

# Minerals, Vitamins, and Antioxidants for Syndrome X

## Background

Syndrome X is a metabolic disorder that significantly increases one's risk of heart attack or stroke. It is estimated to affect nearly 60 to 75 million, or nearly one in four, Americans.<sup>1</sup>

Syndrome X is caused by insulin resistance; in fact, it is also known as Insulin Resistance Syndrome. Insulin resistance (initiated by a deficiency of magnesium) occurs when the body's cells and tissues lose their sensitivity to insulin, a hormone that transports glucose into the body's cells where it is used for energy. In insulin resistance, because the cells no longer respond to insulin, the pancreas secretes higher and higher amounts of insulin to ensure glucose uptake by the cells. High levels of glucose and insulin (hyperinsulinemia) will build in the bloodstream, causing damage to the cells and tissues of the body and increasing the risk of other serious health disorders such as adult-onset (type 2 diabetes) and heart disease.

There is strong evidence that a deficiency of magnesium, an essential mineral, strongly contributes to the development of Syndrome X.<sup>2</sup> According to current research, a low level of magnesium ions in our cells causes insulin resistance, which, in turn, leads to the development of Syndrome X.<sup>3</sup>

Taking magnesium and antioxidant supplements may be practical and necessary,

especially for those people vulnerable to insulin resistance and Syndrome X, and whose dietary habits and preferences preclude them from meeting the RDA for these essential nutrients.

This backgrounder examines Syndrome X and provides information about current research and scientific support of using certain minerals, especially magnesium, plus vitamins, antioxidants, and other nutrients as a valuable approach in preventing and combating Syndrome X.

## External Indicators

A syndrome is a set of symptoms that appear together in a consistent pattern. Syndrome X is a metabolic disorder, but it is characterized by a cluster of serious health disorders that pose a danger to one's health, well being, and life. There are both external and internal indicators of Syndrome X. The external indicators of Syndrome X include

- Obesity (Pot belly)
- Hypertension (High blood pressure)
- Abnormal glucose metabolism
- Elevated or abnormal cholesterol levels
- Abnormalities in blood clotting
- Aging

## Internal Indicator

The internal indicator of Syndrome X is

- Low intracellular ionic magnesium and high intracellular ionic calcium

# Magnesium Deficiency and Syndrome X

Ideally, cells should contain a balanced ratio of magnesium and calcium. However, these two minerals act antagonistically towards each other in the body: calcium stimulates the constriction or tightening of the muscles, including the arteries, while magnesium causes them to dilate.<sup>4</sup>

If our intake of magnesium is low, which it surprisingly is, even in developed countries, calcium floods the smooth muscle cells, constricting blood vessels and leading to insulin resistance, high blood pressure, angina, and heart attack.<sup>3</sup> Low cellular levels of magnesium and high levels of calcium have been found in each of the disorders of Syndrome X.<sup>2</sup> According to Carolyn Dean in her book *The Miracle of Magnesium*, many researchers believe that Syndrome X is the result of a long-standing magnesium deficiency.<sup>3</sup> Low intracellular magnesium and high intracellular calcium are linked not only with insulin resistance, but high blood pressure, abnormal blood cholesterol, obesity, blood-clotting disorders, and many age-related conditions—in other words, Syndrome X.<sup>2</sup>

## Factors that Contribute to High Calcium/Low Magnesium

Magnesium deficiency is common and can occur as a result of two factors. First, most people don't meet the RDA for magnesium. For men, the RDA for magnesium is 400 milligrams (mg); for women, it is 320 mg. According to Dr. Mildred Seelig, results from several dietary intake surveys consistently show that in the United States, Asia, and Europe, many people don't consume diets that provide the RDA level for magnesium.<sup>5</sup>

Second, as magnesium intakes have fallen, intakes of calcium, phosphate, fat, and sugar—elements and substances that affect magnesium retention—have increased.<sup>5</sup> Dr. Larry Resnick of Cornell University believes that Syndrome X is caused by a high calcium to magnesium ratio diet, which is common in North America.<sup>3</sup>

