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REPORT

SAMe Part 4: Treatment for Arthritis Possibly the Safest, Most Effective Treatment Ever Discovered

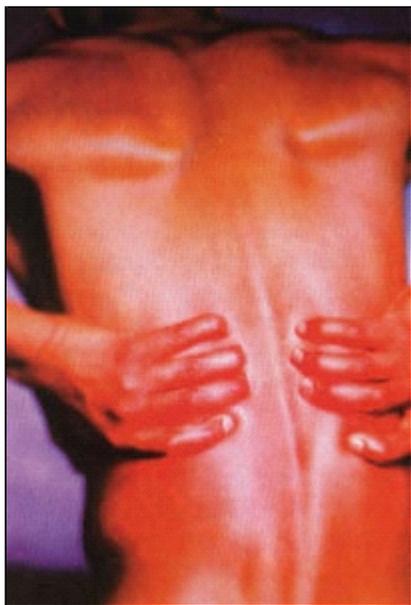
Note to Readers: This is Part 4 of an ongoing series on the use of S-adenosyl-methionine (SAMe) for health and longevity. We were initially skeptical that one product could have such diverse health effects. It was only when we discovered that SAMe is utilized by almost every cell in the body that we understood how it could have so many different effects.

SAMe is the activated form of methionine. It has been compared to ATP in importance. According to one authority, "the only known methyl group transfer that does not involve SAMe is the synthesis of methionine itself." Because it has so many actions in different parts of the body, SAMe can have a lot of health benefits that seem unrelated, but in fact all depend on SAMe.

Research shows that SAMe is a treatment* - for arthritis. According to the Arthritis Foundation, 15.8 million Americans have osteoarthritis. Another 2.1 million have rheumatoid arthritis, and 3.7 million have fibromyalgia. These and other rheumatoid diseases cost over \$50 billion a year in lost wages and treatments. Osteoarthritis is one of the most prevalent causes of disability not only in the U.S. but worldwide. After age 65, a person can almost count on having some degree of osteoarthritis or osteoporosis (luckily, the two may be mutually exclusive).

The standard treatment for arthritis hasn't changed in decades: aspirin, steroids, NSAIDs (non-steroidal anti-inflammatory drugs), gold treatments, immune-suppressing drugs, exercise and weight loss, walking sticks and surgery. Anyone who has tried them knows they sometimes work, but none of them is a panacea. Now, however, better treatment is at hand.

NEW RESEARCH



Three exciting new studies are out about arthritis. They not only help unravel the underlying processes, they also shed light on the biochemical underpinnings of SAMe. Although arthritis is usually thought of as a cartilage disease, researchers at the University of Bristol have discovered that bone is also involved. An enzyme that degrades collagen is breaking down the lattice network inside bone called "cancellous bone". Incredibly, researchers found that the thick part of the bone near the joint is breaking down faster in osteoarthritis patients than in osteoporosis patients.

The second study concerns free radicals and rheumatoid arthritis. Researchers in the Netherlands have discovered that the synovial fluid in rheumatoid arthritis patients contains non-functioning T-cells. The deficit is caused by a lack of interleukin-2 (IL-2), a cytokine crucial for T-cell activation. Free radicals are to blame, although all the science hasn't been worked out. However researchers did find that N-acetyl-L-cysteine (NAC) restores T-cell activity. (NAC naturally elevates the body's antioxidant, glutathione).

A third study was recently published in the British Journal of Rheumatology. Researchers demonstrated for the first time that S-adenosylmethionine (SAMe) reverses the effects of a different, deleterious cytokine in synovial cells. Damage caused by tumor necrosis factor (TNF) was reversed when SAMe was added to cells at the same time as TNF.

