Strontium: The First Bone Builder

The Rediscovery of a forgotten Bone Health Mineral

We sometimes think of our bones as being like the columns of an ancient Greek building: rigid "pillars of strength" that are built in our youth but are then slowly worn away by the forces of time. But in fact, bone is a dynamic, living tissue, like any other tissue in your body. While they seem unchanging, healthy bones are actually in a continuous process of remodeling and renewal. Old bone is torn down (resorbed) by one class of specialized cells (osteoclasts), while another kind of bone cell (osteoblasts) is responsible for building up new bone tissue to replace it. The constant balance of resorption and new bone formation allows for the replacement of old, stressed, damaged tissue with healthy new bone, and also lets the body adjust its skeletal structure when it is subjected to new or changing stresses.

But as we age, the creative equilibrium which governs the forces of remodeling becomes disrupted. In women, this is most obvious at menopause. Because the hormone estrogen suppresses the tearing down of bone by osteoclasts, the sudden reduction in the body's estrogen production causes a dramatic increase in bone loss.

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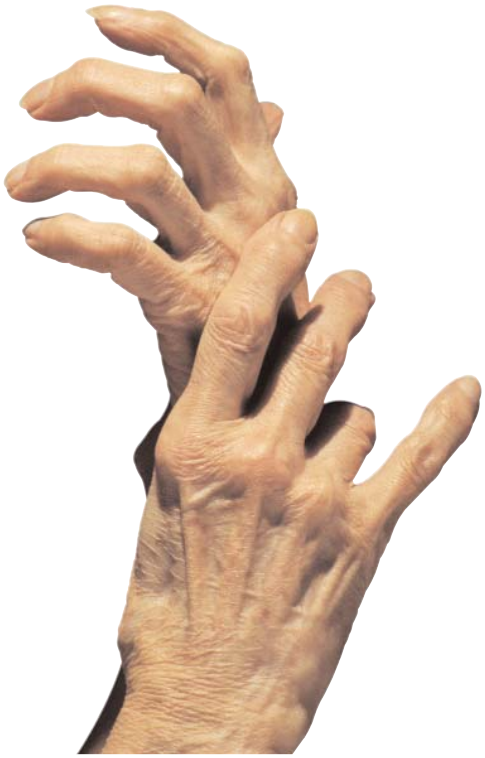
But while the process of bone loss accelerates suddenly in women at menopause, it actually begins when we're still seemingly in our physical prime. While menopause brings with it a ravaging increase in bone resorption, there is also a much less obvious slowdown in the formation of new bone which starts to take hold much earlier, in men as well as women – in our twenties, in fact.[1] At this time, while bone formation is reduced, bone resorption is still under control, so the result is a gradual, almost imperceptible loss of bone mass over the course of the following decades. When the menopausal surge in bone resorption kicks in on top of decades of reduced bone formation, you get the ruinous degradation of bone that we call osteoporosis.

All of the existing, approved drugs on which mainstream medicine relies to treat osteoporosis – including bisphosphonates like alendronate (Fosamax®), hormone replacement therapy, selective estrogen receptor modulators (SERMs, such as raloxifene (Evista®)), and calcitonin (Calcimar® or Miacalcin®) – are "antiresorptive agents." That is, they are all substances that work by slowing down runaway bone resorption.[2-5] Even calcium and vitamin D supplements have an antiresorptive mechanism of action, keeping the body's stores of calcium at levels high enough to keep calcium from being leeched out of your bones by parathyroid hormone. They don't actually increase the body's ability to build new bone.[5]

In other words, these drugs – as well as calcium and vitamin D – don't actually build bone at all. They just keep old bone from being destroyed. And not only that. Believe it or not, recent research has shown that, despite what your bone mineral density (BMD) reading might say, real bone mass continues to fall while you take Fosamax® and other antiresorptive drugs. When you take antiresorptive drugs, the increase in BMD reported by DEXA machines is not caused by an increase in true bone tissue, but by increased mineralization of the tissue you're left with … even as the amount of tissue continues to decline.[6,7]

There are two problems with this approach. The first is the issue of bone "quality." All existing osteoporosis drugs result in bone which is, on average, made up of older, poorer-quality material. Because this older bone tends to be more brittle, the overall architectural integrity of the bone is decreased.[8-10]



But there's an even more fundamental issue at stake. Conventional osteoporosis treatments are one-sided, halfway measures. That is, while bisphosphonates, HRT, SERMs, and the like are effective in treating one part of the osteoporosis problem (excessive bone resorption), they fail to address the other underlying factor in the disease process: the age-related decline in bone formation. A doctor who treats osteoporosis with an antiresorptive drug is like a sports coach so obsessed with defensive strategy that he has his team spend all of their time learning to keep their opponents from scoring, without ever helping them learn to score goals of their own.