Calcium is an important element and research shows its effectiveness in building and maintaining bone density and strength. However, consuming a diet that contains a high ratio of calcium to magnesium alters the intracellular balance of ions. Remembering that calcium and magnesium act antagonistically towards each other, high calcium displaces magnesium in our cells, which can lead to the accumulation of calcium in the soft tissues including the arteries and kidneys.<sup>5</sup> For individuals concerned about calcium and bone loss, Dr. Seelig states that high intakes of magnesium don't interfere with calcium retention, but actually *improve* calcium retention unless calcium intake is very low.<sup>5</sup>

Phosphate is another mineral that interferes with magnesium absorption. Phosphate intake has increased in recent years, due to its addition to processed foods and soft drinks.<sup>5</sup> Human studies have demonstrated the effect of high-calcium, high-phosphate diets on magnesium retention. One study of elderly men found that a magnesium deficiency occurred when their calcium levels were raised to 1,400 mg/day and, similarly, when phosphate levels were increased to 1,500 mg/day—an amount Dr. Seelig says is common in the American diet.<sup>5</sup>

Besides calcium and phosphorous, high levels of fat and sugar interfere with magnesium retention.<sup>5</sup> Fat in the intestine impairs the body's ability to absorb magnesium.<sup>5</sup>

Sugar contributes to magnesium loss in two ways. First, according to research by Dr. Abram Hoffer, the process of refining sugar strips essential and important minerals and trace minerals including chromium, manganese, cobalt, copper, and zinc. Consuming refined sugar requires the body to draw from its own reserve of minerals and vitamins so it can metabolize sugar.<sup>3</sup> Second, high sugar intake and high blood sugar levels (hyperglycemia) increase the loss of magnesium in the urine.<sup>5</sup> An optimal intake of magnesium is necessary for normal insulin metabolism and to avoid diabetes (and its complications), high blood pressure, heart disease, and obesity.<sup>2,3</sup>

## Nutritional Support for X Magnesium

Magnesium is *the* most important nutritional supplement one can take for nutritional support against Syndrome X. It exerts several protective effects in the body. In addition to regulating the intracellular flow of calcium ions, it has anti-hypertensive, glucose-regulatory and cardio-protective activity.<sup>6</sup> It promotes the dilation of blood vessels and inhibits platelet aggregation (blood clotting within the arteries and blood vessels).

The following paragraphs provide a brief review of current nutritional research of magnesium and its effectiveness in combating Syndrome X.

### Magnesium and Insulin Resistance

According to Dr. Larry Resnick, Syndrome X is not caused by hyperinsulinemia, but, instead, by a low level of magnesium in the body.<sup>3</sup> Studies show that when a magnesium deficiency is induced in animals, they develop insulin resistance.<sup>3</sup> Magnesium is directly involved in insulin secretion and utilization. When insulin is

released from the pancreas, magnesium is needed so that the cell can “open” and glucose can enter. But in the case of magnesium deficiency and insulin resistance, the cellular mechanisms don’t work, and insulin resistance (and Syndrome X) can develop.<sup>3</sup>

Magnesium deficiency and insulin resistance create a vicious cycle. Insufficient magnesium leads to insulin resistance, and insulin resistance impairs cellular uptake of not only glucose, but of magnesium as well.<sup>7,8</sup> Further, insulin resistance increases urinary loss of magnesium, which intensifies the development of Syndrome X. Magnesium supplements can improve insulin function. One study of older, non-obese patients demonstrated that 400 mg/day of magnesium improved insulin response and glucose handling.<sup>9</sup>

### Magnesium and High Blood Pressure

High blood pressure (hypertension) is defined as a consistent reading of anything more than 140 over 90 mm Hg. More than 50 million Americans suffer from hypertension.<sup>3</sup> Hypertension, states Dr. Seelig, is actually a sign of disease that is accompanied by other metabolic abnormalities such as insulin resistance and hyperinsulinemia that can be traced back to cellular ionic abnormality: low cellular magnesium and high cellular calcium.<sup>2</sup>

