VOLUME 3 • ISSUE 4

ADVANCES
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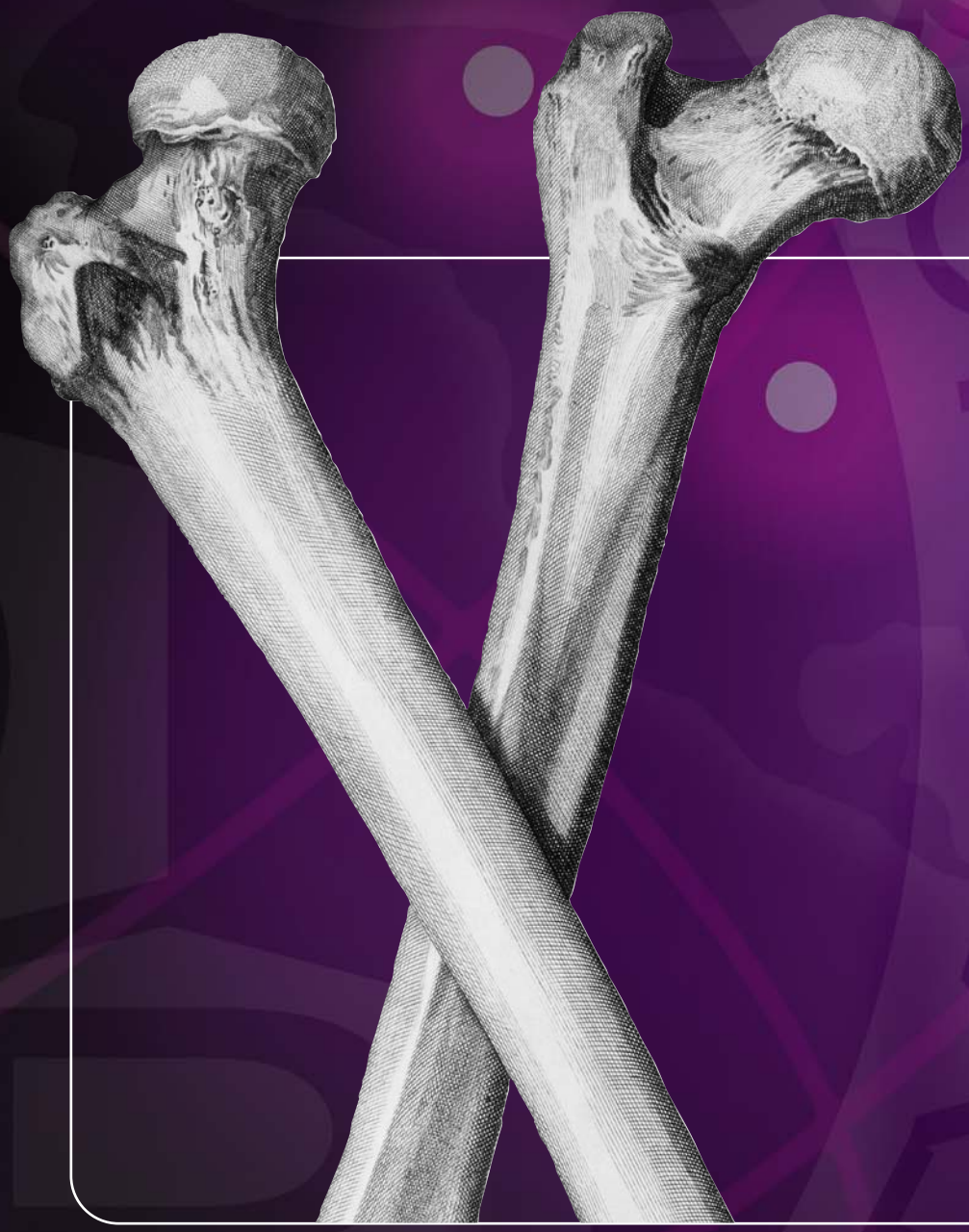

Bone Health

The Rediscovery of a Forgotten Bone Health Mineral

Questions and Answers about Bone Health Supplements

Bone Building Basics

research-driven botanical integrative orthomolecular breakthrough

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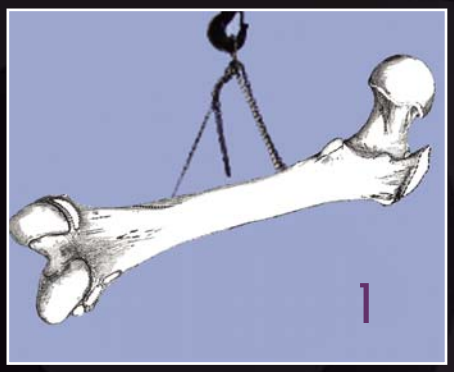

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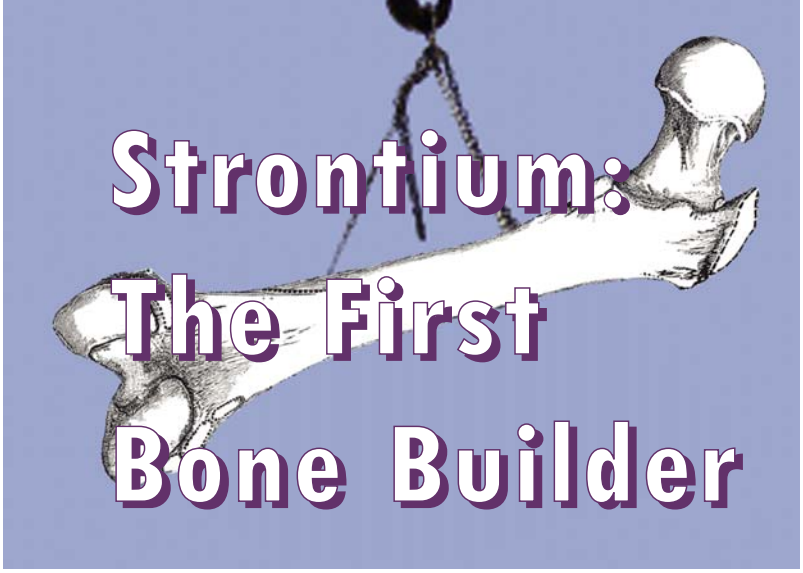


Strontium: The First Bone Builder

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.

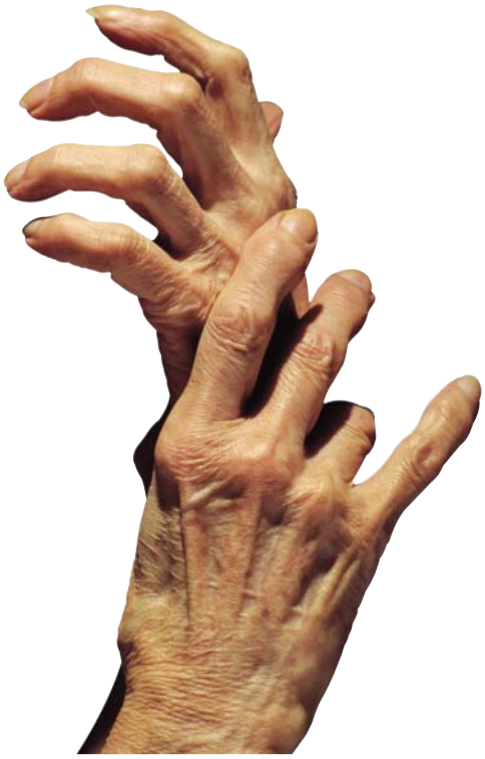
These drugs –
as well as calcium and vitamin D –
don't actually build bone at all.

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.

We need an agent which will not just prevent bone resorption, but also boost the body's ability to create new bone tissue.

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.

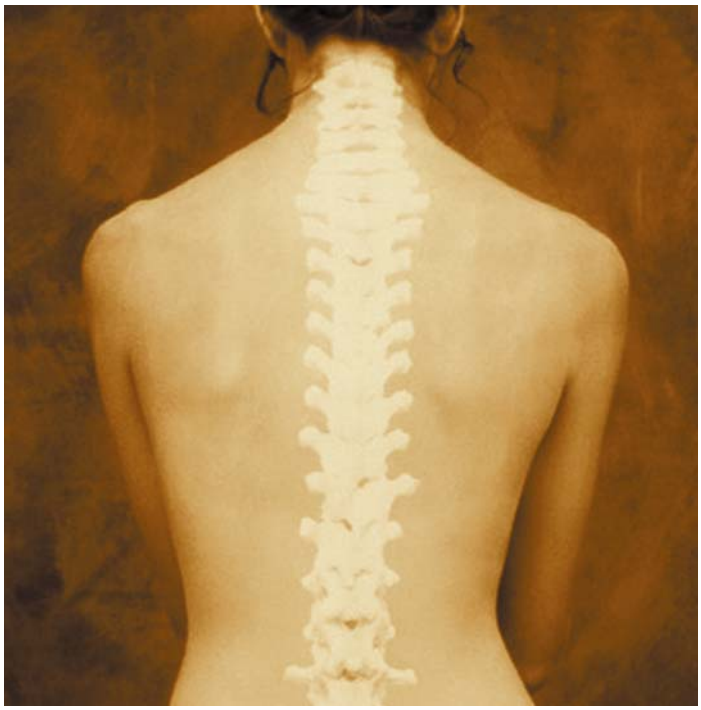
It would again be decades before more human research on Strontium's role in bone health would be tested – this time, in the early 1980s, by McGill University's Dr. Stanley Skoryna. Providing Strontium supplements (both Strontium carbonate and Strontium gluconate)) to 142 people with a range of bone health 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.