To fully address the underlying causes of low bone mass, then, we need an agent which will not just prevent bone resorption, but also boost the body's ability to create new bone tissue. In fact, pharmaceutical companies have been working for some time to develop new drugs that can correct the weakening of the body's bone-building capacity. Such drugs are called "anabolic agents" for bone tissue.[3,4,7] The first fruits of their labors – a drug made by modifying the structure of a fragment of the body's parathyroid hormone (brand name Forteo®) – is expected to hit North American drug stores within a year.

But Nature already has an effective combination bone anabolic/anti-resorption nutrient in her medicine chest. In fact, she's had one since time immemorial, and it's been known to support the health of the skeletal system for over fifty years. But until recently the research supporting its powers was incomplete, and its mechanism of supporting bone health was not understood – so its enormous importance as a bone health nutrient was overlooked.

But all of that has changed in the last decade. Today, in the opening years of the twenty-first century, this nutrient is about to create a revolution in our ability to preserve – and even to restore – the youthful structure and function of bone tissue. That nutrient is the mineral Strontium.

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Two Centuries of Obscurity

Strontium was first discovered in 1790, when the Scots-Irish chemist Adair Crawford discovered a distinct mineral species mixed in with the barium crystals commonly found in ore around the Scottish town of Strontian. While some patent medicines using Strontium were sold from the late nineteenth century until the mid-50s, none of them was used for bone health, and none was ever supported by hard scientific evidence. Strontium was also used in making fireworks, paints, and TV picture tubes … a radioactive form of Strontium (90Sr) gained a certain notoriety because it was contained in nuclear fallout … and strontium was used as a delivery vehicle in some cancer treatments. But outside of these narrow fields, Strontium seemed doomed to obscurity. Certainly, few suspected that the mineral was important to human health as a nutrient, in the same sense as calcium, iron, iodine, or other essential minerals.

That began to change in the 1940s, when research began to suggest that Strontium was in fact vital to the development of a healthy skeletal system. One hint was the finding that the human body actually contains a fair amount of the mineral – and that 99% of it is concentrated in the skeleton. Scientists found that giving animals Strontium in their diets increases the buildup of bony dentin tissue in their teeth,[11] and that healthy human teeth contain more Strontium than do teeth with cavities.[12] In fact, areas with more Strontium in the water were later found to have a lower incidence of dental caries[13] – a finding which was to be reinforced by the findings of at least eight more studies over the course of the next few decades.[14]

More significantly, a French researcher reported that a lack of Strontium in the diet causes defective mineralization of the bones and teeth in rats and guinea pigs.[15,16] This suggests that mammals need Strontium for normal development, and suffer from Strontium deficiency if they don't get the mineral in their diets – just as they would if their diets lacked calcium, magnesium, or zinc.

Strontium supplements improve the retention of calcium, phosphorus, and protein in women with menopausal osteoporosis.

Indeed, calcium and Strontium are almost always found together in natural foods, because plants, animals, and people absorb and store the two minerals in similar ways.[17-19] Therefore, when studies find that calcium-rich foods support bone health, they may actually be revealing the bone-health properties of getting both minerals in the diet.

The First Clinical Trials

Even in those early days, some scientists were convinced that there was enough evidence for Strontium as a bone health nutrient to start doing some small-scale trials in people with osteoporosis. In fact, doctors Ephraim Shorr and Anne Carter at the Russell Sage Institute of Pathology began an open trial of Strontium for osteoporosis as early as 1942,[20] citing as their inspiration the even earlier clinical experience of a German physician, who had used Strontium to restore mineralization of the bones in children with bone loss caused by calcium deficiency.[21] In the Russel Sage Institute study, people with osteoporosis took a 1700 milligram (elemental) Strontium supplement daily (in the form of Strontium lactate), usually for three to four months but sometimes for as much as four years, along with a diet carefully controlled for its calcium, protein, and phosphorus content.

Several important observations were made in this study. The first was that Strontium supplements improve the retention of calcium, phosphorus, and protein in women with menopausal osteoporosis, as well as in people with osteoporosis resulting from other causes. In fact, these scientists found that when intake of calcium got high enough that retention plateaued (so that eating more calcium resulted in no more calcium being retained by the body), adding a Strontium supplement could break the glass ceiling, causing a further increase in calcium retention.

