Micronutrients: Manganese

Transcript

Hello and welcome to our micronutrients presentation on manganese. Manganese is an important trace mineral. It's needed in somewhat small amounts but it's powerful, very, very powerful in a widespread number of metabolic and structural components throughout the body. Before we begin, just make sure you know that this presentation is not intended to replace a one-on one relationship with a qualified healthcare provider. It's not intended as medical advice. It's just me sharing and educating you. Make sure that any decisions you make based on this are in conjunction with a healthcare practitioner. When you are working with a client, you make sure that you keep them aware of the disclaimer so people are not coming back and charging you with practicing medicine without a license.

Let's look at manganese. I put this really beautiful picture up there because I thought so many of the minerals don't look so attractive as that but that's actually a picture of some manganese, pink manganese, and it's really striking, the color of the manganese. It's needed in small quantities, very small milligram quantities. It's not like iodine where supposedly it's only needed in micrograms, like a 150 micrograms, or chromium and selenium which are micrograms. Manganese is needed in milligram quantities but very small, like between 1 and 2 milligrams. It's nutritionally essential but it also can be potentially toxic, especially when it's inhaled. The word that manganese derives from, the Greek word for “magic”.

It's thought that when they first discovered what manganese could do it was considered magical. Really there's not a lot of agreement on the various effects of the deficiency, and they're finding more and more, and also of manganese toxicity. There's just a lot of speculation and a lot of very mixed studies but not a whole lot of strong evidence either way for certain things. This is a list of the various functions that manganese has been attributed to and we'll go through some of these in more detail.

Some of them have really good evidence and really good biochemistry behind them to explain them and others don't. It's an antioxidant, in particular superoxide dismutase, a very powerful antioxidant, is a manganese-dependent enzyme. It's important for metabolism, and we'll look at a few of the enzymes for which it's a co-factor in the manufacture of various components of metabolism like carbohydrates and proteins, et cetera.

It's important in bone development and wound healing and, oftentimes, it's part of combination formulas to help people in healing. I know there's a few of these.

Collagenics® is a formula that comes to mind that has a lot of manganese in it that is used for connective tissue healing. Bone, wound, and connective tissue. It's got some issues, some relationship to blood clotting although that's not as clearly studied, some relationship to sex hormone synthesis, fat and carbohydrate metabolism, calcium absorption, blood sugar regulation, and brain and nerve function. We'll look at as many of these as there's clear evidence for us to look at.

Let's start by looking at manganese as an antioxidant. It's a co-factor for superoxide dismutase. Manganese superoxide dismutase, which is a super important antioxidant in the mitochondria. Everything that we do in our body is not without cost. If you have to run away from a tiger and you get stressed out, your adrenals produce cortisol and as a result, it also produces a whole bunch of oxidative by-products that you have to do clean-up crew on. In the mitochondria, it's similar. In the mitochondria, all the metabolic activity to create ATP, the cellular currency, creates oxidative by-products. Manganese superoxide dismutase catalyzes the conversion of these radicals, these superoxide radicals. Superoxide radicals being those that have the O_3 as part of it. It basically converts it to hydrogen peroxide.

Hydrogen peroxide is then reduced to water by other antioxidant enzymes. Superoxide dismutase starts that breakdown. The superoxide radical is one of the most reactive oxygen species that's produced in the mitochondria. It's super reactive, meaning that it can do super amounts of damage. That's one important function for manganese.

Another one is as part of different enzymes. Gluconeogenesis, which is the production of sugar from non-carbohydrate sources, meaning basically the breakdown of protein or the breakdown of fat, although actually it's not the breakdown of fat because that's usually called lipolysis or lipolysis, so really it's the breakdown of proteins and turning them into carbohydrate, turning them into sugar. That's in cases where there's not enough glucose or glycogen stores, or when you're under stress and cortisol is getting in the picture.

Cortisol favors gluconeogenesis to add blood sugar so that you can run away from tigers. Two of the enzymes that are involved there are pyruvate carboxylase and phosphoenolpyruvate carboxykinase. The names, they're all very hard to say. I don't like saying them out loud. I don't mind reading them but anyway, PEPCK is the abbreviation that's used. Those are manganese-dependent enzymes.

Manganese is important for creating glucose from protein stores. Arginase is an enzyme that works inside the urea cycle. The urea cycle is in the liver for the detoxification of ammonia and ammonia is generated during amino acid metabolism so arginase is a manganese-dependent enzyme in the urea cycle. Then we have glutamine synthetase. Glutamine synthetase converts glutamate to glutamine in the brain.