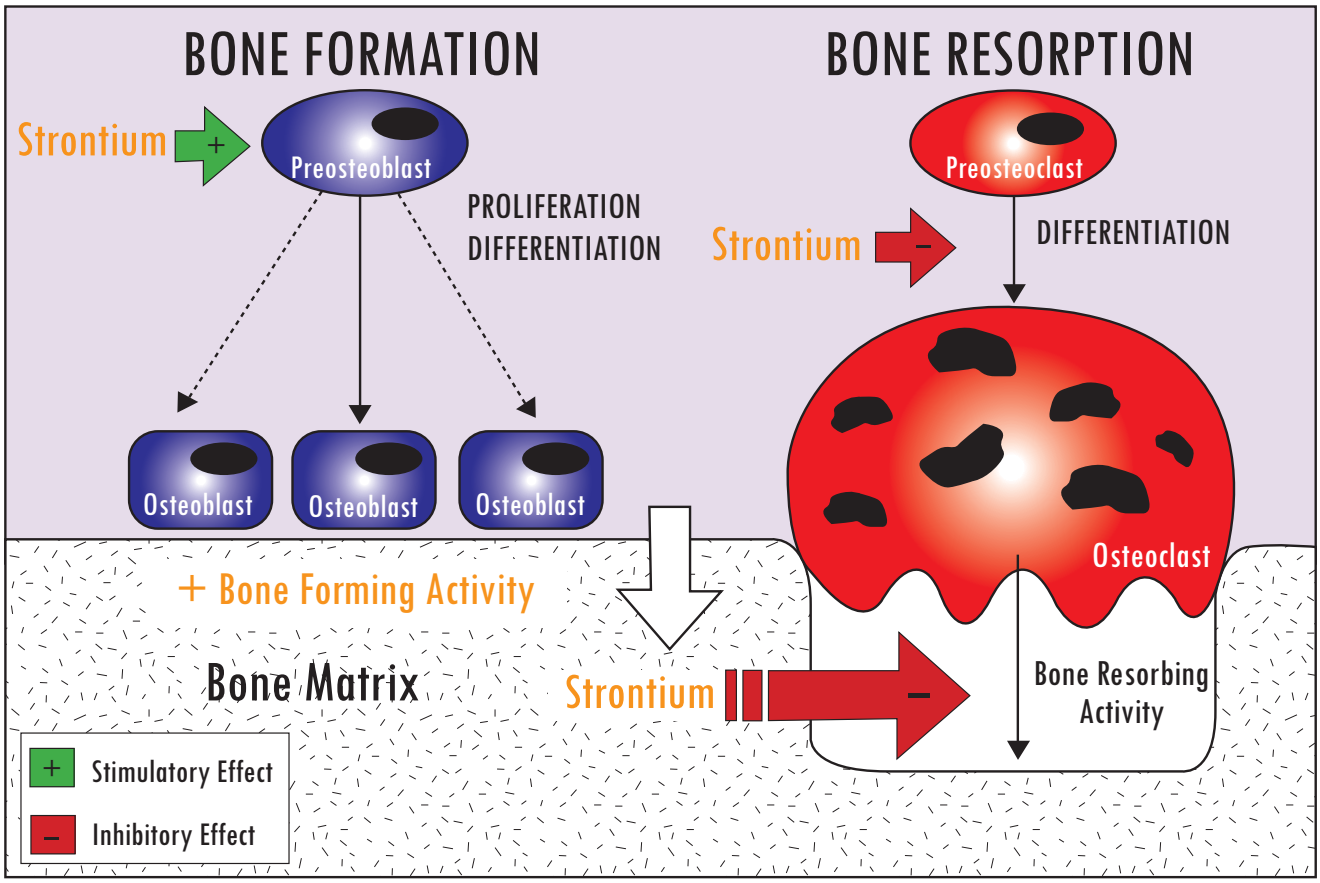
The animal evidence of increased formation of new bone is consistent with Dr. Shorr's early speculations about osteoblast activity,[22] and with the preliminary results seen in Dr. Skoryna's pilot study.[26] But the ultimate vindication of Strontium's bone-building powers has come from the new European 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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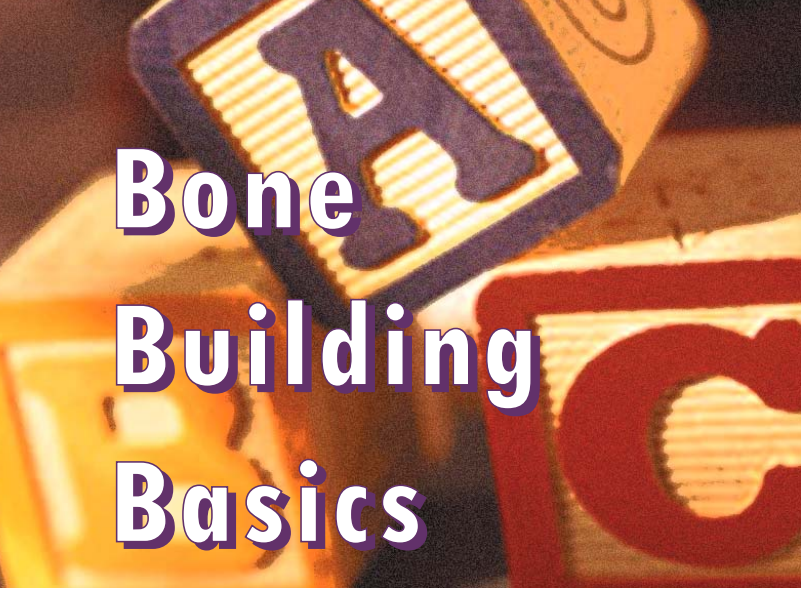


Bone Building Basics

Surprising New Research About the Foundations of Bone Health

In this special issue of Advances, we've heralded the coming of Strontium, a revolutionary new supplement which has only recently stepped out of the research clinic and into the hands of people wanting to take good care of their bones. But in our excitement over this vanguard bone-health nutrients, we should also remember that bone health is a total lifestyle commitment. While most people know the importance of "the basics" (like calcium, magnesium, and vitamin D), there are controversies that need to be addressed even surrounding the right dose and form of even these well-known nutrients. The facts about these and other lifestyle choices may surprise you.

1300-1600 milligrams of calcium is more effective for lowering fracture risk.

- Get Enough Calcium. 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.[1] But these numbers are your total calcium need. The more calcium you get in your diet, the less you need from supplements. There is little evidence that ever-higher intake of calcium does your bones any additional good, and indeed taking too much calcium can inhibit the absorption and utilization of other important bone nutrients, such as zinc and copper.[2]

The best food sources of calcium are skim milk and many other low-fat dairy products. Contrary to what you may have heard, the balance of the evidence overwhelmingly favors the conclusion that milk is good for your bones.[3]

- Get the Right Kind of Calcium. Too many health-conscious people believe that conventional calcium supplements (or conventional calcium plus vitamin D) can put an end to bone loss. They can't. As multiple studies have documented, conventional calcium supplements – such as calcium gluconate, calcium citrate, calcium carbonate, and even calcium citrate-malate – slow, but do not halt or reverse, menopausal bone loss, whether taken alone or with vitamin D.[4-18] Even a total daily calcium intake of 3000 milligrams of calcium from conventional sources isn't enough to stop bone loss, let alone turn the decline around.[12] You simply can't force the bones to take in more calcium, and build more bone, by taking more and more calcium: the mineral itself can only support your existing bone mass, or the building of bone induced by the other factors in your skeletal health program.[1,22]

But there is one seeming exception. Ossein microcrystalline hydroxyapatite complex (MCHC) consistently halts, or even reverses, bone loss in controlled human trials.[14-21] When put head-to-head against other calcium supplemental forms, MCHC consistently trumps the conventional calcium supplement.[14-18,21,23-26] But actually, this is the exception that proves the rule, because MCHC's bone-building powers do not lie in the calcium itself.

True MCHC is not just a form of calcium, but is a calcium-based crystalline nutrient complex, which is how the mineral is actually stored in your bones. Supplements do exist which contain "calcium hydroxyapatite" which lack this crucial nutrient matrix, either because the "calcium hydroxyapatite" is not derived from bone but from chemical synthesis (this is also known "calcium orthophosphate"), or because it uses bone meal, which is heat-treated ("ashed"), breaking down the MCHC crystalline structure and destroying the non-mineral components of the complex. But these supplements, even though they contain the same chemical form of calcium, fail to reproduce the unique effects of MCHC on parameters of bone health.[17,24-26]

Thus, the unique support for bone health provided by MCHC is probably due to a combination of its intact crystalline structure, and the vibrant blend of peptides, mucopolysaccharides, and growth factors which accompany the calcium in true MCHC supplements[27,28] – factors which are not present in conventional calcium supplements, in bone meal, or in synthetic hydroxyapatite. The bottom line is that the effects of MCHC derive from the whole supplement, and not just from its calcium content.

Unfortunately, of course, vegetarians cannot consume MCHC because it is an animal product (although premium MCHC supplements use free-range, pasture-fed livestock from countries like New Zealand or Australia as sources for the raw materials). For vegetarians, the best calcium source is calcium citrate-malate.

Ossein microcrystalline hydroxyapatite complex (MCHC) consistently halts, or even reverses, bone loss in controlled, scientific studies.

Calcium citrate-malate is not the same thing as calcium citrate, or as a simple admixture of calcium citrate and calcium malate. Calcium citrate-malate is prepared in such a way that a significant number of its calcium atoms are bound to both citrate and malate molecules at once. This unique structure makes calcium citrate-malate six[29] to nine[30] times more easily dissolved in the stomach than plaincalcium citrate.

This superior solubility may be at least part of the reason for the fact that calcium citrate-malate is considerably better-absorbed than calcium citrate. In fact, despite what is often said, nearly all studies have reported that plain calcium citrate is actually no better absorbed than calcium carbonate when taken with food.[30-36] Most studies find that about 22 to 26% of calcium from calcium carbonate or citrate is absorbed, whereas calcium citrate-malate absorption is consistently found to be around 36 to 37%% in capsules and tablets,[29,36-38] and can be as high as 42% when dissolved in orange juice.[39]

Calcium citrate-malate has been used successfully in many controlled trials to support bone mass and/or to lower fracture risk.[5,7,8,11,13,43-48] Some of these trials have involved a direct face-off between calcium citrate-malate and other forms of calcium. Such trials demonstrate that, as might be expected from its greater bioavailability, calcium citrate-malate gives better protection to the bones than other vegetarian calcium sources – although its effects are still not as impressive as those of MCHC.

