vitamin D3 also have been shown to normalize calcium malabsorption that occurs as result of aging. Patients taking calcitriol should be monitored for serum and urine calcium response to the drug. As is common with most FDA-approved drugs, dangerous side effects are a significant risk. Prescription of calcitriol for the treatment of osteoporosis should be reserved for physicians and their patients with a special interest in the treatment of metabolic bone disease. The taking of high doses (over 1100 IU a day) of vitamin D3 also should be under physician supervision.

Severe Osteoporosis and Alternative Treatment

Instead of using potentially toxic FDA-approved drugs such as calcitriol and calcitonin to treat severe bone loss, European doctors have found that the biphosphonate drug clodronate safely protects and restores bone density. In one study, the effectiveness of different clodronate regimens in postmenopausal osteoporosis was evaluated. Sixty women were randomly assigned to one of

three treatments: Oral calcium, 1000 mg/day; oral calcium plus oral clodronate, 400 mg/day; oral calcium plus oral clodronate, 400 mg/day for 30 days, followed by a 60-day period of calcium supplement alone. This last regimen was repeated four times in the 12-month study period. The results showed that patients who received calcium alone showed a decline in spinal bone mass, both after 6 and 12 months; femoral density in this group also decreased after 6 and 12 months. On the other hand, both clodronate-treated groups had increased levels of lumbar bone mass compared with controls, both after 6 and 12 months of therapy. At the end of the study, it was found that patients treated with cyclical clodronate had higher spinal bone mass compared with those treated continuously. After 6 months, femoral bone density was significantly higher in subjects treated with clodronate, both cyclically and continuously, compared with controls who only received calcium. Continuous clodronate treatment resulted in a clear fall in biochemical indices of bone degradation. The doctors concluded that one-year treatment with clodronate induces a gain in bone mass, especially in the spine.

Another study of 60 women with postmenopausal bone loss showed that just 400 mg a day of clodronate taken by mouth produced a progressive and significant increase in lumbar bone density, both at 6 and 12 months. In contrast, there was a progressive and significant decline of bone mineral density in untreated patients. The doctors concluded that cyclical low-dose clodronate therapy induced a gain in lumbar spine bone mass in patients with postmenopausal osteoporosis.

While the FDA has approved expensive drugs such as Fosamax (alendronate) that work in a similar way to clodronate, the side effects of these drugs can be severe. Clodronate, on the other hand, is virtually free of side effects. The dose used to treat osteoporosis is 400 mg a day (about 1/4 the dose used to treat cancer patients with bone metastasis). Blood tests to measure serum calcium levels and kidney function should be done ten days after initiating clodronate therapy and then every one-to-two months thereafter. The concern for a small minority of people is that clodronate will cause too much calcium to be pulled from the blood for deposition onto the bone. Regular blood testing will detect a serum calcium deficit. One study warns against taking clodronate in those suffering from severe renal insufficiency. The kidneys normally remove excess clodronate, and dialysis may not efficiently remove clodronate from the blood. Another study encourages clodronate to be used in renal disease when hypercalcemia is present. Regular blood tests can detect kidney problems early, though clodronate dose not appear to cause kidney disease in-and-of itself. Do not use clodronate if pregnant because it could adversely effect calcium metabolism to the fetus. Clodronate is banned by the FDA, despite its extraordinary 15-year track record for safety and efficacy.

For those with severe osteoporosis, higher amounts of calcium and vitamin D3 may be required, along with a six-month regimen of growth hormone-replacement therapy. A parathyroid hormone (PTH) test must be performed to see if calcium is leaving the bones—that is, if the process of bone demineralization is occurring. An elevated parathyroid hormone level indicates the possibility of osteoporosis, secondary to calcium deficiency.

Osteoporosis & Men

It is important for men to utilize the same nutritional guidelines as women. Attention to testosterone level is especially important. DHEA* and melatonin may be helpful in men as well. In some cases a consideration for the use of some progesterone should be made. Lastly, the importance of exercise cannot be overemphasized. This should be done under the care of a physician especially for men with a history of prostate cancer.

Chelation Therapy

Chelation therapy is a non-conventional treatment for arteriosclerosis and a number of other diseases not yet approved by the FDA. Chelation therapy is available in this country because the primary ingredient EDTA has been approved by the FDA for other uses. In an article published in *The Journal of Advancement In Medicine* in 1988 by Rudolph, McDonagh, & Wussow, chelation therapy was found to increase bone mineral density. The mechanism is believed to be the pulsing of the hormone parathyroid hormone which is made by the parathyroid glands and is essential in calcium metabolism. This pulsing probably results in deposition of calcium in the bones.