Resnick has documented that people with high blood pressure and insulin resistance have low levels of magnesium ions and high levels of calcium.<sup>10-12</sup> The hypertensive effect of this ionic abnormality can be attributed to calcium’s constrictive effects on the smooth muscle of the arterial walls, whereas magnesium causes their dilation.<sup>4</sup>

Magnesium supplements have shown promise in reducing high blood pressure. In a double-blind, placebo-controlled study, 33

people who took a magnesium supplement (providing 411 - 548 mg/day) for four weeks experienced a drop in blood pressure and an improved response to insulin.<sup>13</sup> In a separate study, patients who took 240 mg of magnesium/day experienced a drop in blood pressure and triglyceride levels.<sup>14</sup>

## Diabetes

Diabetes is the seventh most common cause of death in the United States.<sup>2</sup> There are two types: Type I, which is caused by insufficient production of insulin, and Type II (adult onset), which is the insulin-resistant form. Adult-onset diabetes is quickly becoming a worldwide epidemic. World Health Organization officials predict that more than 300 million people will have adult-onset diabetes by 2025.<sup>15</sup> Diabetes significantly increases the risk of heart attack and stroke, but it can also cause nerve damage, kidney disease, blindness, increased susceptibility to infection, and foot ulcers, which result in limb amputation.

Magnesium deficiency is common in people with diabetes. In a recent analysis of 22 scientific papers on type-2 diabetes, nearly half of patients were deficient in magnesium and a third more had suboptimal levels.<sup>16</sup> In addition, research has shown that people with insulin resistance and diabetes excrete higher amounts of magnesium in their urine than those with normal glucose metabolic function.

Several studies have demonstrated that magnesium supplements have improved both insulin sensitivity and insulin secretion in diabetic patients. In addition, magnesium supplementation can prevent diabetes' debilitating complications including cardiovascular disease, eye and nerve damage.<sup>3</sup>

## Magnesium and Obesity

Obesity, especially upper body or abdominal obesity (more common in men), in and of itself is associated with the disorders

of Syndrome X: high blood pressure, diabetes, high triglyceride, and insulin levels. For years, researchers have called it "the deadly quartet" because it is often seen in men who die from heart attack or stroke.<sup>20</sup> Findings from a study of obese patients both with and without high blood pressure revealed they had impaired magnesium balance, which the study's authors said could have been caused by insulin resistance or hyperglycemia.<sup>21</sup> This study suggests that magnesium supplements may correct insulin resistance and improve blood pressure by repairing the intracellular ratio of magnesium to calcium.

## Magnesium and Elevated Cholesterol

People with Syndrome X often have high total cholesterol levels (above 240 mg/dl) and high triglycerides (above 160 mg/dl), but low levels of high density lipoprotein (HDL-C), the good form of cholesterol. Results from animal studies show animals fed a diet deficient in magnesium develop changes in lipid metabolism that mirror those found in people with Syndrome X. Specifically, they have high triglycerides, low HDL-C, decreased insulin response, and decreased function in lecithin-cholesterol acyltransferase or LCAT, an enzyme that helps clear triglycerides from the blood.<sup>22-23</sup>

Magnesium supplementation has been shown to have a positive effect on cholesterol: it decreases the level of harmful cholesterol (LDL-C) and increases the good cholesterol (HDL-C). Researchers believe that magnesium's cholesterol-lowering effect is due, in part, to its ability to activate LCAT.<sup>24</sup> In a clinical study comprised of children, researchers found that higher levels of ionic magnesium corresponded with a higher level of HDL-C and greater LCAT activity.<sup>25</sup>

## Magnesium and Blood-Clotting Disorders

One of the disorders included in Syndrome X is thromboembolic or blood-

clotting disorders. That is, blood coagulation that occurs in the blood vessels, which causes blood clots to form that lead to heart attack or stroke.<sup>2</sup> Once again, the intracellular high calcium/low magnesium ratio in Syndrome X has been identified as a likely factor in the development of these disorders. Calcium is known to enhance blood coagulation while magnesium inhibits it.<sup>26,27</sup> Insulin has also been shown to increase platelet aggregation.<sup>28</sup>