More important were the observations they made of Strontium's effects on the disease. In the 1940s, the diagnostic technology we use today to test bone mineral density, bone formation, bone resorption, or bone quality didn't exist. But Shorr and Carter's studies[20] revealed that subjective symptoms and objective performance tests all improved when people with osteoporosis took Strontium supplements. Women and men experienced relief from their bone pain, and began taking up more physical activity – and their progress more strongly reflected the total retention of calcium and Strontium combined than their retention of calcium alone.

It was clear that Strontium's effects on calcium absorption and retention alone weren't enough to explain why the Russel Sage Institute patients were improving so much. But what could underlie the Strontium effect? One attendee at a scientific conference raised the possibility that the results meant "that strontium stimulates osteoblastic activity." As a careful scientist, Dr. Shorr refused to engage in wild speculation; none the less, he responded that while "We have to remain uncertain for the present as to the mechanisms … Osteoblastic activity might be stimulated".[22] But it would be fifty years before science would have the tools to test this guess – and as we shall see, to prove it right.

In the meantime, a second human trial using Strontium supplements in men and women with osteoporosis was performed by physicians at the Mayo clinic.[23] Over the course of five years, a number of their patients with osteoporosis took supplemental Strontium (again as the lactate, and again at a 1700 milligram elemental daily dose), this time for periods of three months to three years. A consistent pattern emerged in the 28 women and four men who fully completed the study. Whether they had begun the study only mildly affected by osteoporosis, or severely affected but mobile, or completely bedridden, all

people suffering with osteoporosis experienced improvements in their mobility after taking Strontium supplements. "Marked" improvements in subjective symptoms were experienced by 84% of Strontium supplement users, with the remaining people still obtaining moderate improvements. "No patient failed to improve subjectively" on Strontium, the investigators reported.

The effect of Strontium was also evaluated using X-rays; unfortunately, technical factors surrounding early X-ray methodology and equipment, combined with the relatively subjective nature of evaluating them, resulted in their being no consensus among the six evaluators as to whether most X-rays showed improvement.[23] Indeed, it was exactly these kinds of difficulties with simple X-rays that created the push for clearer, less subjective, and much more precise results – a demand that ultimately drove the development of DEXA technology. But based on their clinical results, the Mayo Clinic physicians concluded that "the therapeutic value of [Strontium] appears to be established." Yet, like Shorr and Carter before them, they couldn't say just what it was about the supplement that caused the results experienced by their patients.

Strontium supplementation increased the parameters of bone formation in osteoporosis patients.

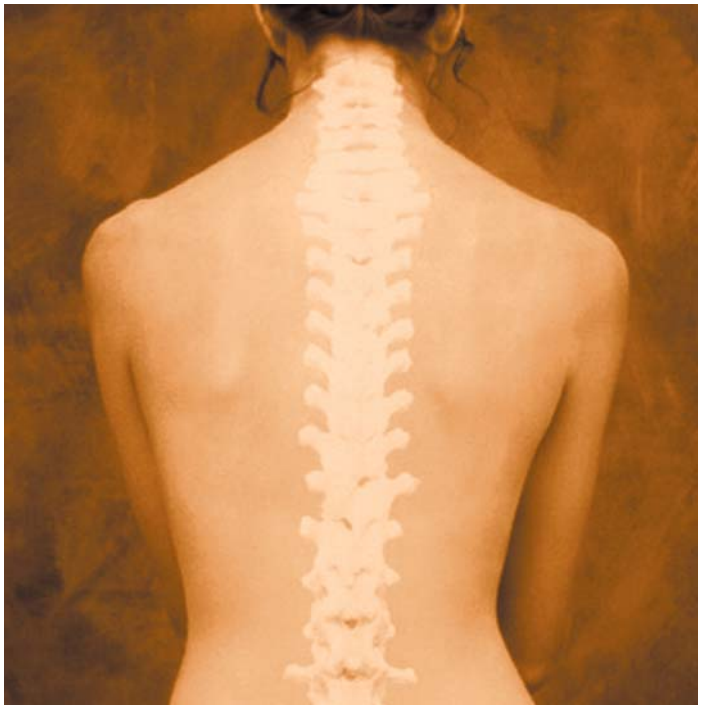
It would again be decades before more human research on Strontium's role in bone health would be tested – this time, in the early 1980s, by McGill University's Dr. Stanley Skoryna. Providing Strontium supplements (both Strontium carbonate and Strontium gluconate)) to 142 people with a range of bone health issues (including people with osteoporosis, bone loss due to not disease-related weight loss, nutrient malabsorption from liver disease, and cancer victims whose disease had spread to their skeletons),[24,25] Skoryna showed that "patients treated with SST [stable Strontium therapy] have less disability than they would have had they been untreated" as judged "from radiologic findings and physical examination".[24]

