Strontium

The First Bone-Building Supplement!

Bone loss accelerates suddenly in menopausal women because the drop in estrogen levels causes an increase in the resorption (teardown) of existing bone. But resorption is only half of the story. Age-related bone loss is also caused by a decrease in the formation of new bone tissue.

Existing drugs for treating osteoporosis, as well as calcium and vitamin D supplements, work by reducing bone resorption. But they do not support the formation of new bone. These drugs and nutrients increase the mineralization of bone, but they do not help the body to build new bone tissue. And in fact, within weeks of starting use of antiresorptive drugs like Fosamax,® the body’s formation of new bone actually decreases. The resulting bone is less prone to fracture, but is not the same as youthful, healthy bone.

Strontium is a mineral found along with calcium in most foods. Research has long suggested that it may be an essential nutrient required for the normal development, structure, function, and health of the skeletal system. Clinical trials going back into the 1940s have supported this conclusion, but recent studies have provided evidence that it can offer unique nutritional support against loss of bone structure and function.

Animal studies have shown that Strontium supplements both decrease bone resorption, and increase the formation of new bone tissue.

• In animal models, Strontium (in various forms, such as chloride, carbonate, and ranelic acid salt) causes “baby” osteoblasts (bone-building cells) to multiply more quickly.
• Bone tissue cultures which are exposed to Strontium synthesize more bone matrix and new bone collagen. The same amount of calcium (in various forms, including the ranelic acid salt) has no effect on these parameters.
• In bone tissue culture, Strontium reduces bone resorption at concentrations at which calcium has no effect, prevents the resorption caused by excessive parathyroid hormone, and slows the rate at which immature osteoclasts develop.
• Strontium-supplemented diets boost bone strength in experimental animals without a negative impact on bone quality, even at extremely high doses.
Human clinical trials also support Strontium’s ability to both support new bone formation and prevent excessive resorption.

• The results of early clinical trials using Strontium (lactate) led researchers to speculate that Strontium increased osteoblast activity.
• Bone biopsies from a small human pilot trial revealed an astounding 172.4% increase in new bone formation after six months of Strontium (gluconate) supplementation.
• The bone-building activity of osteoblasts can be measured using bone-specific alkaline phosphatase, while crosslinked N-telopeptide (NTx) and C-telopeptide (CTx) mark the degradation of bone collagen by ravaging osteoclasts. The use of these tests in large clinical trials (using the ranelic acid salt of Strontium) has confirmed that Strontium supplements decrease bone resorption and also stimulate bone-building osteoblast activity and new bone formation in women with osteoporosis.

Recent large-scale, double-blind, placebo-controlled trials using the ranelic acid salt of Strontium have proven that Strontium supplements combined with calcium and vitamin D dramatically build bone mass, reduce the incidence of spinal deformities, and slash hip fracture risk compared to calcium and vitamin D alone.

• In a three-year trial involving 1649 women with postmenopausal osteoporosis, women receiving only calcium and vitamin D suffered the loss of 1.3% of their lower spinal BMD, while women also taking Strontium supplements at 680 milligrams per day increased their bone mass by an astounding 14.4% at the spine, and by 8.3% in the large bone at the top of the thigh.
• Women taking Strontium supplements were spared 41% of the new vertebral fractures that befell women taking calcium and vitamin D alone.

A second trial showed that Strontium supplements are just as effective against hip fractures. In this study, 5091 postmenopausal women with osteoporosis received calcium and vitamin D supplements, along with 680 mg of Strontium or a dummy pill. Taking Strontium supplements allowed women to avoid 41% of the hip fractures suffered by women taking only calcium and vitamin D. Although it was a three year study, the benefit began to manifest in just a year and a half.

A third trial shows that Strontium supplements can also protect the bones of women who do not yet have osteoporosis. In this study, 160 women in early
menopause, but without osteoporosis, took either calcium supplements alone, or calcium plus Strontium for two years.