How Rumors Get Started

The widespread myth of calcium citrate's superior absorption is in part the result of poorly-designed studies, which used calcium excretion as a measure of absorption. The reasoning for using this method is based on the fact that, once your body has used all of the calcium which it can at the time that a dose of calcium is taken in, any extra calcium initially absorbed will then be passed out in the urine. Thus, by giving a dose of calcium so high that the body can't use it all, and then measuring how much calcium passes out through the urine, the comparative bioavailability of two calcium forms can in theory be gauged by seeing how much calcium excretion they cause.

That's a sensible-sounding and inexpensive testing method, and in many cases it probably gives a good picture of calcium absorption. But it falls down in comparing calcium citrate with the carbonate salt. First, the alkalinizing effect of the carbonate reduces the amount of calcium excreted through the urine, making its absorption look lower; and then, some studies suggest, the citric acid in calcium citrate increases the body's excretion of calcium, making its absorption look higher![32,40,41]

Faith in calcium citrate's higher bioavailability was also shored up by a recent "meta-analysis" paper.[42] Meta-analysis is done by combining the results of several separate studies into one mondo-report, which gives a clearer picture of the overall results of the available scientific evidence. But the authors of this meta-analysis made one critical mistake: in combining studies, they assumed that calcium citrate was basically the same as calcium citrate-malate, and lumped the results for the two forms together. In fact, of course, the two forms are considerably different. By combining studies on calcium citrate with studies on the much more bioavailable citrate-malate form, the citrate salt aquired an undeserved glitter, reflected from citrate-malate's radiance.

On the other hand, the hype surrounding so-called "ionic coral calcium" is not the result of understandable errors in otherwise solid science, but of a lack of even the most elementary scientific credibility. Not one clinical trial has ever been performed using this calcium source to show that it is better absorbed or better utilized than other conventional calcium sources. Instead, astoundingly, the claims of high bioavailability for "coral calcium" are not based on controlled studies in humans, but on the stuff's ability to dissolve in water; and as has been shown, such a silly test bears little relationship to the ability of a living body do absorb calcium.[36] Indeed, this kitchen-counter method of testing absorption leads to ridiculous exaggerations of calcium absorption, such as 50% absorption for calcium citrate, or 95% absorption for "coral calcium" itself. In the real world, no calcium source has such a high bioavailability.

In one such trial,[13] a subgroup of women in late menopause and a low dietary intake of calcium took 500 milligrams of calcium (either calcium citrate-malate or calcium carbonate) or a dummy pill for two years. By the end of the trial, all of the women in the study had lost some bone mineral density: again, conventional calcium supplements can slow, but cannot reverse, the loss of BMD over the body as a whole that accompanies menopause. The women receiving the placebo were in the worst shape, having lost 2.27% on the BMD in their spines. Women given calcium carbonate did get some benefits – they endured 15% less loss of BMD than the women receiving the fake pills – but women taking calcium citrate-malate fared much better than women receiving the more common calcium supplement, having escaped 60% of the loss of spinal bone mineral density suffered by the placebo group in the same period.[13]

Both calcium supplements were more protective at the hip. While women receiving only a dummy pill lost 2.11% of their hip BMD, women taking calcium carbonate held their hip BMD steady as a group (with most women ranging from a gain of 1.16% to a loss of 0.90%). But again, calcium citrate-malate demonstrated its superiority, with women taking this form of calcium actually experiencing a gain in hip BMD (on average, 0.87%, although the typical change in these women ranged from a gain of 1.88% to a loss of 0.14%). Similar results were seen in the lower arm bone.[13]

Bottom line: take your calcium in the form of MCHC if you are comfortable with animal products; choose calcium citrate-malate if you're not.

- Rock Around the Clock. Several recent studies have suggested that when you take your calcium can make a big difference in terms of both the amount of calcium you'll absorb, and the effects of that calcium on your bones.

For starters, take your calcium with food, as doing so will increase absorption.[36,37] It's also important to spread your calcium supplements over the course of the day. Taking a smaller dose of calcium at each meal has several advantages over taking it all at once. For one thing, it will increase your total absorption of calcium (by as much as 80-100%!).[49] And by keeping calcium levels in your serum high throughout the day and night, a multi-dose approach keeps parathyroid hormone (PTH) under control throughout the day, whereas a one-shot dose of your entire day's calcium supplementation causes only a temporary lowering of this hormone.[50,51] (Keeping PTH under control is important: the hormone is released in response to low serum calcium, triggering your body to rob the bones of this mineral to meet needs elsewhere in the body). And to get the best possible results, take the largest single dose of calcium later in the day, at dinner or with a late-night snack. Studies show that this last daily calcium dose does a better job of reducing markers of bone teardown,[52,53] perhaps by keeping PTH low while you're sleeping (and thus not taking any calcium).

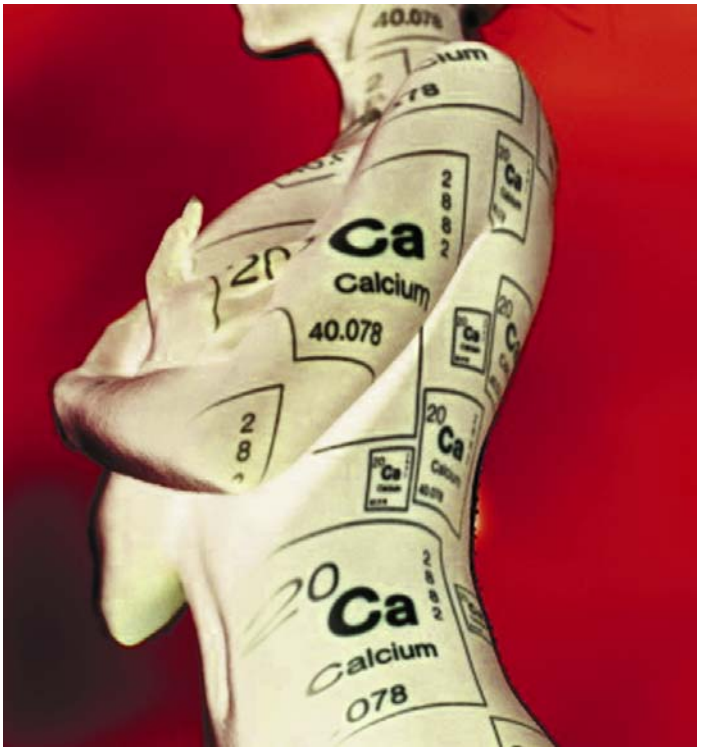
So, for instance, if you were taking a total of six calcium capsules a day, you might take one with breakfast, one with lunch, and three with dinner – or you might take two with each meal, and then go to bed with a nice glass of warm milk to help you sleep (and yes, Mom was right: a late-night glass of milk leads to sounder sleep,[54] probably thanks to its content of the amino acid tryptophan which (along with its calcium and magnesium content) increases levels of the sleep hormone melatonin).

- Almost Everyone has Vitamin D Insufficiency! Aside from improving calcium absorption, vitamin D is needed for proper muscle function, which may play a role in protecting against fractures by reducing falls.[55] So getting enough vitamin D is important. And you simply can't rely on the sun to meet your requirements, especially in Northern climates. Flat-out vitamin D deficiency is found in one third of otherwise-healthy Canadians at least once over the course of the year.[56] Indeed, the whole reason that our milk is now fortified with vitamin D is that rickets (bone disease caused by vitamin D deficiency) was epidemic in children in the Northern United States at the turn of the twentieth century – when kids spent a lot more time out-of-doors than do today's adults. There's a good reason for this: studies in human skin show that the amount of ultraviolet light that reaches the skin in Boston or Edmonton on cloudless winter days is not enough to make the body produce the vitamin.[57] But even in sunny Spain, researchers have found that 80% of children have inadequate vitamin D levels in March and October,[58] and the situation is much the same throughout central and western Europe,[59,60] including France, Italy, and Greece.[60] Even in sunny Santiago, Chile, about one third of older men with normal sun exposure are suffering from frank vitamin D deficiency.[60a]

From what we now know, the old RDA of 400 IU will not protect you from vitamin D insuffciency except in the sunniest of climates. A controlled trial in teen and preteen girls in Finland showed that a 400 IU vitamin D supplement was not enough to keep serum levels of the active vitamin above the cutoff for insufficiency,[61] and studies in the health of large populations confirm the finding in Canadian[62] and Danish[63] women lead to the same conclusion. More importantly, the use of standard 400 IU supplements have not been shown to reduce fracture rates,[64,65] and neither 300[66] nor even 600 IU has detectable effect on BMD.[5]

It's clear that the caution surrounding vitamin D toxicity has been overblown.[67,70] Indeed, the "lowest observed adverse effects level" (LOAEL) recognized by the RDA committees (2000 IU) was based on a single report in which a person taking this dose exhibited unusually high calcium levels in the blood – with no actual negative clinical effects. Indeed, doses as high as 4000[68] to 50 000 IU per day[69] have been used for months with apparent short-term safety

Vitamin D, together with calcium, helps to reduce the risk of fracture at a dose of 800 IU per day.



So how much vitamin D do you need? For optimal bone health – as opposed to simply avoiding a case of obvious rickets – scientists are now suggesting that the proper test is to see how much of the vitamin it takes to minimize the elevation of parathyroid hormone,[70] which as we've noted leeches calcium from the bones when serum calcium levels are low. To reliably reach this target, authorities are now recommending that people take vitamin D_3 supplements of 800 to 1000 IU[67,71-73] – even in pregnant and lactating women.[74] Controlled studies show that vitamin D_3, alone or together with calcium, increases BMD,[75] reduces the risk of falling,[75,76] and most importantly lowers the risk of fracture[10,77-79] at a dose of 800 to 1000 IU per day. And a body of evidence is emerging that there are an astounding range of other benefits to ensuring a high intake of vitamin D, including reduced risk of breast and prostate cancers, type 1 diabetes, heart disease, rheumatoid arthritis, and multiple sclerosis.[60,67]

It's also important to know that vitamin D_2 (ergocalciferol) is significantly less effective than vitamin D_3 (cholecalciferol) at improving real vitamin D activity in the body.[80,81] Unfortunately, many vegetarians feel ethically bound to refuse the use of D_3 supplements, because they are produced using lanolin, which comes from sheep's wool – an animal product. So while D_3 may be the preferable form, it will not be acceptable to all.