Glutamate is an excitatory neurotransmitter. Glutamine is actually a source of nutrition and healing for various cells, including the endothelium in the gut, as well as the brain. These are very important enzymes. There's just a handful of them and these are some of the most important things that manganese plays a role in.

Manganese also plays a role in bone development. It is actually the preferred co-factor of enzymes called, "Glycosyltransferases." It's not the only cofactor, but it's the preferred cofactor. In the absence of manganese, other things can substitute, but they don't work quite as effectively. It's required for creating proteoglycans needed for the formation of healthy cartilage and bone. Proteoglycans are specific chemicals that are needed to create healthy cartilage and bone. Manganese is important. Deficiencies of manganese can theoretically affect the production of bone and there are some studies relating it to osteoporosis which we'll look at.

Glycosyl transferases catalyze the transfer of saccharides, which is, you remember, from our macronutrients module, are sugars and so we take these saccharides from the nucleotide sugars and create carbohydrates, glycosides, oligosaccharide, polysaccharides, and other types of chemicals. They're important transferases. They transfer sugars from one place to another and they're important in bone development.

Let's look at wound healing and collagen formation. There's an enzyme called prolidase, which splits dipeptides, meaning two amino acids put together. If those dipeptides contain proline or hydroxyproline, which we know are important amino acids for the production of cartilage, it actually breaks those bonds and provides that protein so that collagen formation can occur.

Glycosaminoglycan, you may have heard of this, they're also called GAGS, G-A-G-S, the synthesis of those are manganese-dependent. Some of these other chemicals, which I'm sure you've heard of is chondroitin sulfate, a very important thing used a lot in creating products that are helpful for building the cartilage up. Keratan sulfate and also hyaluronic acid, all of these are very important in the synthesis of collagen.

There is a rare genetic abnormality of manganese that can result in the prolidase deficiency and abnormalities of collagen synthesis that are very, very severe. It's a very rare genetic abnormality. The reason I bring it up is not that you're going to see this much when you're speaking with clients, but that you understand that if there's a disease that creates a deficiency of this enzyme on a very large scale, and it's a genetic abnormality, what you might see is a lesser scale of this where people are deficient in manganese and they're not activating the prolidase as effectively, and they're having some healing, wound healing and cartilage formation kinds of problems.

Let's look at some nutrient interactions. We have manganese and iron. We'll come back to some of the other deficiency symptoms in a little while. Manganese interacts with iron. They share a common absorption and transport pathway, so they competitively inhibit each other. When you absorb more manganese, you absorb less iron. When iron absorption increases, the absorption of manganese decreases.

Large-dose iron supplementation, about 60 milligrams for four months was what we've studied, was associated with decreased blood manganese level and, more importantly, is the decreased manganese SOD activity in the white cells, which means that there's going to be more oxidative damage as a result of excess iron supplementation.

We're aware of this. You've probably heard it before to be careful of too much iron supplementation because of oxidative damage. It's competitive inhibition of manganese can be part of that picture. Whenever there's a deficiency of iron in the body, intestinal absorption of manganese has been shown to increase. Whenever you have increased ferritin, it's associated with decreased manganese absorption.

If you have a lot of iron and the stores of iron, called ferritin, are increasing, it's going to have decreased manganese absorption. What this says to me is that in people with a disease called hemochromatosis, which is very high ferritin levels, dangerously high ferritin levels, it's a genetic disorder. It's actually in my lineage. I'm a carrier for hemochromatosis. One of my brothers actually has it. It's associated with decreased manganese absorption which would mean that people with hemochromatosis may have more likelihood of poor wound healing, poor bone strength, and structural abnormalities like that.

Men absorb less manganese. It's believed that the reason for that is because women have less iron, men have more iron. They're going to absorb less just because they don't go through the menstrual losses each month like women do. Iron deficiency has been shown to increase the risk of manganese accumulation in the brain, which can cause some issues with cognition and neurotransmission.

Let's look at manganese and magnesium. Supplemental magnesium of about 200 milligrams a day, which is not a high dose magnesium, has been shown to slightly decrease manganese bioavailability in healthy adults, where it was studied. The theory is magnesium either decreases absorption or increases excretion. Now, this is a very small dose. If we have 400, 800 milligrams like sometimes we're having people take because they're very low in magnesium or they're in the process of doing some healing that needs more magnesium, then we'd see some more.

My guess would be for whenever you're giving people more magnesium, that maybe a little bit of manganese would be useful as well, or manganese-containing foods.