• Women taking calcium alone were subjected to a loss of 0.5% of their lumbar bone mass per year, but women taking calcium plus Strontium (340 milligrams daily) experienced a 0.66% gain annually. The net benefit to Strontium users was 2.46% more lumbar bone mass by the end of the trial. Lower doses (42.5 or 170 milligrams of elemental Strontium) were not effective.

• Likewise, women adding Strontium to their supplement regimen experienced gains of 2.46% in bone mass at the neck of the femur, and 3.21% in the hip as a whole, compared to women taking calcium alone.

• Strontium users’ lab tests revealed significant increases in markers of bone formation, with no change in markers of bone resorption.

Unlike the range of side-effects that accompany antiresorptive drugs, no clinical side-effects have ever been reported that could be clearly attributed to Strontium. Transient changes in some laboratory tests have been observed in some studies but not others, and in one study people experienced no symptomatic, chemical, or physiological signs of toxicity after taking Strontium supplements for as long as four years, at two and a half times the dose of elemental Strontium that’s used in today’s clinical trials. In studies where laboratory changes have been observed, none have been associated with real-world clinical problems, and most have reversed themselves over the course of the study.

Calcium and Strontium: the Dynamic Tension

Calcium and Strontium can both play key roles in the health of your bones – if you use them properly. On the one hand, animal studies suggest that Strontium is not effective, and may even be counterproductive, if your calcium intake is not adequate. Current “official” recommendations suggest an intake of 1000 milligrams of calcium for younger adults, and 1200 milligrams for people over the age of 50. Some evidence suggests that a still higher intake (1300-1600 milligrams) of calcium is more effective for lowering fracture risk in the elderly. But remember that these numbers are your total calcium need. The more calcium you get in your diet, the less you need from supplements.

At the same time, however, it’s important not to take your Strontium supplement at the same time as your calcium supplements. This is because calcium and Strontium use the same pathways for absorption in the intestinal tract, so that swallowing a calcium supplement along with your Strontium can dramatically reduce absorption. So obviously, putting
Strontium and calcium in the same pill is a recipe for bone health disaster, in which you don't get the benefits of either nutrient!

The best protocol – and the one used in the most recent clinical trials – is to take your Strontium either three hours after your last meal of the day, or one hour before breakfast in the morning, or both. Because studies suggest that one last dose of calcium just before retiring can help prevent excessive resorption of bone overnight, it may be best to take all of your Strontium before breakfast, leaving you free to take a calcium supplement just before you go to bed.

Like the Strontium carbonate crystals (strontianite) from which it was first isolated, Strontium’s role in bone health has long been hidden in obscurity. But its strength has allowed it to endure, waiting for the day that it could emerge and reveal its power.

References

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The usefulness of strontium as an adjuvant to calcium in the remineralization of the skeleton in man.
Shorr E, Carter AC.

The results are described of a current investigation of the possible value of Sr as an adjuvant to Ca in the remineralization of the depleted skeleton in a variety of derangements of bone metabolism in man. Sr, in amounts sufficient to achieve significant retention of this element, has been well tolerated over several years of administration and without toxic effects. The retention of Sr is augmented by agents such as Vitamin D, estrogens, and androgens in a similar manner to Ca. When given in equal amounts, Sr is found to have certain distinct advantages over Ca for the remineralization of the skeleton. There is greater retention of Sr; and when the ceiling for Ca retention has been reached, the addition of Sr results in a retention of the latter. Hence, the deposition of Ca plus Sr is greater than the total Ca storage which can be achieved with Ca alone, regardless of Ca intake and auxiliary therapy. This combination should hasten the rate of remineralization of the skeleton as compared with Ca alone, an inference that is supported by the objective and subjective improvement observed under the combined regime. Maximal retention of Sr and Ca is achieved with the assistance of three auxiliary agents-Vitamin D, estrogens and androgens. Finally, the usefulness of Sr as a means of measuring mineral salt turnover in bone is suggested.