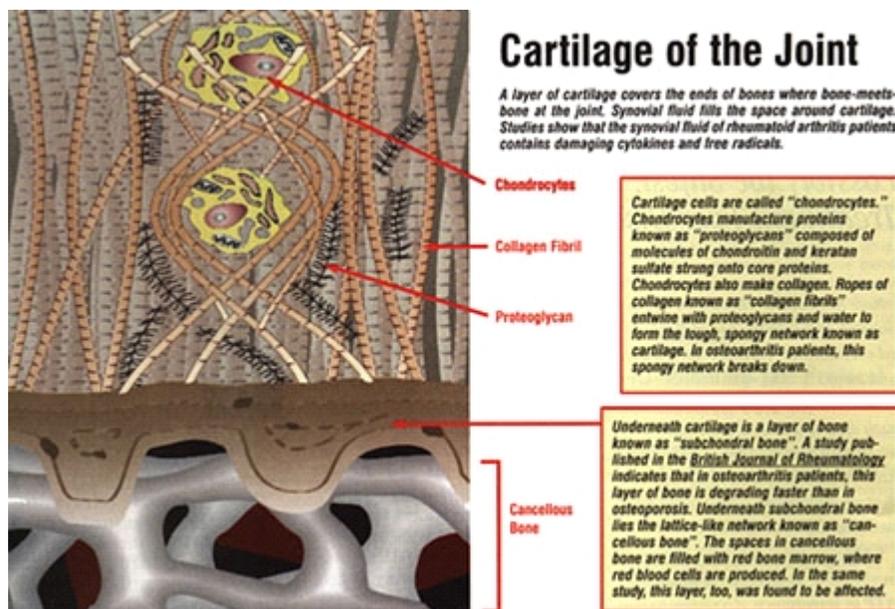
Researchers theorize that SAMe, like NAC, protects synovial cells by reversing glutathione depletion. (SAMe is naturally converted to cysteine in the body). But in addition to its antioxidant protection, they believe SAMe has other important effects. It may protect synovial cells by blocking the enzymes that degrade cartilage. This would occur through its role in the polyamine pathway that leads to protein synthesis. It may also protect important cartilage proteins called "proteoglycans" by lowering homocysteine levels.

OSTEOARTHRITIS

Osteoarthritis is a localized disorder, while rheumatoid arthritis is a systemic autoimmune disease. Both are predominantly female diseases, with two-thirds of osteoarthritis sufferers being female. The first symptoms of osteoarthritis usually occur in middle-age or later, whereas rheumatoid arthritis may strike someone in their 20s or 30s. Rheumatoid arthritis is associated with inflammation in the joints, and osteoarthritis is mostly associated with joint degeneration. Sometimes called "degenerative joint disease", osteoarthritis is far more prevalent than rheumatoid arthritis. Studies show that most people in their 60s have some degree of osteoarthritis, although they may not have symptoms.

Almost all of the arthritis studies done with SAME involve osteoarthritis. In the test tube, SAME increases the number of chondrocytes (cartilage cells) and proteoglycans (protein). This suggests that SAME treatment may reverse the underlying process of osteoarthritis by stimulating cartilage to grow. Cartilage acts like a spongy cushion where bone meets bone at the joint. In osteoarthritis, this cushion gradually disintegrates.

The other main component of the joint is synovial fluid, which acts as a lubricant. The cancer-killing cytokine, TNF, has been found in the synovial fluid of people with rheumatoid arthritis, and it plays a role in bone and cartilage destruction. Until recently, scientists did not know the effects of SAME on synovial fluid. As mentioned above, it was recently discovered that SAME reverses the damaging effects of TNF.



In 1987, the American Journal of Medicine published a series of articles on the use of SAME for treating osteoarthritis. The company that manufactures SAME provided it for the studies, which were spread out among numerous physicians and clinics (in one case, 33 different medical centers). The studies confirmed that SAME works as well as the most popular treatments on the market. The series is published under the title "Osteoarthritis: The Clinical Picture, Pathogenesis, and Management with studies on a New Therapeutic Agent, S-Adenosylmethionine".

Ten years earlier, studies had been done in Italy showing the benefits of SAME. One of the studies involved more than 20,000 patients. This large-scale trial lasted two months. Participants were not allowed to take any pain medication or other arthritis treatment during the study. Doctors found that patients taking SAME improved steadily from the beginning. At the end of the study, about 80% of the people who took SAME reported improvement. Seventy percent of the people with the most severe knee pain improved significantly. Side effects were minimal, and only 2.3% of the group stopped taking it because it didn't work. The most severe side effect reported was gastrointestinal upset.

SAME, ASPIRIN AND THE GUT

The gastrointestinal upset sometimes caused by SAME in high doses is different from that caused by aspirin and NSAIDs. The latter can damage the mucosal lining of the stomach and cause life-threatening gastrointestinal bleeding. NSAIDs and aspirin work by inhibiting "bad" prostaglandins which promote inflammation, pain, and free radicals. Although inhibiting prostaglandins in joints relieves the symptoms of arthritis, it creates problems in the gut where the same prostaglandins are beneficial.

Unfortunately these pain killers are not selective. If a person takes them long enough or in high enough doses, they can end up with holes in the lining of their stomach. The only thing standing between killer stomach acid and the stomach is the mucosal lining.

SAMe does not affect the gut in the same way. The upset stomach that SAMe sometimes causes is probably due to its effect on the brain rather than the stomach - much like motion sickness which affects the stomach indirectly through the vomiting center of the brain.