Combined with the slow trickle of animal studies which had continued to document the nutrient's skeleton-strengthening powers over the ensuing years, these results gave Skoryna the ammunition he needed to spearhead a new human study of Strontium's potential in osteoporosis. In a small pilot study involving just six people diagnosed with osteoporosis,[26] his team of researchers found that, using Strontium carbonate at a dose of 600 to 700 mg daily for six months, Strontium supplementation increased the parameters of bone formation in osteoporosis patients: the surface covered by osteoblasts increased by 120.8%, and the rate of new bone formation jumped by an astounding 172.4%!

Women taking Strontium supplements were spared 41% of the new vertebral fractures.

This result was unheard of. Could Strontium actually be increasing the formation of new bone in these patients? Skoryna's results were not "gold standard" proof – there were too few patients, and no control group was used for comparison – but with these new findings the scientific community was forced to take notice of Strontium's potential.

Finally, then, European scientists launched the first rigorously scientific studies to evaluate Strontium's bone-building abilities.[27,28] Moving beyond the animal studies and small, uncontrolled pilot trials, these researchers initiated the large-scale, double-blind, randomized, placebo-controlled human studies that have today conclusively demonstrated the safety and effectiveness of Strontium as a mineral to build bones.



Proof Positive

The first of these new clinical trials[29] involved 353 women with osteoporosis and at least one previous fracture in the vertebrae of their spines. As in the following trials, this study used the ranelic acid salt of Strontium (ranelic acid is an almost entirely unabsorbed, unmetabolized, and inactive synthetic molecule which plays no role in Strontium's effects

on bone cell metabolism[30]). The women quit any existing osteoporosis drugs, and for the next two years took calcium and vitamin D3 supplements, along with either a Strontium supplement or a look-alike dummy pill (placebo). The Strontium supplements came in three strengths, providing 170, 340, or 680 milligrams of elemental Strontium a day; however, no one – not the women taking the supplements, nor the doctors who cared for them and evaluated their progress – knew who was getting a placebo and who was taking the real thing – or at what dose.

Two years later, the women's results spelled out a testament to Strontium's power. Strontium supplements had increased the women's bone mass – and the more Strontium they took, the more bone mass they gained. Women taking calcium and vitamin D3 alone (but whose Strontium supplements were dummy pills) still gained some bone mass in their lower spines: about 0.5% per year over the course of the trial. But women taking real Strontium experienced much greater gains: 1.35% when taking 170 milligrams of Strontium a day, or 1.65% at 340 milligrams, and a remarkable 2.97% increase in bone mineral density at a dose of 680 milligrams of Strontium.

Even more striking were the results in the hip bone. Despite the calcium and vitamin D3 supplements they had been taking, women who did not take supplements of Strontium actually lost 0.57% of the bone mineral density in their hips each year of the study.[29] (While some may find that result surprising, the failure of calcium to stop bone loss is actually to be expected: see "Choosing the Right Calcium" in the article, "Bone Building Basics" in this issue of Advances).

By contrast, women who took Strontium supplements even gained bone mass in their hips. And again, the more Strontium, the more bone mineral density they gained. At 170 milligrams of elemental Strontium, women gained 0.24% more hip bone mass a year. At 340 milligrams, the annual gain was 1.41%. And again, the most impressive results were seen at the highest dose: a 680 milligram Strontium supplement supported a gain of 3.05% in hip bone mass per year over the course of the trial. Of even greater significance, the trial also reported that women taking Strontium supplements suffered only 56% as many new vertebral deformities, compared with women taking calcium and vitamin D3 alone.[29]

A second, larger, and even more ambitious study was initiated to test an even more important parameter: Strontium's effects on risk of fractures. In this study,[31] 1649 women with postmenopausal osteoporosis again took calcium and vitamin D3 supplements, this time for three years. But in addition, one group of women were given "strontium" placebos, while the other group took a 680 milligram elemental Strontium supplement – without anyone knowing which was which.