Manganese also interacts with calcium. Supplemental calcium about 500 milligrams a day, which again, given the way that people are supplementing calcium is not much. You may be seeing people that are coming in, taking 1500 milligrams because their doctors told them to, so they prevent osteoporosis as they age. That's going to slightly decrease manganese bioavailability.

Really looking at what your clients are taking when they come in, and making sure that it's not interfering with other nutrients, and, if it is, that you can help them to supplement with those other nutrients as well. It was interesting that milk has the least effect on the manganese bioavailability and calcium carbonate and phosphate have the greatest effect. This says to me that maybe the calcium in milk is not as bioavailable as a lot of people think it is when recommending people drink high doses of milk for osteoporosis.

Also, because of the high protein content in the milk, it might be drawing out some of that calcium and eliminating it, so it's not available to interfere with the manganese. Several other studies found minimal effects of supplemental calcium on manganese metabolism. There have been mix studies. You have to look each study and think, and make your decision as to whether you think it was a well-constructed study. There's clearly some interaction there, just to keep on the forefront of your mind.

What are some of the references? These are just some of those articles that I quoted in some of the different nutrient interactions above. They didn't all fit on the slide with the particular information. I gave them to you as a separate slide if you want to look into it in more detail. Manganese deficiency is really not that common. In most circles, we're talking more about toxicity being an issue, but possibly increased risk of osteoporosis, diabetes or epilepsy.

Children on long-term TPN, which is total parenteral nutrition that doesn't have manganese added to it, have been found to show impaired growth and demineralization of bone. Once they were correctly supplemented with manganese, those problems seemed to correct themselves. Young men on a low manganese diet showed decreased serum cholesterol, a transient skin rash and elevated blood levels of calcium, phosphorous and alkaline phosphatase.

That goes back to that manganese calcium interaction. If we have excess calcium intake, it might interfere with the manganese, but if we have low calcium, it's going to cause elevated blood levels of the manganese because the calcium is not interfering. It's all a matter of balance and finding the right balance for each particular client you're working with.

Then in another study, young women fed a manganese-poor diet had mildly abnormal glucose tolerance in response to an IV infusion of glucose. There is a link there where you can find some of the more detailed information about manganese. Osteoporosis, there are definitely were some studies looking at this.

Women with osteoporosis were found to have decreased plasma or serum levels of manganese, kind of interesting, and an enhanced plasma response to an oral dose of manganese.

In post-menopausal women, with and without osteoporosis, there didn't seem to be any difference in the plasma levels of manganese. It seems like after menopause, the manganese doesn't seem to have as much of an impact as it does before menopause. When they did a study of healthy post-menopausal women, and gave them a supplement of 5 milligrams a day, which is about three times the RDA, with copper at two and a half milligrams a day and zinc at 15 and a combination with calcium supplement of a 1000. They found that this was more effective than calcium alone in preventing the spinal bone loss over a two-year period.

Because they had other minerals in there, they're not a 100% sure that it was the manganese and really haven't done a study to share what it was like if you just take the calcium with just the manganese or the calcium without. It's clearly that combination of nutrients is much better than calcium alone. It's easy to talk to people about either taking supplements or using the foods that are high in these minerals.

Diabetes. Mixed results in the studies with diabetes. In one study, whole blood manganese levels didn't differ significantly between 57 diabetics and 28 non-diabetics. Urinary magnesium excretion tended to be slightly higher in the diabetics compared to a 185 non-diabetics. Another case looked at 250 diabetic and non-diabetic individuals and found that Type 2 individuals had a higher serum magnesium than non-diabetics, which says that maybe they need more. I'm not sure how that relates. It's not really consistent and congruent with the rest of this.

In another study, 257 Type 2 diabetics and 166 non-diabetics, found that the lower blood levels of manganese was found in diabetic patients. In some, it was higher and in some it was lower. It's really very confusing to know. Another study of magnesium status on the activity of the superoxide dismutase was lower in white blood cells of diabetics than non-diabetics. The diabetics may have more of the deficiency of manganese.

They looked at giving groups either 15 or 30 milligrams of oral manganese. None of them seem to include the glucose tolerance when given an oral glucose challenge. In other words, when you do a glucose tolerance test where somebody's given 100 milligrams of pure glucose syrup and they took people in that glucose challenge situation and neither the 15 milligram nor the 30 milligrams of manganese improved their balance. They all didn't do very well as you would expect with a large load like that. It's just not real clear the role in diabetes, but clearly you want to err on the side of making sure that people have sufficiencies of all their trace minerals.