The drop-out rate of SAMe trials on osteoarthritis has been very low. In a two-year study involving 108 patients, only 2 people dropped out the first year, and 9 in the second. More than 90% of the physicians and 85% of the patients in that study rated SAMe therapy as "good" or "very good". Patients' moods improved too. Other studies show that SAMe alleviates depression caused by organic diseases, including osteoarthritis. The mechanism of action in depression is unknown.

CLINICAL TRIALS

Several double-blind studies have compared SAMe with NSAIDs. The first compared people who took 1200 mg of SAMe with people who took 1200 mg of ibuprofen for four weeks. Both therapies gave an overall improvement in symptoms of about 50%. Both were well-tolerated, and no one dropped out of the study.

In an earlier study, SAMe relieved "active movement pain" better than ibuprofen (1200 mg each), with other parameters being about the same. Side effects were better with SAMe. Sixteen ibuprofen patients experienced side effects versus 5 for SAMe. Again, there were no drop-outs due to side effects.

Another study compared SAMe to indomethacin. (Indomethacin was recently rated the most effective NSAID, while at the same time causing the most side effects). Again, improvement was almost identical, with SAMe causing fewer side effects (11% versus 39%).

Comparison with naproxen was similar. More than 700 people took part in a 30-day, double-blind, placebo-controlled study. At the end of the trial, SAMe was rated almost as well as the drug by both physicians and patients, although it took SAMe longer to be effective. This is similar to another study where SAMe's effects increased over time.

FIBROMYALGIA

Fibromyalgia is a kind of mystery disease. No one knows what causes it. The basic symptoms are pain in muscles and bones, plus fatigue. Other symptoms include disturbed sleep and depression. Doctors diagnose it by pressing on various parts of the body. Lab tests for fibromyalgia can look perfectly normal unless special muscle testing is done. Fibromyalgia can occur by itself or as part of another disease. The Arthritis Foundation considers it a type of arthritis.

In 1987, a double-blind, placebo-controlled study was done on 17 people with fibromyalgia not complicated by any other disease. Five participants had suffered from it for 10 years or longer. Researchers found that SAMe reduced pain and caused no major side effects.

In a study published in the Scandinavian Journal of Rheumatology, 44 fibromyalgia patients took 800 mg of SAMe for 6 weeks. Results showed that SAMe reduced pain at the tender points, as well as fatigue, morning stiffness and resting pain. Being free of pain apparently put people in a better mood: they chose more "happy faces" in psychological tests.

Results of treatment
with SAMe for
Fibromyalgia
IMPROVED

- n Tender Points
- n Morning Stiffness
- n Resting pain
- n Fatigue

(Adopted from Jacobsen, et al.)

TAKING SAME FOR ARTHRITIS

Clinical trials have proven that SAME works for fibromyalgia and osteoarthritis. New data indicates it may help rheumatoid arthritis patients. It alleviates pain as well as NSAIDs, without the side effects. Not only does it work as well as NSAIDs, it may protect against the side effects these drugs cause. SAME works somewhat differently than glucosamine and chondroitin sulfate which are building blocks for cartilage and potential enzyme modulators. In this regard, it may turn out to be the perfect compliment to these therapies. Although the story is not complete, SAME apparently counteracts cytokines, protects cartilage, inhibits destructive free radicals, and may reverse the effects of homocysteine on cartilage and/or inhibit enzymes. In clinical trials, SAME alleviated pain and improved mood.

Based on data from published studies, 600 to 1200 mg of SAME should be taken per day to start. If gastrointestinal upset occurs, SAME should be reduced by half, then gradually increased again. In a long-term study, patients were given 600 mg of SAME per day for the first two weeks, then 400 mg daily. In other studies, patients were consistently given 1200 mg of SAME from day one. People taking SAME should experiment with the 400-1200 mg range to find the best dose for them. Several studies indicate that it may take several weeks or months for SAME to achieve its full effect. SAME is a substance which is naturally made in the body. No serious side effects have ever been reported with SAME, even in high doses administered intravenously.

PART 1 of SAME (S-adenosylmethionine)

PART 2 of SAME (S-adenosylmethionine)

PART 3 of SAME (S-adenosylmethionine)

FURTHER READING

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Jacobsen S, et al Oral S-adenosylmethionine in primary fibromyalgia. Double-blind clinical evaluation. *Scand J Rheumatol* 20: 294-302, 1991

Fassbender HG, Role of chondrocytes in the development of osteoarthritis. *Am J Med* 83 (Suppl 5A):17-24, 1987

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