As in the previous study, Strontium boosted bone mineral density. Even on this parameter, the news was exciting: while women receiving only calcium and vitamin D3 suffered the loss of 1.3% of their lower spinal bone mass over the course of this large three year study, women taking Strontium supplements increased their bone mass by an astounding 14.4%.[31] To put this result in perspective, the most powerful of the bisphosphonate drugs (alendronate/Fosamax®) increases BMD at this site by no more than 5.5%, even when combined with other therapies.[32-34]

But what was new about this study was that it was large and long-term enough to evaluate fracture risk. And Strontium proved itself. At the beginning of the study, 87.5% of the women had at least one vertebral fracture. In fact, the average woman had 2.2 such fractures. Yet using either one of two analysis methods, women taking Strontium supplements were spared 41% of the new vertebral fractures suffered by women taking calcium and vitamin D3 alone over the course of the trial![31] And unlike the range of side effects that accompany bisphosphonates and other antiresorptive drugs, no side effects were reported that could be attributed to Strontium.

Strontium not only inhibits the excessive breakdown of existing bone, but also powerfully boosts the body's ability to build new bone.

And that's not all. A separate five-year trial is also underway, designed specifically to test the effects of 680 milligrams of elemental Strontium in reducing the incidence of fractures other than fractures of the spine, such as broken hips and ribs. In this study, 5091 postmenopausal women with osteoporosis are taking calcium and vitamin D3 supplements, along with 680 mg of elemental Strontium or a dummy pill. A preliminary analysis of this trial[35] has found that Strontium supplements allow women to avoid 41% of the hip fractures suffered by women taking only calcium and vitamin D3. Although it is planned to be a three-year study, the benefit began to manifest in just a year and a half.

An additional trial shows that Strontium supplements can also protect the bones of women who do not yet have osteoporosis. In this study,[36] 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 (elemental) 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.[36]

The Only True Bone-Builder

With the new wave of research into Strontium, new techniques of molecular investigation have begun to shed light on the mysteries of the mineral's effects on bone. And this new research has confirmed what Dr. Shorr had merely guessed in 1950,[22] and what Skoryna's research had appeared to show in the early 1980s: namely, that Strontium not only inhibits the excessive breakdown of existing bone, but also powerfully boosts the body's ability to build new bone (see Figure 1).

One basis for this conclusion has been studies in experimental animals, which have shown that the actual volume of their bones increases when they are given Strontium-supplemented diets.[37-39] In one especially revealing study,[40] scientists removed the ovaries of three groups of laboratory animals, as a way to simulate menopause's low-estrogen hormonal environment. The researchers then measured the ability of estrogen replacement therapy or a Strontium-supplemented diet to prevent the loss of bone volume in their tibias (the bone that runs from the knee to the ankle). They found that, while estrogen replacement prevents the loss of bone volume caused by ovariectomy, Strontium supplements actually boost bone volume to a level 30 to 36% greater than it is before the onset of "menopause"! The loss of bone ash and bone mineral content caused by the mock-menopause was also prevented by Strontium.[40]

These same studies have revealed the underlying reasons for Strontium's powerful effects on bone volume. Strontium supplements cause an increase in the area of bone covered by bone-building osteoblasts, along with decreases in the number of bone-dissolving osteoclasts in bone tissue and the amount of surface that they occupy.[37] Chemical and physiological signs of new bone formation are also boosted by Strontium supplements.[39] The pseudo-menopause created by the removal of the ovaries in adult mice causes an increase in the rate of bone resorption and a decrease in the rate of new bone formation; Strontium prevents these changes.[41] Parallel effects have been observed in monkeys given a Strontium-supplemented diet.[42]

More precise details have emerged from looking at Strontium's effects on cultured bone tissue – a model that lets researchers directly study the growth, development, and activity of osteoblasts. Using this model, scientists have found that Strontium causes "baby" osteoblasts to multiply more quickly.[43] An increase in the synthesis of DNA is also seen in these cells, underlying the increased growth which Strontium stimulates.

With all of these new osteoblast recruits on hand, bone tissue cultures which are exposed to Strontium synthesize more bone matrix – the mineral-enriched collagen that forms the bedrock of bone tissue.[43] A similar model suggests that this is due to a direct increase in the formation of new bone collagen in Strontium-fortified bone tissue.[43]

The possibility that Strontium might merely be stepping in for calcium (which is in many ways metabolized very similarly to Strontium) can be ruled out, because the same amount of calcium has no effect on these parameters.[43] (There is also no such effect from ranelic acid, the inert acid salt to which Strontium has been bound in many of the more recent clinical trials.[30]) In fact, recent research appears to show that there is a receptor in the osteoblast which responds specifically to Strontium, and which is unaffected by calcium, aluminum, or other metallic elements.[50] This is consistent with the fact that, while calcium is needed for the building of new bone, it does not stimulate it (although an abundance of calcium does help to suppress bone teardown).[5] It also confirms the many other studies showing that conventional calcium supplements slow – but do not reverse – the age-related loss of bone mass (see "Bone Building Basics" in this issue of Advances).