- Are You Absorbing that Magnesium? Magnesium is central to various aspects of bone metabolism, and borderline magnesium deficiency is surprisingly common. Unfortunately, far too many bone health formulas rely on magnesium oxide as the source of this mineral, for the simple reason that it takes up less room in a capsule, and therefore requires fewer capsules to be taken to reach the daily dose. But compared to other sources of the mineral, magnesium oxide has "extremely low" bioavailability (22.8%).[82] Additionally, magnesium oxide is an antacid, which can impair digestion and nutrient absorption. This is an especial concern in many older people, whose low stomach acid may even trigger pernicious anemia (flat-out B_{12} deficiency).

Magnesium citrate is certainly somewhat better, at 29.64% absorption,[82] but much of the supposed "magnesium citrate" on health-food store shelves is not true, fully-reacted magnesium citrate, but a mixture of magnesium oxide and magnesium citrate. And indeed, much better absorption is available from other forms of magnesium. Among the available options, fully-reacted magnesium monoaspartate stands out as the best, with a remarkable 41.7% bioavailability.[82]

- "Vitamin K" is Not All The Same! The importance of vitamin K to bone health is one of the more recent nutritional discoveries, but many bone health supplements do now contain some form of the nutrient. Unfortunately, nearly all are using phylloquinone (Vitamin K_1), the form of the nutrient produced in plants. By contrast, a large body of research has now clearly identified Menatetrenone (MK-4 – a form of vitamin K_2), the metabolite of K_1 produced in mammals for their specific use, as having unique bone health properties not shared by phylloquinone.[83] (The role of other forms of vitamin K_2, such as the bacterial menaquinones (most prominently MK-7), remains unclear).

Protein – makes a positive contribution to bone health.

The current Dietary Reference Intake (DRI) for vitamin K, established jointly by the Institute of Medicine in the United States and scientists from Health Canada, is 120 micrograms – but epidemiological and other evidence suggests a much higher intake is appropriate to maintain bone health in healthy people (in the range of 200 to 500 micrograms).[83,84] At least 22 clinical trials have also documented that Menatetrenone supports bone structure and slashes the risk of a fracture at true "megadose" levels: 45 milligrams (45 000 micrograms) a day in women whose bone health has already suffered significant decay.

MK-4 has recently been made available in the United States at these doses – but buyer beware, because many companies are also trading off of the confusion between Menatetrenone and the other, bacterial "vitamin K_2" forms to pawn cheap bacterial menaquinones off as equivalent to genuine MK-4 – despite the fact that all of the clinical trials use the latter. In the mean time, Health Canada continues to deny access to this crucial bone health supplement to Canadians, limiting supplemental dosages of all forms of vitamin K to just 120 micrograms – which does not even meet the DRI established by their own expert panel!

- Remember the Neglected Nutrients. Calcium, magnesium, and vitamin D are very well-known as nutrients with an important place in bone health. By contrast, you may never have heard of the powerful support that Menatetrenone and Strontium can lend your bones before reading about them in Advances. But there are a host of nutrients important to bone health that are too often neglected in putting together a total lifestyle program. These would most prominently include manganese, zinc, and copper,[2,46,85-87] and would extend to other, even more commonly-neglected nutrients such as silicon,[88,88a] boron,[89] and vitamin C.[83] Methylating nutrients such as vitamin B_{12} and folic acid are also emerging as important bone health supplements: low levels of these vitamins are associated with poor bone health,[90-94a] as are high levels of the toxic amino acid homocysteine (levels of which climb when B_{12}, folic acid, or TMG levels are low).[94a-96] This may be because homocysteine itself exerts toxic effects of on the protein fibers in bone,[97,98] or it may be because B_{12} is needed for the normal functioning of bone-building osteoblasts.[99]

- The Phosphorus Paradox. It's widely believed that Western diets are too rich in this mineral, and that excess phosphorus is bad for bone health. But phosphorus is an essential mineral, which makes up more than half of the mineral content of bone and which is needed for osteoblast function. And nearly a third of older Americans don't get the DRI of this essential mineral.

"just" 5000 or 6600 IU of preformed vitamin A is enough to roughly double your risk of a fracture

The concerns with phosphorus stem from theoretical speculations related to its effects on parathyroid hormone, and the belief that phosphorus causes you to lose calcium in

Table 1. "Alkaline-Ash" and "Acid-Ash" Foods. Average values for a class of food are given after the class name, which is given in full capitals; exceptional specific foods are also listed beneath the category name. Foods assigned more "negative" values are more alkaline; those with higher "positive" values are more acidic. Values are per 100g of food. Data taken from (132).

FATS AND OILS:	**0**	**MEATS:**	**+9.5**
FISH:	**+7.91**	Corned beef:	+13.2
Brown trout:	+10.8	Lean pork:	7.9
FRUITS:	**-3.1**	**MILK AND DAIRY:**	**+8.7**
Raisins	-21	Buttermilk:	+0.5
Currants	-6.5	Cheddar Cheese:	+26.4
NUTS:	**+4.1**	Cottage Cheese:	+8.7
Peanuts	+8.3	Soft Cheese:	+4.3
Hazelnuts	-2.8	Whole Milk:	+0.7
Walnuts	+6.8	Parmesan:	+34.2
GRAINS:	**+5.7**	Yogurt:	+1.5
Bread:	+3.5	Ice Cream:	0.6
Rye bread:	+4	Skim Milk:	+1.2
Whole wheat:	1.8	**VEGETABLES:**	**-2.8**
Flour:	+7.0	Spinach:	-14
Spagetti:	+6.7	Zucchini:	-4.6
White rice:	+1.7	Cauliflower:	-4.0
Brown Rice:	+12.5	Carrots:	-4.9
Oats	+10.7	Asparagus:	-0.4
LEGUMES:	**+0.53**	Cucumbers:	-0.8
French Beans:	-3.1		
Lentils:	+3.5		
Peas:	+1.2		

your urine. But studies show that it's the form of phosphorus that counts: phosphoric acid (the acidic phosphorus compound in some sodas) may cause increased calcium excretion because of its acidifying effect, but neutral phosphorus forms do not;[100] and indeed, one study[101] found that even when sodas contain phosphoric acid, they don't increase calcium excretion unless they also contain caffeine.

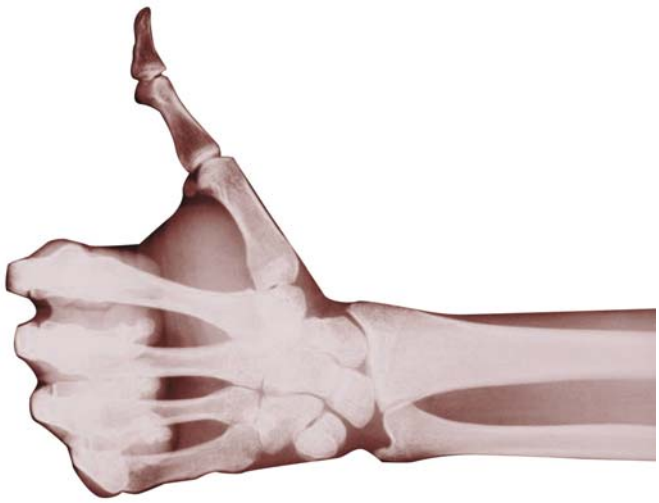
In fact, a recent study[102] has raised concerns that, with so many people taking calcium as supplements instead of drinking milk (in which calcium and phosphorus come together as a bone-building team), folks who don't get plenty ofphosphorus in their diets (such as persons on low-protein diets and many of the elderly) may actually become phosphorus deficient, because calcium supplements can reduce phosphorus absorption. Several recent reviews in the scientific literature have emphasized the importance of getting enough of this "black sheep" in the bone-health nutritional family.[83,85,103]

- Eat an "Alkaline-Ash" diet. When the body metabolizes minerals bound to certain organic ligands, alkaline ions are produced. These alkaline ions help to keep the body's acid-base load in balance. When the body becomes too acidic, calcium phosphate is leeched from the bones in order to bring the balance back, contributing to the destruction of your bones.[104]
  Foods rich in such minerals are called "alkaline-ash." The most important "alkaline" foods are vegetables and fruits (see Table 1). As you can see from the Table, the widespread belief that whole grains and fish are "alkaline-ash" foods is a myth: in fact, these foods are "acid-ash" – that is, they contain moieties which, when metabolized, tend to acidify the body. Many grains are as acidic as beef and other meats, whose acidifying properties are more widely known. The more "acid-ash" foods you consume, the more important it is to get plenty of "alkaline-ash" fruits and vegetables to balance them. The "alkalinity" of these foods is probably a big part of the reason why people eating diets rich in fruits and vegetables have better bone health and metabolism.[102,105-107]

- Get Enough Protein. Like phosphorus, protein has a bad rep' in many health-conscious circles because of its "acid-ash" properties. Surprisingly, however, the latest and best research consistently reports that protein – including animal protein – makes a positive contribution to bone health, especially when protein intake is somewhat higher than the RDA.[43,108-111] The authors of studies which have commonly been presented as "proof" that animal protein is bad for bone health[112,113] have come forward to state that their results have been misrepresented.[114,115]

In fact, higher protein intake increases the bone-health benefits of taking calcium supplements.[43] Furthermore, research clearly shows that low protein intake results in impaired bone metabolism, reduced calcium absorption, and bone-draining elevations in parathyroid hormone.[116,117] And, importantly, the RDA does not provide enough protein to prevent impaired calcium metabolism.[118,119]

So despite its "acidifying" influence – which can be countered with a rich intake of fruits and vegetables – the overall effect of protein on bone health is favorable. The optimal intake of protein to support a healthy skeletal system appears to be in the range of 1.0 to 1.5 grams per kilogram of body mass, or 0.45 to 0.68 grams of protein for each pound that you weigh.[83] This is an intake significantly higher than the RDA for protein, which is set at 0.8 grams of protein per kilogram of body mass.