Studies based on a magnesium dosage of 400 mg/day have demonstrated magnesium's ability to inhibit platelet aggregation in people with low magnesium levels, even when subjects were exposed to various aggregating (clotting agents).<sup>29-32</sup>

## Magnesium and Aging

As we grow older, cells become more vulnerable to ion disturbances (high intracellular calcium/low magnesium) and, consequently, insulin resistance and Syndrome X are common among the elderly.<sup>2</sup> According to Seelig, the ionic hypothesis of aging maintains that alterations in the cellular mechanisms that maintain homeostasis of cellular calcium and magnesium levels govern the aging process. When cells become depleted of magnesium, it sets the stage for the onset of many age-related disorders including adult-onset diabetes and high blood pressure.<sup>2</sup>

Another condition associated with aging is increased free radical formation. Free radicals are electrically charged molecules that are the normal by-products of our body's metabolic process.<sup>3</sup> They are created when molecules in our body react with oxygen. A free radical lacks an unpaired electron, so it will try to replace this missing electron by "stealing" one from another molecule. Although free radicals are a normal part of the metabolic process, increased production of free radicals is harmful because they damage cells and tissues, and are linked to many degenerative diseases.<sup>3</sup>

Elevated blood levels of free radicals are associated with aging, diabetes, and atherosclerosis.<sup>2</sup> In healthy individuals, elevated free radicals and low antioxidant levels are linked to hyperglycemia, elevated free fatty acids, and hyperinsulinemia.<sup>2</sup>

There are certain external and internal conditions that increase the production of free radicals. An external condition that increases free radical release is exposure to drugs, pollution, and irradiation.<sup>2</sup> Internally, certain conditions increase free radical release. One is insulin resistance and the other is magnesium deficiency.

Individuals who suffer from impaired glucose and insulin metabolism (including diabetes) generate more free radicals than those with normal glucose metabolic function.<sup>2</sup> Several studies have shown that a magnesium deficiency lowers the level of antioxidants in the tissues and increases free radical release.<sup>2</sup> Animal studies have shown that magnesium deficiency lowered the level of antioxidants in many tissues, including the heart and aorta of animals, thus making them more susceptible to heart attack. One such study revealed that as plasma magnesium levels dropped in mice fed a magnesium-deficient diet, the levels of heart and liver antioxidants decreased as well.<sup>33</sup>

Magnesium can play a role in maintaining health and longevity due to its ability to correct an imbalanced ratio of intracellular calcium and magnesium ions and act as an antioxidant, thereby protecting the body (including the heart) from oxidative damage caused by free radicals.<sup>2</sup> Several studies have demonstrated magnesium's positive effect on cardiovascular health including high blood pressure, atherosclerosis, sudden cardiac death, and cardiac arrhythmias.<sup>6</sup>

## Additional Antioxidants

Besides magnesium, vitamins C, E, alpha-lipoic acid, and selenium have been shown to magnify the protective effects of magnesium and combat Syndrome X due to their antioxidant, blood-thinning, and circulation-enhancing properties.

### Vitamin C

Vitamin C is an essential vitamin that has antioxidant properties. There is evidence that people with high blood sugar (hyperglycemia) and diabetes have low plasma vitamin C levels.<sup>34</sup> Vitamin C can protect the body from the harmful complications of diabetes. Researchers have found that high blood sugar levels cause an excess production of sorbitol through aldose reductase, an enzyme. An accumulation of sorbitol in the cells contributes to chronic diabetic complications.<sup>35</sup> Clinical studies using high levels of vitamin C have shown that vitamin C lowers sorbitol levels by inhibiting aldose reductase, which suggests vitamin C can be an effective means to prevent many complications of diabetes.<sup>36</sup>

Vitamin C has also demonstrated cardioprotective effects. It's been shown to slow atherogenesis and improve blood flow. As an antioxidant, vitamin C protects against the oxidation of low density lipoprotein (LDL), which is believed to be an early step in atherogenesis.<sup>37</sup> In a separate study, vitamin C was found to improve blood flow in patients with coronary artery disease due to its ability to dilate the blood vessels, increasing blood flow.<sup>37</sup>