Toxins

There is ample evidence that fluoride found in drinking water and toothpaste may contribute to bone destruction. The use of properly filtered water and toothpaste without fluoride is recommended.

Summary

The prevention and treatment of osteoporosis depends largely upon several factors:

- Proper nutritional supplementation with vitamins and minerals, in particular calcium -Exercise -DHEA* and melatonin
- Avoidance of fluoride in water and toothpaste
- Soy extract in women

- Progesterone cream in women
- Consider hormone replacement in women: Natural estrogens, progesterone, testosterone, oral or implant
- Consider hormone replacement in men: Testosterone, progesterone
- Consider chelation therapy
- Consider clodronate

Osteoporosis is a progressive reduction in bone mineral density that can be corrected by the proper use of nutrients, hormones and exercise to promote overall health and reduce the risk of numerous other diseases. Bone loss resulting from causes other than aging is often very difficult to reverse without addressing the underlying cause. This is particularly true for patients who are on anti-inflammatory steroids for chronic conditions because the bone loss is a side effect of the drug itself. Conventional medicine has for years emphasized the role of estrogen in preventing osteoporosis. Physicians were largely unaware of the fact that progesterone is more important for preventing and treating osteoporosis. Our current knowledge is based largely on the work of Dr. John Lee. Readers are referred to the Life Extension Protocol on Hormone Replacement (www.lef.org) or in the Disease Prevention and Treatment Protocol book for more details regarding current thinking relating to both proper estrogen and progesterone therapy.

*DHEA Precautions

DHEA replacement is becoming a very popular anti-aging therapy that may also help prevent bone loss. However, there are some precautions that should be exercised when taking DHEA.

A DHEA blood test should be taken three-to-six weeks after beginning DHEA therapy to help determine optimal dosing. Some people take a DHEA blood test before beginning DHEA replacement therapy, but The Life Extension Foundation has found that every person evaluated who is over 39 years of age shows marked DHEA deficiency.

For the DHEA test, blood should be drawn between the first and second daily dose of DHEA. While this test can be costly, it can save you money in the long-run if it shows that you should take less of the hormone to produce youthful DHEA levels.

Take antioxidant supplements after every DHEA dose to protect your liver against free-radicals that could be generated in response to DHEA's metabolic-enhancing effects.

CAUTION: Men with prostate cancer or severe benign prostatic hypertrophy should not take DHEA because it can be converted into metabolites estrogen and dihydrotestosterone, which could promote prostate cell proliferation.

Men over 40 who take DHEA should also take an extract of saw palmetto (320 mg) and nettle root extract (240 mg) every day, or another 5-alpha reductase inhibitor, to reduce the conversion of testosterone to dihydrotestosterone. Men over 40 should also consider checking their PSA (prostate specific antigen) levels when they have their first DHEA blood tests, and every year thereafter. This test can reveal the presence of prostate cancer. Do not take DHEA if you have prostate cancer.

DHEA can increase serum estrogen levels in women. It could reduce or eliminate the need for estrogen replacement therapy by naturally elevating estrogen levels in the body. To help protect cells (especially breast cells) from excessive proliferation in response to estrogen in the blood, women should consider taking 500 mcg to 3 mg of melatonin every night, especially if they take DHEA. High doses of soy provide phytoestrogens that may also reduce breast cancer risk.

Note: Women taking DHEA or any form of estrogen therapy are strongly advised to take a soy supplement that provides at least 50 mg of elemental genistein for the specific purpose of reducing the overall risk of breast cancer. Women with an estrogen-dependent cancer may want to avoid taking DHEA. However, some physicians find physiological DHEA replacement is beneficial for patients with such cancers. Women should consider estrogen testing when they take their DHEA blood test, in order to evaluate DHEA's effect on their blood levels of estrogen when a follow-up test is performed.

If you have liver disease, it is more important that you take DHEA sublingually (under your tongue) to reduce the amount of DHEA entering your liver. Check your liver enzyme levels to make sure DHEA is not making an existing liver disease worse. Some animal studies suggest the possibility of liver damage from large doses of DHEA. Antioxidants should be taken to protect against DHEA-induced free-radical damage to the liver.

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