- Avoid Vitamin A Toxicity. Ultra-conservative medical "authorities" have cried wolf on the dangers of nutritional supplements so often that many health-conscious people simply tune out when they raise an alarm. But recently, one example of a genuinely crippling result of long-term, chronic supplement overdose has emerged: the association between excessive preformed vitamin A (retinol/retinyl esters) and the loss of bone health. It's long been known, from animal studies, that getting too much vitamin A is bad for the skeletal system. In recent years, these findings have been confirmed in humans. Several large, well-designed population studies (and a few smaller and less rigorous ones) have now reported that men and women with the highest intake[120,121] or serum levels[122,123] of retinol are at the greatest risk of suffering a fracture; taking in the most retinol also associates with having the lowest bone mineral density (BMD).[118,124-126] (It's important to understand that this refers to preformed vitamin A: beta-carotene and other 'provitamin A' carotenoids have not been associated with loss of bone health).

Frighteningly, the amount of retinol which these studies have found to put consumers at risk of broken bones is right in the ballpark found in many – and perhaps most – multivitamins: "just" 5 000[118] or 6 600[119] IU of preformed vitamin A is

enough to roughly double your risk of a fracture. It's extremely unlikely that you'd get dosages like these from food – you'd have to spend all day gorging on liver, eggs, and fortified milk – but it's all too easy to exceed the safety limit if you're taking the kind of multivitamin designed around an unthinking 'more is better' paradigm. And indeed, nearly no one in these studies would have reached the extreme levels of intake associated with increased fracture risk if it were not for the badly thought-out supplements they were letting into their systems.

But this doesn't mean that you should avoid all intake of retinol, or depend entirely on carotenoids to get your vitamin A. The rate of conversion of "provitamin A" carotenoids into retinol varies nearly ninefold from person to person,[127] and can be altered by age, genes, body weight, and alpha-tocopherol intake. Remember that retinol is an absolutely essential nutrient – and in fact, one of its most important functions in the body is in normal skeletal metabolism! Indeed, some of the same studies that reported the impairment of bone health caused by years of retinol overdose have found that people with the lowest vitamin A levels[121] or intake[122] also suffer an elevated fracture risk[121] and lower BMD.[122] It appears that the ideal retinol intake for bone health – from diet and supplements combined – is in the ballpark of 2000 IU.

But remember that, because of government-mandated fortification, a single serving of low-fat milk or yogurt contains between about 500 and 750 IU of vitamin A, and a standard 85g (3 oz) slice of liver contains an astounding 22 000 IU! So it's very easy to overshoot your safe vitamin A intake if your supplement contains more than 1000 IU of retinol. The goal of supplementation should be to put you into that happy medium where bone health is optimized, supporting the balance of the diet instead of overbalancing it with levels you'd never get from well-chosen foods.

- Keep Active. Exercise clearly helps build bone mass in young people. And it also improves balance, muscle mass, and strength, which reduces your chances of taking a fall by about 25%. Despite these facts, it isn't totally clear whether exercise actually increases bone mass, or protects against fracture risk, when people don't get started until their middle years or beyond.[127,128] Despite this uncertainty, getting active is clearly a good idea, if only for the many other ways that it will improve your life, from energy levels to heart health to looking good. The kinds of exercise most likely to specifically support bone health are weight-bearing and/or high-impact activities, such as weightlifting and jogging.[126]

- Maintain a Healthy Weight. While there are all kinds of good reasons to avoid the overweight that's creeping its way across every sector of our society, it's also important not to lose too much weight – or to lose weight too quickly. Low body weight, and quick weight loss, are associated with thinner bones, and higher fracture risk.[127]

- Quit Smoking. Smokers are between half-again and twice as likely to suffer a fracture as nonsmokers,[83] apparently because the toxins in cigarette smoke interfere with normal estrogen metabolism and calcium absorption, and brings on early menopause.[129] For help quitting – especially if you've tried to quit before and have not yet escaped the addiction – see the resources at: http://www.hc-sc.gc.ca/hecs-sesc/tobacco/quitting/index.html, or talk to your doctor.

- If you Drink, do so in Moderation. Heavy drinking (more than two drinks a day) definitely puts you at risk for bone loss.[83] But more moderate drinking – say, between one and two drinks a day – doesn't seem to harm the bones, and some studies even suggest that it might be protective in women,[83,127] though there's no real reason to believe that's true of men. If there is a bone-shielding effect, it might be related to the fact that a drink or two daily increase the body's formation of some estrogens from their precursors.[130]

But the very changes in estrogen metabolism which might help shield a woman's bones can also promote breast cancer – and even one drink a day is linked to greater risk of this killer, especially (though not exclusively!) if you're taking estrogen replacement therapy.[131] Throw in the well-known heart-health benefits of moderate drinking, and trying to fit together the total puzzle of alcohol's risks and benefits can be a frustrating, dizzying challenge. Best advice: don't start or increase your drinking just to support your bones – but if you already make a glass of wine a part of your dinner every day, talk with your doctor, weigh your priorities and family history, and choose carefully.

To some, this "to do" list for bone health will seem too long, and they may become discouraged. But remember that each of these choices also has positive impacts on other aspects of your lifestyle. And there really aren't that many steps along the way. A single, well-designed multinutrient bone-health supplement can help ensure that you're getting the right kind and amounts of the basic vitamins and minerals you need for bone health. The shift to a diet rich in fruits and vegetables, which includes adequate protein, is a simple goal which can be reached in easy – and delicious! – steps. Exercise and a healthy weight are good for you in a lot of ways, and can be rewarding in themselves; alcohol is a grey zone, where individual priorities play heavily into the mix. And if you smoke, quitting is a contest that you can win – and the greatest prize (your health) is then yours to reclaim.

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Another Piece of the Bone Health Puzzle

Finding A Place In A Crowded Room

Bone health. It is arguably one of the most scrupulously studied health conditions known. This is due in no small part to its fundamental nature, and that same fundamental nature has produced a body of dietary knowledge for bone health that is both long-established and widely accepted. Calcium comprises over 40% of bone mass, making its supplementation essential. Calcium cannot be absorbed adequately without vitamin D, which in turn depends intrinsically on a steady supply of magnesium for its active transport. These essential vitamins and minerals, as well as a handful of other nutrients, have earned a place as staples in the bone health regimen, with a myriad of advanced delivery systems manifesting around them.

Over and above these staples for the optimal sustenance of bone health, certain research-based organizations have introduced innovations such as strontium to help those whose needs exceed that of preventative maintenance. One therefore cannot be faulted for at least questioning the need for yet further nutraceutical developments in the area of bone health. One such development is Milk Basic Protein, or MBP(r).

What Is Milk Basic Protein ?

The simplicity of the name is deceiving. It is well-known that bovine milk is rich in calcium and vitamin D (the latter being mainly a synthetic addition from the 1930's to fight rickets), but it has recently yielded yet another bone-building nutrient to science.

Milk in general (and bovine milk in particular) arguably contains more growth factors than any other single food source. Growth factors are specific proteins which act as intracellular signaling molecules by affixing themselves to the receptors of certain categories of cells and promoting their differentiation and growth. Transforming Growth Factor (TGF-ß), Insulin-like Growth Factor 1 (IGF-1), and Vascular Endothelial Growth Factor (VEGF) are among the more well-known of these proteins that are particularly present in mammalian milk. Nearly all of the growth factors in milk possess what are called basic isoelectric points.[2]

Basic isoelectric points are derived from one of the most common techniques used for separating mixtures of proteins, namely the two-dimensional polyacrylamide gel. In these gels, proteins are separated in one dimension which is determined by their molecular weights and in another dimension which is determined by the pH level at which they take on a negative charge. That pH level constitutes the isoelectric point of that protein.

Scientists in Japan used this method to isolate the biologically active components of whey protein which they had determined to have positive metabolic effects on bone health. These determinations included studies reporting whey's ability to suppress osteoclast (bone teardown) cell formation and resorption[3] as well as stimulate the proliferation and differentiation of osteoblast (bone building) cells.[4]

Protein constitutes less than 3.5% of the molecular weight of milk, and less than one-fifth of that amount (0.6% of milk's molecular weight) consists of whey. The remaining 2.9% majority consists of casein, but it was within the minority whey fraction that the scientists found what they were looking for.

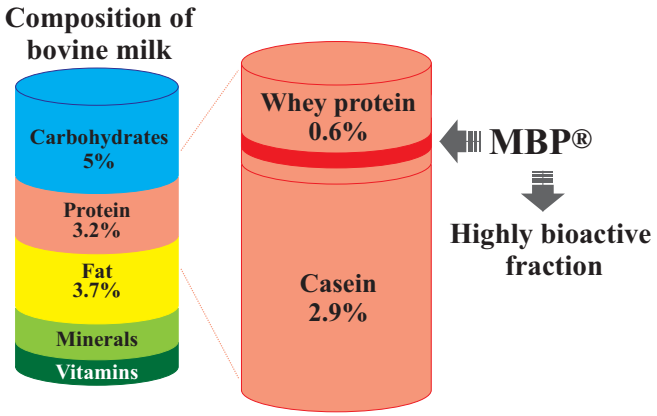
MBP is a compounded protein fraction separated from bovine whey.

What they found, using the isoelectric points as bioactivity markers, were the compound alkaline fractions most directly responsible for the bone-enhancing properties of whey protein. The Japanese scientists designated this series of fractions as a proprietary discovery known as Milk Basic Protein, or MBP. The terms 'milk' and 'protein' refer to the source and type of nutrient respectively, while the term 'basic' refers to its alkaline nature. The protein strains within MBP have basic isoelectric points ranging from 7.0 to 10.5 and contain much higher amounts of the essential amino acid lysine and the conditionally essential amino acid arginine than casein does.[5]

The Science of MBP

At first glance, the mechanism of action through which MBP exerts its effects seems remarkably similar to that of its bone-enhancing nutrient predecessors. For example, MBP assists in the absorption and retention of calcium, just as vitamin D does. Unlike vitamin D, MBP does so via the inhibition of cystein protease due to the presence of the protein strain known as cystatin C, which is part of the structure of MBP itself.[6] Cystatin C also inhibits the release of calcium from bones stimulated by thrombin, interleukin-1 and prostaglandin E2.[7] The essential nature of this function cannot be understated, as calcium is the "mortar" for the collagen matrix- together contributing to form the complex that is bone.