### Vitamin E

Vitamin E is a fat-soluble vitamin that has strong antioxidant activity.<sup>38</sup> It has been shown to prevent oxidative damage to cell membranes<sup>2</sup> and reduce oxidation of LDL-cholesterol.<sup>38</sup>

A 1995 survey measuring epidemiologic and clinical studies found that a high intake

of vitamin E—lasting at least two years—was associated with a significant reduction in cardiovascular disease.<sup>38</sup>

Researchers theorize that vitamin E's and C's cardioprotective effects are due to their ability to dilate blood vessels and arteries and relax vascular smooth muscle.<sup>2</sup> Another heart-healthy benefit of vitamin E is that it has been shown to reduce platelet aggregation, a factor in blood-clotting disorders and heart disease.<sup>38</sup>

### Alpha-lipoic Acid

One of the most common and severe complications of diabetes is nerve damage or neuropathy. Alpha-lipoic acid is a vitamin-like compound that has strong biological antioxidant properties that prevent nerve dysfunction.<sup>2</sup>

One study found that 600 mg/day of alpha-lipoic produced promising results in diabetic patients with nerve damage. Patients reported reduced foot pain, burning, paresthesia, and numbness.<sup>39</sup> Another study, based on a 1,200 mg/daily dose, was shown to significantly increase capillary blood flow. The study authors theorized that alpha-lipoic improved microcirculatory blood supply which, in turn, improved nerve function.<sup>40</sup> In Germany, alpha-lipoic acid supplementation is an approved treatment for neuropathy.<sup>2,38</sup>

In addition to its positive effects on neuropathy, alpha-lipoic acid has been shown to improve glucose control in diabetic patients.<sup>2,38</sup> One four-week study of oral alpha-lipoic, which varied the dosage from 600 mg/ once, twice, or three times daily, was shown to improve insulin sensitivity with no difference between the different daily doses.<sup>41</sup>

Several other studies have demonstrated alpha-lipoic's antioxidant effects both in diabetic patients with poor glycemic control and kidney damage<sup>2</sup> and in slowing the development of atherosclerosis<sup>38</sup>, for which people with insulin resistance and diabetes are at risk.

## Selenium

An essential trace mineral, selenium has been shown to activate several antioxidant enzymes in the body.<sup>2</sup> Epidemiologic studies show an inverse relationship between intakes of selenium and cardiovascular disease and certain forms of cancer.

## Conclusion

In summary, Syndrome X is a deadly metabolic disorder that affects a significant proportion of the population. Syndrome X is predicted to become a major health problem, especially as the numbers of adult-onset diabetes are expected to explode within the next twenty years.

Magnesium plays a crucial role in the development of Syndrome X. Low intakes of magnesium are common throughout the world. A deficiency of magnesium alters the delicate intracellular balance of ions, creating excess intracellular calcium and low intracellular magnesium. This ionic abnormality is found in each of the disorders of Syndrome X. Magnesium deficiency has been shown to cause insulin resistance, and insulin resistance is associated with Syndrome X. People who are diabetic are commonly deficient in magnesium; therefore, supplementation may be necessary for those at risk for Syndrome X and who do not get enough magnesium from their diet. Magnesium supplementation has been shown to improve glucose tolerance and insulin function, lower high blood pressure and cholesterol, reduce platelet aggregation, and protect the body from damage caused by free radicals.

In addition to magnesium, other antioxidants such as vitamins C, E, alpha-lipoic acid, and selenium may also be useful in preventing or delaying Syndrome X. According to renowned medical researcher Mildred Seelig, “Combinations of the antioxidant nutrients that protect against

free radicals, in combination with the minerals that is likely to be deficient in the occidental diet, and deficiency of which releases free radicals—magnesium—are the most promising approaches to controlling the diseases that comprise the Metabolic Syndrome X.”<sup>2</sup>

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