The effect of strontium lactate in the treatment of osteoporosis.
McCaslin FE Jr, Janes JM.

A study has been made of the case records of 32 patients treated for osteoporosis with strontium lactate, or strontium lactate with hormones, and then traced for various periods with repeated physical and roentgenographic examinations. Marked subjective improvement was experienced by 84 percent of the patients. Although the mechanism of action of strontium lactate in the treatment of osteoporosis remains to be elucidated, the therapeutic value of the drug appears to be established.

Histomorphometry of Bone Changes in Stable Strontium Therapy
Marie PJ, Skoryna SC, Pivon RJ Chabot G, Glorieux FH, Stara JF

Previous studies in rats have shown that low dosage of stable Sr2+ added to drinking water stimulates bone formation (7). Low doses of Sr2+ are currently used in treating metastatic bone cancer and osteoporosis (17). In the present paper, histomorphometric changes in transiliac bone biopsy material obtained in six patients, before and after 6 months of Stable Strontium Therapy (SST), are reported. All cases had clinically diagnosable osteoporosis. Sr2+ was administered as Sr carbonate, 600-700mg per day. No side effects were observed. Serum Sr:Ca ratio changed from pre SST of 1:1250 (〓) to 1:12 (〓5) post SST. Bone Sr:Ca ratio changed from 1:1276 (〓) to 1:166 (〓). Mean bone Ca2+ increased slightly but not significantly. Following SST, all histological parameters of bone formation increased, while bone resorption remained unchanged. An increased amount of osteoid tissue was observed, associated with stimulation of bone formation at the tissue level. No significant elevation of trabecular bone volume was found. Clinical observations suggest that the response to SST is better in younger (post-menopausal) cases than in senile osteoporosis. Long-term studies are necessary to determine whether the increase in trabecular calcified bone volume observed in rodents, following low dosage of Sr2+, also occurs in human subjects.

Preclinical and clinical studies have demonstrated that strontium ranelate (S12911) is a bone forming agent with anti-resorptive activity which increases bone mass and bone biomechanical resistance. A dose-ranging clinical study (STRATOS) has determined the 2g-daily dose to be the optimal dose in increasing lumbar BMD.

A randomised double-blind, placebo controlled, phase 3 clinical trial (SOTI study), involving 72 centres in 12 countries, was designed to assess the anti-vertebral fracture efficacy and safety of S12911 (2g/d orally) in women with postmenopausal osteoporosis over a 3 year period. Patients also received daily calcium and vitamin D supplements. The patients (n = 1649) were included in two parallel groups [age: 69.7 (7.3); Lumbar BMD: 0.73 (0.12); mean (SD)], 87.5% of them having at least one prevalent vertebral fracture (2.2 prevalent VF per patient).

A 41% reduction in relative risk (RR) of experiencing a first new vertebral fracture (semi-quantitative assessment) was observed with strontium ranelate throughout the 3 year study compared to placebo, 139 patients with VF versus 222 respectively (RR = 0.59, 95%CI [0.48;0.73], p<0.001) in the intent-to-treat population. These results have also been confirmed when combining both diagnostic methods (semi-quantitative + quantitative) for incident vertebral fracture. Bone specific alkaline phosphatase increased while serum CTX decreased. The lumbar BMD increased in the treated group when compared to the placebo group (+11.4% versus △% respectively, p<0.001). S12911 was well tolerated without any specific adverse event and no deleterious effects were observed on rates of non-vertebral fractures. We infer that strontium ranelate is a new orally effective and safe treatment of vertebral osteoporosis with a unique mechanism of action.

The effects of strontium ranelate on the risk of vertebral fracture in women with postmenopausal osteoporosis.