Cystein protease also digests collagen in the bone matrix, further testimony to the benefit of its inhibitory effect from the cystatin C in MBP.[8] The collagen factor brings us to another interesting link between MBP and its predecessors, namely MBP's effect on the relationship between osteoblast cells and osteoclast cells. Like strontium, MBP cultivates both the proliferation and activity of the bone-building osteoblasts while conversely bridling the same proliferation and activity among the osteoclasts responsible for the resorption (breakdown) of older bone tissue.[9] Even more revealing is the extent of MBP's inhibition of osteoclasts, suppressing the activity of even the most isolated osteoclast cells.[10]



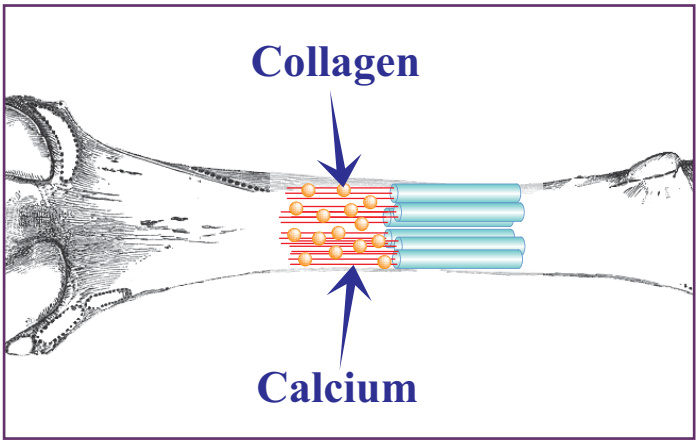
The association between the osteoblast/osteoclast relationship and collagen lies in the ability of osteoblasts to produce collagen, and it is here where MBP comes in to its own. The ability to specifically manipulate osteoblasts into producing more collagen in a manner that is more pronounced than that of its osteo-nutrient predecessors is an additional factor that makes MBP unique. Furthermore, MBP also increases serum concentrations of osteocalcin (BGP, also called Gla protein), which is the major non-collagenous protein in bone.[11]

A Brief Summary of the Effects of MBP

- Stimulates the activity and proliferation of bone-building osteoblast cells
- Stimulates collagen production
- Suppresses the activity and proliferation of osteoclast cells responsible for bone resorption
- Greatly improves the absorption and retention of calcium within bones

Science In Action: What The Studies Say

The recent scientific isolation and practical procurement of MBP has lead to numerous studies with excitingly impressive results.



The latest among these studies examined the effects of MBP on the demographic that is undoubtedly the most vulnerable to the onset of osteopenia/osteoporosis, namely menopausal women. In this study, thirty-two healthy menopausal women were randomly assigned to treatment with either a placebo or MBP (40 mg per day) for 6 months. The bone mineral density (BMD) of the lumbar vertebrae of each subject was measured by dual-energy X-ray absorptiometry (DXA) at 0 and 6 months of treatment. Serum and urine indicators of bone metabolism were measured at 0, 3 and 6 months. Twenty-seven subjects who

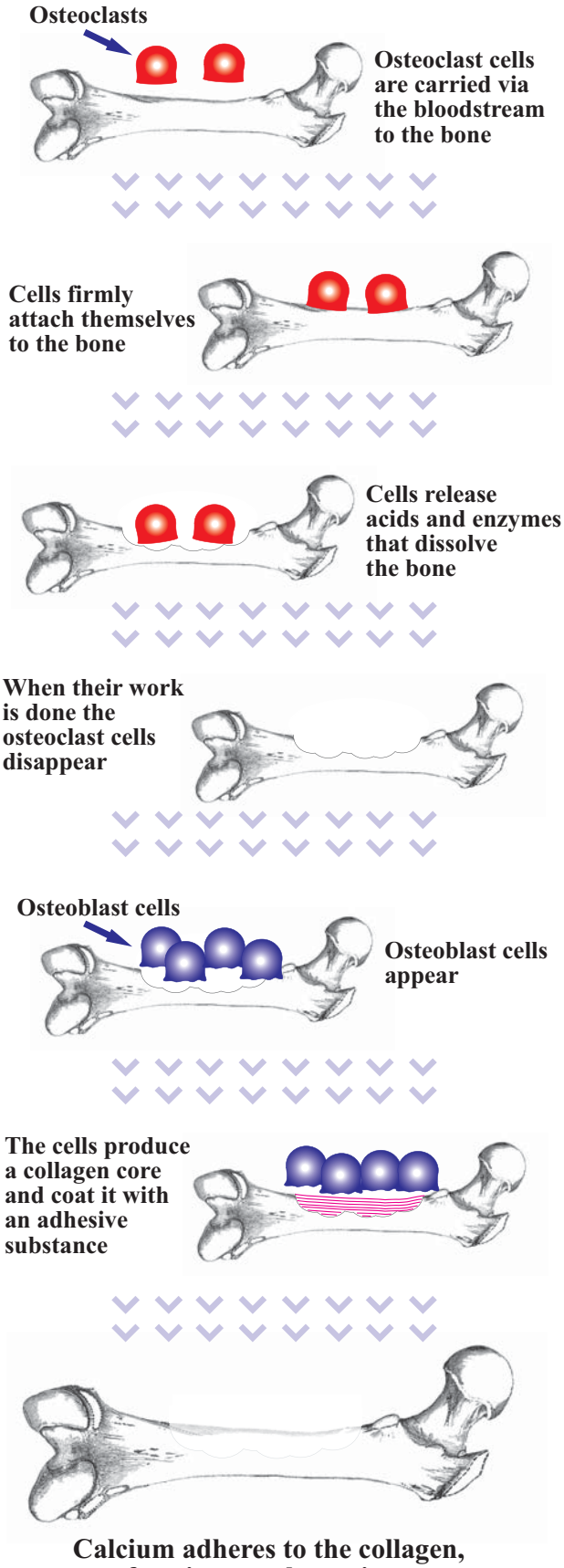
completed the study in accordance with the protocol were included in the analysis. The MBP group had a bone mineral density (BMD) increase of 1.21% while the placebo group lagged significantly behind with a 0.66% BMD decrease.[12] When compared with the placebo group, urinary markers indicating a loss of type-I collagen were significantly decreased in the MBP group at 6 months. The urinary excretion markers were found to be related to serum osteocalcin in the MBP group at 3 and 6 months, indicating that MBP maintained the balance of bone remodeling. These results suggested that MBP supplementation 'was effective in preventing bone loss in menopausal women'.[13]

MBP was eventually identified as a result of in-vitro studies that were done to identify more accurate methods of measuring the effects of various interventions on osteoclast formation and activation.[14] The more effective interventions were identified and sequestered for further study. Whey protein quickly emerged as superior, and was further investigated to isolate the source (MBP) of its influence on the osteoblast/osteoclast dynamic. A 1996 study revealed that whey protein increased the incorporation of the nucleotide thymidine as well as the overall DNA content within osteoblast cells.[15] More revealingly, it had a particularly enhancing effect on the hydroxyproline content of those cells, as hydroxyproline is a major constituent of collagen.[16]

The authors of this study began a process to isolate the bioactive ingredients in whey protein which were responsible for these and numerous other biological actions. This trend continued in another study conducted the following year, when in addition to fortifying osteoblasts, whey protein was also shown to suppress osteoclast-mediated bone resorption and osteoclast cell formation.[17] This was done using the highly reliable method of evaluating the number and area of pits formed on the surface of the bone by the osteoclasts.[18] This in-vitro research showed that the area of the pits formed in those treated unfractionated bone cell cultures were up to 2.4 times smaller than those of the untreated control group on a dose-dependent basis.[19]

The isolation process continued until the active component of whey protein that the Japanese scientists were looking for was determined to have an amino-terminal sequence identical to that of bovine high mobility group protein (HMG).[20] HMG is a family of proteins involved with the structure of chromatin and thus plays a precursory role in DNA replication. This led to the short-term designation 'HMG-like protein', a name that lasted until a successful in-vivo study involving laboratory rats took place in 2000, when the term 'Milk Basic Protein' was coined.

The Interaction of Osteoblasts, Osteoclasts, Collagen, Calcium and Bones



After further success with laboratory animals, the first study among humans was finally conducted the following year. In it, thirty-three healthy women were randomly assigned to treatment with either a placebo or MBP (40 mg per day) for six months. The bone mineral density (BMD) of the left heel bone of each subject was measured at the beginning of the study and at the end. Serum and urine indices of bone metabolism were measured at the base line, three-month intervals, and again at the end of the study. Daily intake of nutrients was monitored by a three-day food record made at three and six months.[21] When standard BMD testing was conducted at the end of the study, the women in the MBP group gained approximately 70% more bone mineral density than the control group.[22] Furthermore, urinary markers of bone loss - in this case, cross-linked type-I collagen/creatinine and deoxypyridinoline/creatinine, were 'significantly decreased' in the MBP group.[23]

A study among healthy adult men was similarly impressive,[24] as well as another study among healthy adult women in 2002. This particular double-blind, placebo-controlled trial measured radial bone mineral density, and once again the mean BMD value of the MBP group was 'significantly higher' than that of the placebo group.[25]

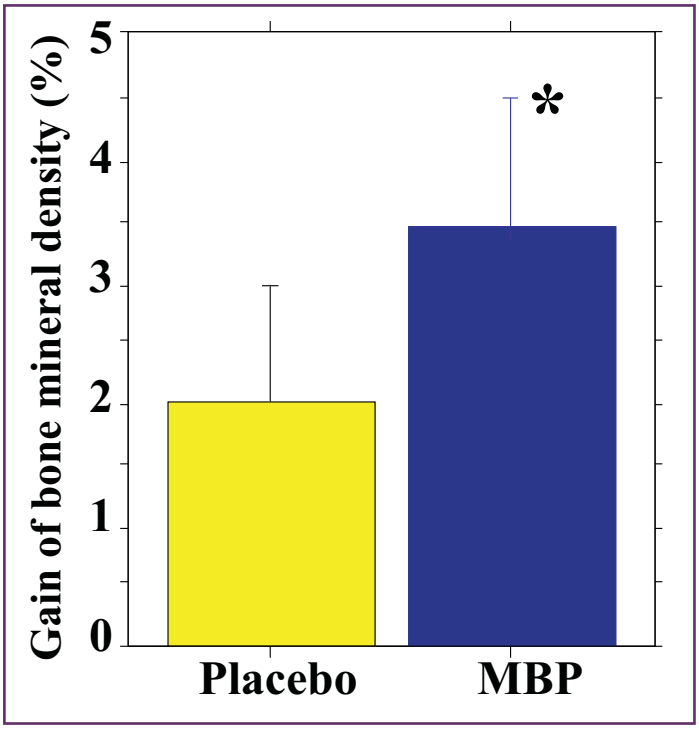
A Brief Summary of the Results of MBP Studies

- In a study among healthy menopausal women, the MBP group reported a bone mineral density (BMD) increase of 1.21% while the placebo group recorded a 0.66% BMD decrease.[26]
- In another study among healthy adult women, the MBP group gained approximately 70% more bone mineral density than the control group.[27]
- MBP reduced the number of pits on the bone surface caused by bone resorption by approximately 85% in an in-vitro study.[28]
- In yet another study among healthy adult females, the MBP group displayed a 3% increase in the BMD of the radius (a forearm bone near the wrist) compared to a 1.3% BMD decrease in the placebo group.[29]

In Conclusion

Milk Basic Protein offers certain advantages some over other osteo-nutrients. The following is a brief summary of these advantages.