Yet even at preventing resorption, Strontium's powers appear to outshine calcium's. Similar organ culture studies have found that Strontium reduces bone resorption at concentrations at which calcium has no effect.44 Strontium also prevents the resorption caused by excessive parathyroid hormone in this model.[45] And unlike bisphosphonate drugs,[46,47] Strontium doesn't kill existing osteoclasts; instead, it slows the rate at which immature osteoclasts develop.[44]

This one-two punch – the coming together, in one supplement, of strong bone anabolic and antiresorptive powers (see Figure 1) – creates the best of all worlds for total bone health. And indeed, animal studies have shown us that Strontium supplements don't just increase bone mineral density (as the clinical trials affirm happens in human Strontium users): they also report that bone strength is improved by Strontium, without an increase in brittleness or a negative impact on bone quality, even at extremely high doses[48] – unlike what's seen in the case of the lopsided approach of bisphosphonates and other exclusively antiresorptive drugs.

Strontium supplements not only decrease bone resorption, but also stimulate bone-building osteoblast activity and new bone formation in women with osteoporosis.

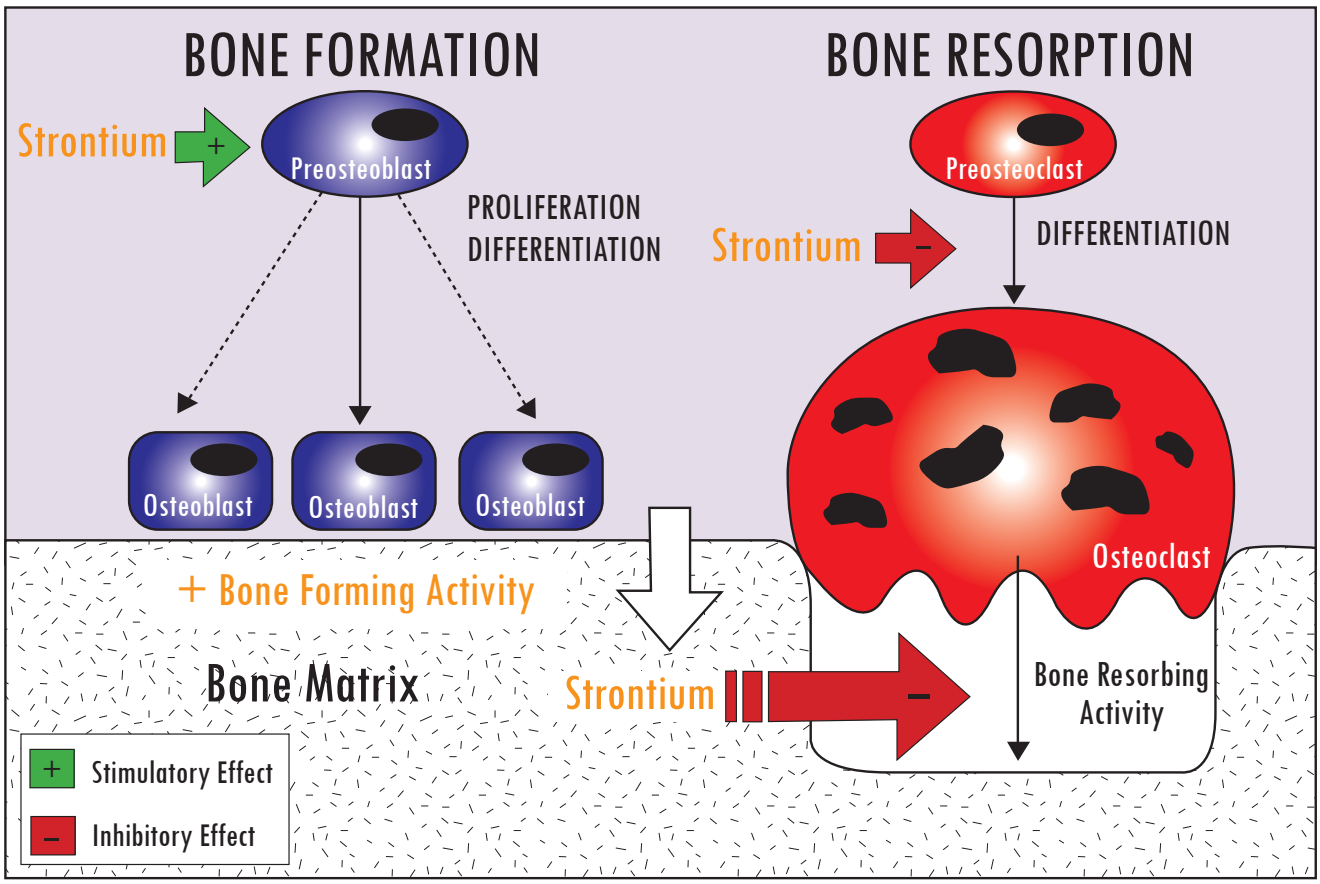
The animal evidence of increased formation of new bone is consistent with Dr. Shorr's early speculations about osteoblast activity,[22] and with the preliminary results seen in Dr. Skoryna's pilot study.[26] But the ultimate vindication of Strontium's bone-building powers has come from the new European Strontium trials. Instead of being caught between engaging in idle theorizing and performing invasive bone biopsies, the new trials have been able to take advantage of new, easily-performed blood and urine tests. 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.