BACKGROUND: Osteoporotic structural damage and bone fragility result from reduced bone formation and increased bone resorption. In a phase 2 clinical trial, strontium ranelate, an orally active drug that dissociates bone remodeling by increasing bone formation and decreasing bone resorption, has been shown to reduce the risk of vertebral fractures and to increase bone mineral density. METHODS: To evaluate the efficacy of strontium ranelate in preventing vertebral fractures in a phase 3 trial, we randomly assigned 1649 postmenopausal women with osteoporosis (low bone mineral density) and
at least one vertebral fracture to receive 2 g of oral strontium ranelate per day or placebo for three years. We gave calcium and vitamin D supplements to both groups before and during the study. Vertebral radiographs were obtained annually, and measurements of bone mineral density were performed every six months. RESULTS: New vertebral fractures occurred in fewer patients in the strontium ranelate group than in the placebo group, with a risk reduction of 49 percent in the first year of treatment and 41 percent during the three-year study period (relative risk, 0.59; 95 percent confidence interval, 0.48 to 0.73). Strontium ranelate increased bone mineral density at month 36 by 14.4 percent at the lumbar spine and 8.3 percent at the femoral neck (P<0.001 for both comparisons). There were no significant differences between the groups in the incidence of serious adverse events. CONCLUSIONS: Treatment of postmenopausal osteoporosis with strontium ranelate leads to early and sustained reductions in the risk of vertebral fractures.

Mechanisms of action and therapeutic potential of strontium in bone. 
Marie PJ, Ammann P, Boivin G, Rey C.

The processes of bone resorption and formation are tightly governed by a variety of systemic and local regulatory agents. In addition, minerals and trace elements affect bone formation and resorption through direct or indirect effects on bone cells or bone mineral. Some trace elements closely chemically related to calcium, such as strontium (Sr), have pharmacological effects on bone when present at levels higher than those required for normal cell physiology. Indeed, strontium was found to exert several effects on bone cells. In addition to its antiresorptive activity, strontium was found to have anabolic activity in bone, and this may have significant beneficial effects on bone balance in normal and osteopenic animals. Accordingly, strontium has been thought to have potential interest in the treatment of osteoporosis. This review summarizes the mechanisms of action of strontium on bone cells, the evidence for its beneficial effects on bone mass in vivo, and its potential therapeutic effects in osteopenic disorders.

Prevention of early postmenopausal bone loss by strontium ranelate: the randomized, two-year, double-masked, dose-ranging, placebo-controlled PREVOS trial. 
Reginster JY, Deroisy R, Dougados M, Jupsin I, Colette J, Roux C.
Early postmenopausal women (n = 160) were randomised to receive placebo or strontium ranelate (SR) 125 mg/day, 500 mg/day or 1 g/day for 2 years (40 participants per group). All participants received calcium 500 mg/day. The primary efficacy parameter was the percent variation in lumbar bone mineral density (BMD), measured using dual-energy X-ray absorptiometry. Secondary efficacy criteria included hip BMD and biochemical markers of bone turnover. At month 24, SR 1 g/day significantly increased lumbar BMD compared with placebo [mean (SD) +5.53% (5.12); p<0.001] for measured values and [mean (SD) +1.41% (5.33%); p<0.05] for values adjusted for bone strontium content. The annual increase for adjusted values was +0.66% compared with -0.5% with placebo, with an overall beneficial effect after 2 years of about 2.4% with SR 1 g/day relative to placebo. There were no other significant between-group differences in adjusted lumbar BMD. Femoral neck and total hip BMD were also significantly increased at month 24 with SR 1 g/day compared with placebo [mean (SD): +2.46% (4.78) and +3.21% (4.68), respectively; both p<0.001]]. SR 1 g/day significantly increased bone alkaline phosphatase at all time points (p<0.05) compared with baseline and between-group analysis showed a significant increase, compared with placebo, at month 18 (p = 0.048). No effect on markers of bone resorption was observed. SR was as well tolerated as placebo. The minimum does at which SR is effective in preventing bone loss in early postmenopausal non-osteoporotic women is therefore 1 g/day.

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