- MBP can be taken with or without food.
- MBP can be taken with calcium.
- MBP comes in very small capsules, making it convenient and easy to swallow
- MBP utilizes different mechanisms of action than its osteo-nutrient predecessors, making it an augmentable or even synergistic addition to any osteo-protective protocol.
- MBP has no known interactions and can be safely consumed by anyone who is not lactose intolerant.



Gain of Bone Mineral Density in Healthy Adult women Given Placebo or MBP Supplementatin for Six Months.
Error bars represent 95% confidence intervals. Significant differences between the groups are indicated by asterisks (P<0.05).

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Q&A

Since we introduced you to the health benefits of stable Strontium in Advances 2(3), we've been inundated with questions about this radical new bone health mineral. We're taking the opportunity to lay out the facts as we know them here.

Q The Strontium supplements I have found are either Strontium citrate or Strontium carbonate. But I keep hearing about Strontium ranelate in the news. Am I getting the wrong kind of Strontium?

A The reason for all the press stories on strontium ranelate is because a major international drug company is now moving this salt form of strontium through the clinical trial process in hopes of marketing it as a drug. So it should come as no surprise if the most recent, most lavishly-funded, and most well-publicized studies in recent years have been the ones performed using this form of Strontium. However, there is nothing "magical" about this particular strontium form. Independent studies have used many different forms of strontium, including strontium lactate,[1-3] gluconate,[4,5] carbonate,[5,6] chloride,[7] acetate,[8] and still other forms of the mineral. Guess what? They all work.

So why is the drug company using the ranelic acid salt? Some of the reasons are revealed in a review of the science on strontium written by Dr. Jean-Yves Reginster, an investigator with the World Health Organization (WHO) Collaborating Center for Public Health Aspects of Rheumatic Diseases, and with the Bone and Cartilage Metabolism Unit of the University of Liège.[9] Dr. Reginster is the author of fourteen peer-reviewed scientific journal articles on the role of Strontium in bone health, and was a principal investigator on three of the largest and best-designed trials.[10,11]

On the other hand, you can get an even higher elemental yield from some other forms of strontium. Strontium carbonate, for instance, has 593 mg of strontium per gram of the compound. But many of these forms of strontium have poor "gastric tolerance" - in other words, they're more likely to cause upset stomach or diarrhea. The ranelic acid salt has good gastric tolerance.[9] They all work.

Independent studies have used many different forms of strontium.

Dr. Reginster also notes that strontium ranelic acid salt has good bioavailability - about 27%.[9] However, this really doesn't make much of a difference in the case of strontium: all forms of strontium have bioavailabilities in the 25-30% range.[7]

But there is likely another reason why this particular pharmaceutical company is now pushing the ranelic acid salt form of strontium through the "drug" development pipeline: control. Strontium lactate, citrate, gluconate, and carbonate are all natural, unpatentable forms of strontium - whereas ranelic acid is a purely synthetic molecule that does not occur in nature. By using the ranelic acid salt, Big Pharma may be hoping to shore up its patent protection and regulatory exclusivity on the "drug" market for what is, fundamentally, a dietary supplement: strontium, a naturally-occurring trace mineral in the diet.

Certainly, the ranelic acid part of the strontium ranelate compound contributes nothing to the effects of strontium on your bones. When you swallow strontium bound to ranelic acid, the compound splits apart into two strontium ions and a molecule of ranelic acid. The two are then taken up into the body separately, and while the body absorbs 27% of the Strontium in a pill, it absorbs less than a tenth as much (2.5%) of the ranelic acid. Of the ranelic acid that is absorbed, 93% to 99% is excreted within 7 days without being metabolized by the body.[9]

Molecular and animal studies have also shown that the effects of the ranelic acid salt of strontium are due to the strontium. In a study on the use of strontium ranelate on bone formation in bone tissue culture, it was seen that strontium bound to ranelic acid enhanced the replication of pre-osteoblastic cells, but that "neither calcium ranelate nor sodium ranelate, at the same concentration, were able to induce similar effects".[9] Again, many other mechanistic studies have used other forms of strontium, such as strontium carbonate and strontium chloride, and shown the same key effects on bone metabolism seen with strontium ranelate.[7] Indeed, it's exactly the many animal studies and clinical trials using other forms of strontium that led to the interest by pharmaceutical companies in strontium for the bones.[9]

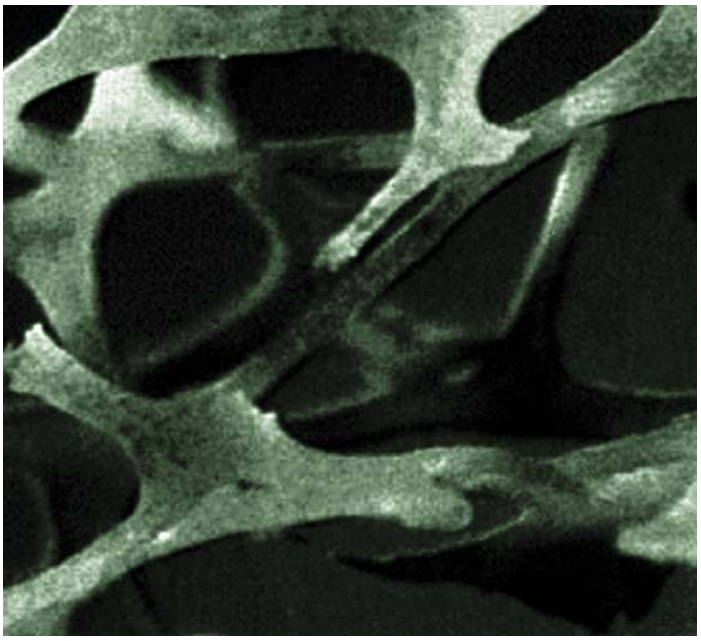
Strontium citrate enjoys the advantages of a relatively high elemental yield (about 300 milligrams elemental strontium per gram of strontium citrate), so you won't be popping fistfuls of pills to get your daily dose, and being very soluble, giving it good gastric tolerance and bioavailability compared to many other strontium forms (such as the carbonate). Citric acid is also a natural ligand, and is available as a dietary supplement.

Q What do you think about all these new supplements which contain a full day's dose of Strontium along with calcium, magnesium, and other key nutrients all in one convenient bottle?

A They're a disaster.

In his review, Dr. Reginster specifically notes (pg. 1914) that "The simultaneous intake of [strontium] and calcium remarkably reduces the bioavailability of [strontium]. This is probably due to competition at the sites of active absorption. Simultaneous food intake also has a negative influence on the bioavailability of [strontium]". Based on this critical factor, Dr. Reginster recommends that high-dose strontium should not be taken "concomitantly with a meal or a calcium intake."[9]

The simultaneous intake of strontium and calcium remarkably reduces the bioavailability of strontium.



The competition between strontium and calcium for absorption has long been known, and all of the trials successful strontium have carefully ensured that the supplement is taken on an empty stomach, away from calcium in food or in supplements.[2,3,6,10-13] In the largest and best-designed trials,[10-13] women have taken their strontium first thing in the morning, half an hour to an hour before breakfast, and/or three hours after dinner in the evening; they took their calcium supplements separately, with a meal. This is the protocol supported by pharmacology and by clinical trials, and it is the one that we recommend unless your doctor specifies otherwise. It is obviously impossible to follow this protocol if you're taking a supplement that combines calcium and strontium in the same pill or powder! Such formulations are, therefore, not the "convenient," "inexpensive" deals they initially seem, but are ill-designed and likely ineffective "kitchen sink" hodgepodges. Persons taking these supplements will not reap the full benefits of strontium documented in the clinical trials. This is a major health issue, especially for people with advanced osteoporosis. If they and their physicians are taking these combination supplements instead of a reliable, separate supplement, or instead of an established drug therapy, the results could be ruinous.

Note that these problems do not hold if there is only a small, nutritional amount of strontium in a core bone health supplement- doses in the range of 500 micrograms to 5 milligrams, which are typical of human dietary intakes. Such doses are appropriate, as they preserve the ratio of calcium and strontium present naturally in whole-food diets. In fact, all natural calcium sources also have a small amount of strontium in them, because of the similar metabolism of the two nutrients in living beings. Calcium supplements with no strontium might be expected to upset this natural balance, leading to suppression of whatever strontium is in your diet, ultimately perturbing the natural balance of minerals in your bone.