By monitoring these tests in women taking Strontium supplements, these large-scale, double-blind trials provided evidence that Strontium supplements not only decrease bone resorption, but also stimulate bone-building osteoblast activity and new bone formation in women with osteoporosis.[29,31] By contrast, these same tests reveal that, while bisphosphonates, HRT, and other conventional treatments for osteoporosis do inhibit resorption, the activity of women's osteoblasts continues to fall when they take Fosamax.®[49]

Beyond "Osteoporosis"

Most of the human research on Strontium's effects on bone structure and function has focused on women with a disease: postmenopausal osteoporosis. But unlike a drug, which would treat a "disease" as such, Strontium's effects on bone health do not involve an alien molecule imposing itself on normal metabolic processes: instead, Strontium's effects are the results of its natural place in bone cell metabolism, as a nutrient in the diet. In fact, it now appears that there is even

Figure 1: Strontium both fights bone teardown and boosts the body's ability to form new bone. Redrawn from (47).



a specific receptor in osteoblastic cells that responds to strontium, and not to other minerals (such as calcium) or toxic metals (such as aluminum).[50]

Human studies have confirmed that the benefits of Strontium on bone health are not confined to people with some specific disease state: in addition to women with postmenopausal osteoporosis,[20-23,26,29,31] Strontium has also been found to benefit bone structure and function in bone lesions from metastatic bone carcinoma, degenerative weight loss, or liver disease,[24,25] "Morquio's disease" (also called mucopolysaccharidosis type IV, a genetic disorder which leads to a buildup of keratin sulfate in the bones, deforming them and leading to breaks in the vertebrae),[22] "Milkman's disease" (osteomalacia marked by multiple pseudofractures resulting from either the remodeling of previously-normal bone, or the repair of microscopic stress fractures, with osteomalacic bone tissue),[22] Cushing's syndrome,[20] nutritional osteoporosis,[21] childhood rachitic bone deformities caused by rickets,[51] and male senile osteoporosis[22,23,26] – and indeed, in menopausal women who have no bone disease at all.[36]

Similarly, while many recent animal experiments used experimental animal models of menopausal osteoporosis, studies performed on healthy animals with no bone disease – whether they are still developing or mature – have also confirmed the positive metabolic influence of high-dose Strontium supplementation on bone development when dietary calcium is adequate.[22,30,52]

Calcium and Strontium: the Creative 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.[22,30,52] 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.[53] 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.[30] 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! As well – and surprisingly – food intake has recently been shown to reduce Strontium absorption.

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.

Tomorrow's Solution – Today

Until recently, all that the drug companies had to offer osteoporotic women and others concerned about their bone health was a "choice" among several drugs that slow down resorption of bone, but which do nothing to restore youthful bone formation. This has recently changed: as we mentioned before, pharmaceutical multinationals are beginning to release new drugs with bone-anabolic effects, starting with teriparatide (Forteo®), a snipped-down version of human parathyroid hormone (PTH) that has been modified using biotechnology to include only the biologically active "business end."

But Strontium supplements are available here and now – and controlled clinical trials have proven that they provide powerful protection for bone structure and function, and are free of clinically-significant side effects not seen in the people taking placebos.[29,31,35,36] Indeed, as far back as the early studies at the Russell Sage institute, people experienced no symptomatic or 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 trials.[20] That's doubly good news to anyone waiting, with hunger and a touch of nausea, for the Fosamax® to get clear of her stomach, so that she can safely sit down to breakfast.

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Strontium Update

The research supporting the use of strontium for bone health continues to surface. Clinical trials have already clearly established the benefits associated with strontium. Newer research has mainly focused on understanding the underlying mechanism of action behind the anabolic effect of strontium on bones.