Epilepsy. They found that rats that were manganese deficient had more susceptibility to seizures than the ones that had plenty of manganese. Rats that are genetically prone to epilepsy have lower than normal brain and blood levels of manganese. Is there a connection? Maybe. Certain subgroups of humans with epilepsy reported to have lower whole blood manganese levels than non-epileptics.

Then there was a study who found that blood manganese levels of individuals with epilepsy of unknown origin were lower than those whose epilepsy was induced by trauma. If somebody has seizures and they haven't been hit in the head with a two by four and nobody really knows the cause, that group of folks tends to have lower blood manganese than those who actually did have a trauma which induced the seizures. There may be a connection here.

Another relationship between epilepsy and abnormal manganese metabolism that's been verified or shown or theorized. Then they're saying as a results of all these, that manganese deficiencies don't appear to be a cause of epilepsy in humans, but it may be a coincidental finding or it's possible that it might just be.

The big problem with manganese is inhaled manganese. It's hard to take too much orally because that's a lot of supplements to take and it's not that high in the food sources. Inhaled manganese happens when people are in mines or things like that, welders and smelters who are exposed to manganese dust. The problem is that when you inhale manganese, it's transported right to the brain and it doesn't go to the liver first to detoxify it.

The toxicity symptoms seem to appear slowly. If somebody's in this welding type of a job, they have a lot of exposure over a period of months to years. The scary part is that the symptoms can resemble Parkinson's Disease and they called it, "Manganism." They can have tremors, difficulty walking, facial muscle spasms, and also psychiatric symptoms like aggressiveness, hallucinations, irritability and the like.

When the manganese gets into the lungs, which is not an uncommon thing, it can lead to cough, acute bronchitis and decreased lung function. Inhaled manganese is more critical and more of a concern than oral manganese in excess. There's something, and this is just out there, they're looking at this, there's a particular type of additive that was in Canada in the gasoline for a long time and then in 1995, it was added in the US. It's called methylcyclopentadienyl manganese tricarbonyl.

Now, if you were a chemist I'd say, "Draw that molecule out," just by me saying that and you'd be able to almost draw it out because you'd know what kind of components it had. The safety studies are unclear with this. There are a lot of people who are questioning in safety and whether we should be including it in gas.

The fact of the matter is that the studies that had been done, and again you always have to look at the source of the studies, who created the studies, was it an independent group that got some funding or was it the company that makes the product that is funding it from its own self interests?

I always err on the side of caution, but it just hasn't been thoroughly evaluated, so it's something to keep our eyes on. Manganese ingested. These are some of the studies that people taking in large doses of manganese.

Older adults in Greece found a prevalence of neurological symptoms when they were exposed to amounts of manganese in their water of 1.8 to 2.3 milligrams per liter. If you have somebody that's drinking their obligatory 2 liters, they're getting about 5 milligrams of manganese, which is about four times the RDA upper limit.

A German study didn't find any evidence of neurological symptoms in people drinking water with a manganese from .03 to 2.3. They compared it to people containing less. What's the scoop? I don't know. Drinking filtered water is a good idea, as far as I'm concerned. Another thing about ingested manganese is that kids exposed to high level of manganese through drinking water had some cognitive effects. There was a study of 142 ten-year-olds exposed to about .08 milligrams per liter, which is a lot less than that other German study, found that they had significantly lower scores on three different test of intellectual function.

Another study saw that high levels of manganese in the tap water can create hyperactive behavioral disorders. There's no complete evidence that this is a problem, but it's something to look at. I say, make sure that you're not taking too much or supplementing somebody too much with magnesium, which is hard to do, and that they're drinking filtered water. Manganese can be done IV and neurotoxicity has been found to be associated with excess when it's put too much, just put into their TPN.

Susceptibility and toxicity. The people that have the most susceptibility to manganese toxicity are those with lower immunity, with less of a robust nature to their bodies. People with chronic liver disease because the manganese cannot be eliminated well. Newborns, for sure, because their brains are so much more susceptible. If you're feeding a newborn tap water that might have high levels of manganese plus all the other junk in tap water, you want to make sure that you're explaining to the moms that this is not a thing you want to feed your babies and that they don't want to drink while they're nursing their babies.

Children. Again, because of the growing and immature nervous system, are going to be much more prone to excess and you just have to be careful. Anybody who's iron deficient is going to be absorbing the manganese because of that interaction.