Indeed, some evidence already exists that, over a lifetime, these low, nutritional doses of strontium do have a role to play in your health. For example, it was discovered in the 1960s that areas with more strontium in the water have a lower incidence of dental caries[14,15] - a finding which was to be reinforced by at least eight more studies over the course of the next few decades.[16]

Some of these strontium-calcium combination products further shoot their users in the foot by using poor forms of key ingredients. Some, for instance, use poor forms of calcium, such as cheap calcium carbonate (which has low gastric tolerance and which reduces your absorption of other nutrients by neutralizing stomach acid) and synthetic calcium hydroxyapatite. The latter is an extremely poorly-absorbed synthetic calcium phosphate salt, not to be confused with ossein microcrystalline hydroxyapatite complex (MCHC), an extract of bone-health nutrients contained in an intact calcium crystalline matrix. Others use magnesium carbonate as a magnesium source; this is another antacid, and like calcium carbonate is poorly absorbed. Likewise, one of these products is even poaching the research on menatetrenone (MK-4) - the form of vitamin K2 used in all of the clinical trials - to sell another vitamin K2: the unproven, bacterial menaquinones.

Everyone concerned about their bone health needs a core calcium supplement, along with other key nutrients such as magnesium, vitamin D3, and menatetrenone. In such a supplement, a small, nutritional dose of strontium is a good balancing act, reflecting the trace levels of strontium naturally present in food. If you need the potent support of a "high dose" strontium supplement, it should absolutely not come in a combination with calcium. You need a separate strontium supplement, taken at a separate time.

Q The articles in Advances say that most trials have used dosages of strontium in the 600-700 milligram range. But I keep hearing stories about trials using one or two grams of strontium!

A This comes down to the question of elemental yield: the amount of strontium itself that is present in a given amount of a strontium compound. Strontium, like other minerals, does not come "naked," but as part of a compound - a salt or chelate form of the mineral. Different forms of the mineral are more or less mineral-dense. For instance, one gram (1000 mg) of calcium carbonate contains 400 mg of elemental calcium, while the same amount of calcium citrate contains just 210 mg of elemental calcium. Similarly, to get 420 mg of elemental magnesium takes 5600 mg of true, fully-reacted magnesium aspartate, because this superior form of the mineral is only 7.5% elemental magnesium by weight. By contrast, to get the same amount of elemental magnesium from cheap, dense, low-bioavailability magnesium oxide requires just 696 mg of the compound, because magnesium oxide is over 60% elemental magnesium by weight.

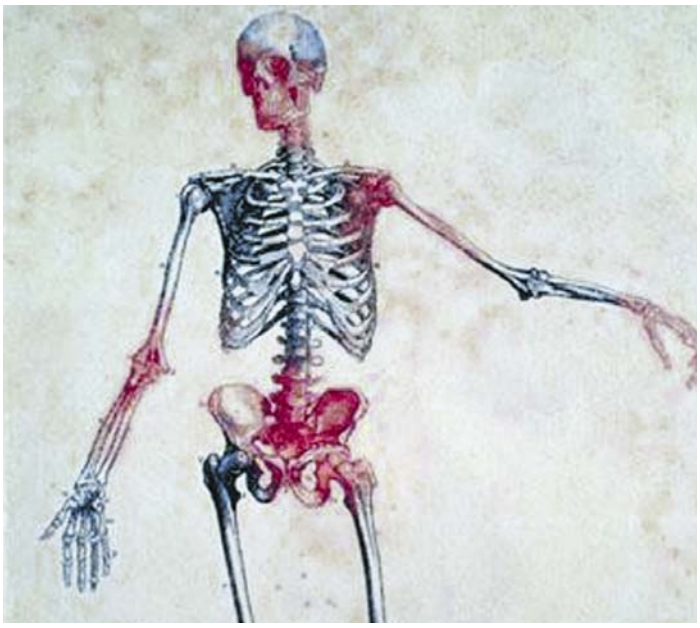
So when you hear that (for instance) some recent trials have used two grams (2000 mg) of strontium ranelate, they are telling you the amount of the compound they used - not the amount of elemental strontium. Two grams of strontium ranelate yield 680 mg of elemental strontium.

Q Can I take my entire daily intake of strontium at the same time?

A Yes, the blood levels of strontium remain fairly constant throughout the day. Strontium has a half life of 60 hours in the body, which means that it takes 60 hours for the strontium blood levels to drop by 50%. This means that there is no reason to divide your strontium intake.

Q How long do I have to wait before I can see results?

A Studies have shown that strontium reduced the incidence of fractures in as little as a year, and that increases in bone density are seen after two to three years of supplementation.[17] Therefore, it is probably better to wait two years before reassessing your bone mineral density.



Q How long do I have to wait before eating?

A Food and dietary supplements can reduce the absorption of strontium by as much as 70%, which is why it is recommended to take strontium on an empty stomach, at least 2 hours before or after food or other supplements.[18] The exception to this is vitamin D, which does not affect the bioavailability of strontium.

Q How long can I safely take strontium and should I stop taking it when my bone mineral density returns to normal?

A The recommendation to discontinue therapy for treatments aimed at increasing bone density comes from studies that have demonstrated that antiresorptive treatments can be associated with a rebound effect if the therapy is continued without interruption.[19] Antiresorptive treatments slow down bone degradation which leads to a slow increase in bone density. When the treatment is stopped, there can be an acceleration in bone

breakdown which significantly reduces the efficacy of the therapy. This rebound effect is more pronounced when the therapy has been ongoing for several years and so, to prevent this problem, the treatment can be halted every few years.[20]

Strontium is an anabolic agent and does not fall in this class of therapies. Strontium increases bone formation while reducing bone breakdown. Strontium does not produce a rebound effect and the follow-up studies have shown that the antifracture efficacy of strontium is maintained over time.

Q Can I combine strontium supplements with a bisphosphonate drug, such as alendronate (Fosamax®)?

A The quick answer is that the trials haven't been done, so we don't know.

There are two ways of addressing a decrease in bone mineral density. Therapies currently available fall in two categories: anticatabolic or anabolic agents. Anticatabolic agents prevent the breakdown of bone by inhibiting the activity of osteoclastic cells whereas anabolic agents stimulate the formation of new bone through their effect on osteoblasts.

At high doses, strontium is an anabolic agent with studies showing that it has the power to help your body create new bone. Bisphosphonates, in contrast, are anticatabolic and designed explicitly to treat a disease (osteoporosis). These drugs don't actually build bone - they work by slowing down the rate at which it is torn down (resorbed).

So the idea of combining a bone-building nutrient like Strontium with a bisphosphonate drug seems to offer a great way to get the best of both worlds. But does it actually work?

The problem is that bisphosphonates reduce both the osteoclastic and the osteoblastic activity in bones. Within weeks after you start taking a bisphosphonate, the drug begins to impair your body's formation of new bone.[17] However, the rate at which old bone is torn down is reduced by much more than that of the bone-building activity, which means that the total mass of bone slowly increases. But by allowing old bone tissue to hang around longer without speeding its replacement, bisphosphonate use results in bone tissue that is, on average, older - and thus, of poorer quality.[21-23] The resulting bone is less prone to fracture, but is not the same as youthful, healthy bone.

Although no trials have been done to determine the combined effect of strontium and biphosphonates, trials combining biphosphonates with teriparatide (an anabolic drug) gave surprisingly disappointing results and showed that antiresorptive drugs, in the long term, wind up reducing the effectiveness of teriparatide.[23,24] The studies showed that BMD was highest in the women taking the bone-building agent only, with no bisphosphonate drug.[24,25] Based on those results, it is reasonable to assume that strontium supplementation may be less effective if it is combined with bisphosphonates. This does not mean that a person using strontium should never use a bisphosphonate - or vice-versa. You may decide - in consultation with your doctor - to adapt a protocol in which you take either strontium or a bisphosphonate drug for a period of time, and then switch over to the other. In fact, there is already such a protocol, where osteoporotic women take teriparatide for two years and then switch over to alendronate.[26]

Although combining biphosphonates with teriparatide or strontium may be ill advised, there may be a way to combine an anabolic with an anticatabolic agent. A protein called cystatin C, extracted from milk and contained in a registered product called Milk Basic Protein® (MBP), protects the collagen in bone from the action of cysteine protease, which is secreted by osteoclasts.[27] Cysteine protease is an enzyme responsible for digesting the collagen in the bone matrix. Since collagen constitutes the underlying structure of the bone matrix, cysteine protease inhibitors such as MBP inhibit the release of calcium from the bone matrix. Studies in women demonstrate that supplementation with MBP significantly increases bone mineral density in as little as 6 months.[28,29]

What is particularly interesting about MBP is that it does not reduce osteoblastic activity like bisphosphonate drugs. Although trials are once again lacking, logic dictates that based on the mechanism of action behind MBP, the product is a good option for those looking for an addition to strontium. Indeed, given that strontium leads to new bone formation by increasing osteoblastic activity while reducing osteoclastic activity and that MBP reduces bone collagen breakdown, the two supplements should have an additive effect on BMD.

Q AOR emphasizes the importance of its use of calcium hydroxyapatite in its bone supplements. Why is AOR advocating the use of this source of calcium over other sources of calcium such as calcium citrate or carbonate?

Many studies have confirmed that conventional calcium supplements - such as calcium gluconate, calcium citrate, calcium carbonate, and even calcium citrate-malate - can only slow menopausal bone loss, whether taken alone or with vitamin D.[30-43] However, MCHC consistently halts, or even reverses, bone loss in controlled human clinical trials.[40-46] When compared against other supplemental calcium forms, MCHC consistently trumps the conventional calcium supplement in its effects on parameters important to bone health.[40-43,46-51]

It is also important (once again) to realize that "calcium hydroxyapatite" is not the same as ossein microcrystalline hydroxyapatite complex (MCHC) - the calcium source used in AOR's Ortho•Bone, and Bone Basics. "Calcium hydroxyapatite" - also known as "calcium orthophosphate" - is a synthetic calcium salt, whereas MCHC is a natural, calcium-containing bone nutrient complex, which contains a variety of growth factors, mucopolysaccharides, and peptides in addition to its calcium content. These nutrients are not found in calcium hydroxyapatite.

Importantly, studies show that neither calcium hydroxyapatite, nor heat-treated MCHC (which destroys its rich nutrient matrix), have the same effects on bone as true, intact lyophilized MCHC.[48-51] Therefore; it is hardly surprising that calcium hydroxyapatite would not deliver on MCHC's promises: it is in no way a comparable supplement.

MCHC remains, on the basis of the primary medical research, the best calcium supplement for bone health.

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