Strontium ranelate is a useful addition to the range of antifracture treatments available for the treatment of osteoporosis in postmenopausal women. Strontium is the only treatment proven to be effective at preventing both vertebral and nonvertebral fractures in women aged 80 and older.[1] Clinical trials have shown that strontium reduces fracture rates at all sites, including hip and vertebral areas which are the most common fracture areas associated with osteoporosis. Strontium also reduces the rate of height loss, prevents 48% of first-time vertebral fractures in osteoporotic women and frees patients of back pain.[2]

Mechanism of action

Animal and human studies have clearly shown that strontium increases the formation of new bone and reduces bone breakdown, which increases bone mineral density in a dose dependant manner.[3] Exactly how strontium does this at a cellular level was poorly understood until recently.

New research shows that strontium activates the calcium-sensing receptor (CaR), an effect that is central to the bone building action associated with strontium supplementation.[4,5,6] Calcium-sensing receptors (CaR) are receptors found throughout the body that are activated by the attachment of calcium. CaRs are present in bones, kidneys, the gastrointestinal system and several glands of the endocrine system - the constituents of the body central to the regulation of calcium levels. Calcium levels are also controlled by hormones such as calcitonin, vitamin D, and most importantly, the parathyroid hormone (PTH). Thanks to the CaR, the cells found in the parathyroid gland can monitor calcium levels. When calcium levels fall, PTH is released, increasing blood calcium levels. On the other hand, when calcium levels rise, the calcium binds to the CaRs on the parathyroid gland cells, which inhibits PTH secretion. For those affected by osteoporosis and bone demineralization, reducing parathyroid hormone secretion is very good, given that PTH stimulates osteoclasts and reabsorbs bones.

The CaR is also responsible for the release of calcitonin from the thyroid. Calcitonin inhibits the activity of osteoclasts and prevents the loss of calcium in the urine.[7]

CaRs are also present on osteoblastic cells. This contributes directly to the anabolic effects of calcium on bones. When calcium attaches to the CaR on osteoblasts, the cells become more active and start depositing calcium in bones - effectively building bone.

Research has shown that strontium can also attach to the CaR, which partly explains the anabolic effects of strontium on bone.[8] This means that strontium increases the proliferation of osteoblasts by activating the genes necessary for that proliferation. Strontium also prevents the release of PTH from the parathyroid gland and increases the production of calcitonin.

This may seem complicated but the effects of strontium are really quite simple. Strontium binds to the calcium-sensing receptor (CaR) - the receptor responsible for the monitoring of calcium levels in the blood. Blood calcium levels must be monitored closely because calcium levels affect the nervous system and influence blood clotting. Any drastic changes in the blood calcium levels would have dire consequences. When strontium or calcium blood levels increase, CaRs are activated and the body starts to clear calcium from the blood by increasing the amount that is deposited in bones and by reducing the amount that is extracted from bones. This explains why the activation of the CaRs increases osteoblastic activity while simultaneously reducing osteoclastic function. This also explains the bone building effects of strontium as they relate to the CaR.

Studies in animals with genetic defects leading to the improper expression of the CaR, have shown that strontium can still induce osteoblastic differentiation (although this ability is significantly attenuated). This indicates that strontium can increase bone mineralization through another receptor or via different mechanisms.
Other researchers found that strontium activates cyclo-oxygenase 2- mediated prostaglandin E(2) production.[9] Prostaglandin E(2) has an anabolic effect on bone and is known to stimulate bone formation in vivo.[10]

Strontium also reduces bone breakdown by upregulating osteoprotegerin, a cytokine that is also known as the osteoclastogenesis inhibitory factor because it inhibits the differentiation of macrophages into osteoclasts. Osteoprotegerin prevents the differentiation of osteoclast precursors into mature osteoclasts thereby reducing bone breakdown.[11]

What is also extremely interesting is that new research has shown that the effects mediated by strontium chloride and strontium ranelate are exactly the same. This led researchers to express their results in terms of elemental

strontium[12] - a clear indication that the effect of strontium on bone is not related to ranelic acid but comes directly from strontium itself.

Compliance is often poor for therapies meant to prevent osteoporotic fractures. This is partly due to the fact that osteoporosis is usually asymptomatic but also because changes in bone mineral density take a long time to be noticed. A recent study reported that for most patients, a daily therapy that is associated with minimal inconvenience is preferred to a weekly or monthly therapy that is slightly more inconvenient.[13] This suggests that the compliance for the supplementation with strontium should be good, since strontium is a daily therapy with minimal inconvenience.

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