Let's look at the amounts of manganese. There's no RDA, because there's nobody's able to say for sure how much we really need. We're looking at adequate intake. Adequate intake for you could …See young children, it's only .003 milligrams. You could see why the drinking water would be really important to watch out for if there's .08 milligrams per liter. As they age, even as early as 7 months, it's a much lower risk of toxicity, and it grows as people age. In the adult population it's somewhere in the 1.8 milligrams whereas it's 2 for pregnant women and 2.6 for lactating women.

It's pretty easy to get that amount in food. Dietary amounts that are estimated from just studies of what people eat, ranges from 2.1 to 2.3 milligrams a day for men and 1.6 to 1.8 milligrams for women. Women seems to be more on the cusp there. People eating vegetarian diets may have manganese intakes as high as 10.9 because of where it's found. However, some of the things in some of the vegetarian foods can interfere with the manganese absorption but just a little bit like phytic acid, which is found in beans and some seeds and nuts if you don't soak them. Same thing with whole grains, you don't soak them and soy products.

That oxalic acid, which some people are very sensitive to, such as cabbage and spinach and sweet potatoes. The tannins in the tea may moderately reduce absorption of manganese. Even though teas tend to have a lot of manganese, it can be not all absorbed. Iron, calcium and phosphorous. We talked about iron and calcium, anyway, and phosphorous also, limit the retention of manganese. Then there's a list of herbs that are good sources. I have listed them here like alfalfa, burdock, chamomile, chickweed, dandelion, eyebright, fennel, et cetera. You can read the list and these are things that you can be using with your clients if you want to help them get more manganese.

The foods avocados, nuts, and seeds, seaweed, whole grains, blueberries, legumes, dried peas, pineapple and greens tend to be good sources of the foods. Here's a list that I got from whfoods.com. This is a list of all the different foods with the serving size, the calories and the amount. I listed the calories because sometimes a food may seem to be a very high source of a nutrient compared to another, but really when you look at the calories it's like, "Okay here in 41, one cup of spinach which is 41 calories is 1.68 milligrams, whereas garbanzo beans, a cup of garbanzos are 269 calories and it's around the same amount."

Now if you're an underweight person, you'll gravitate towards the garbanzos. If you're overweight, you're going to gravitate towards the spinach. Breast milk, infants are exposed to varying amounts of manganese depending on their source of nutrition, so whether it's breast milk or formula. The ranges are given here 3 to 10 micrograms per liter in soy based in breast milk, 3 to 10 micrograms per liter, which is what you want to mimic when you're working with somebody on a baby.

Cow-based is 30 to 50 micrograms per liter and the soy is 200 to 300 micrograms per liter. You could see that if you're feeding an infant purely soy-based formula, they can be really excessive in their manganese. Certainly we know bioavailability of most nutrients is going to be better from breast milk and that's also true of manganese. There's the amounts in water which we already talked about.

Supplements, what are the forms of the supplements? We have manganese gluconate, manganese sulfate, manganese ascorbate and amino acids chelates. These are all pretty well absorbed forms of manganese supplementation.

You can decide on what seems to work best for your client. The drug interactions, anything that's a magnesium containing antiacid will interfere with manganese absorption. Laxatives and Tri-cyclen also. They may decrease the absorption of manganese if you take them together. You always want to get a good drug history on your clients and then chat with them about the best relationship between the drugs and their supplements.

Let's look at some bone and joint health supplements. I mentioned earlier that we saw manganese in a lot of collagen support supplements. Two different studies found that a combination of glucosamine hydrochloride, chondroitin sulfate and manganese ascorbate were beneficial in relieving pain due to moderate osteoarthritis. The dose of elemental magnesium supplied by the supplements was a lot. It was 30 to 40 milligrams a day for 8 weeks. No adverse effects were reported, but it is high enough dose that you'd want to be careful about that.

Neither of the studies actually compared the treatments containing a manganese ascorbate to ones with just the glucosamine hydrochloride without the manganese. It's not as fair of a study as you may like it to be. How do you assess manganese? It's not quite as easy as the iodine. You can look at low whole blood. We don't do it a lot, but whole blood manganese levels are considered to be reliable somewhat. Manganese in the urine is used to monitor exposure or excessive intake, but not really to monitor the overall manganese status.

Hair manganese does correlate well with manganese levels in other parts of the bodies, so getting somebody to take a hair sample, but watching out for hair dyes, which can give false positives. If it shows up with a lot of manganese in that hair, it could be because of exposure so you would switch into a pubic hair as a control.

Finally, some references for you to look up and find out more about all of this great information related to manganese and how you can use it in your practice. This is the end of our manganese talk for the micronutrients module.