# Gnolls.org Opens The Door To Obesity Fight

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**2. HOW SHOULD YOU THINK ABOUT MAGNESIUM AND HOW TO TEST IT CORRECTLY?**
**3. WHAT DOES MAGNESIUM REALLY DO?**
**4. THE MISSING LINK IN TAUBES, GUYENET, LUSTIG, AND EENFELDT'S RECENT COMMENTS?**
**5. ITS THE BRAIN GUYS……WHEN THE SQUABBLE ENDS WE WILL ALL BE SITTING AT THE HYPOCRETIN NEURONS!**

Magnesium (Mg) is an ion that is often spoken about in the blogosphere but its importance has been under-emphasized. After speaking to Gnolls.org blogger/author/hairstylist J. Stanton ……about this issue at the AHS I decided to publish this blog a bit earlier on Magnesium to help clear the air on this cation. I also think it may help bring some clarity to the new paleo "squabble" that has begun with Taubes, Guyenet, Lustig, and Eenfeldt. And I do love this type of passion. It helps solves scientific problems. Failure of the hypothesis should make us all seek the answers. We have heard many podcasts from the paleo community leaders espousing the use of this supplement for muscle aches, constipation, and improving sleep and metabolism. But what we have not heard is why this is important and how should we attack the low magnesium clinically.

Magnesium comes in many forms medically and each formulation has specific benefits based upon its specific chemical structure which confers its ideal biologic availability. Medically-prescribed magnesium supplements such as Slo-Mag and Mag-SR contain magnesium chloride which is slowly released

from its chemical matrix. However, since magnesium is absorbed best by the body in ionic form such supplements have no advantage over any soluble magnesium salt (for example, magnesium citrate or magnesium aspartate). Magnesium threonate is the one version I use clinically in most neurologic applications.

Magnesium citrate works by attracting water through the tissues by a process known as osmosis. Once in the intestine, it can attract enough water into the intestine to induce defecation. This is why Mg citrate is best for constipation. Magnesium aspartate is a salt of magnesium that works to replete Mg but requires a higher dose than other formulations. If one is trying to restore initial sleep disturbances this is a good option. It does not work as well as magnesium malate for these indications. Mg malate is better absorbed from the gut and reaches higher blood levels than most other supplements. This is especially true when you use it in combination with a Mg oil or gel formulation. Supplementation generally takes 30-90 days to replete a minor to moderate deficiency. In diabetes the patients need a much higher daily dose until their diabetes can be reversed. I like to use Mg malate in severe muscle cramping, in diabetics with severe sleep apnea and in patients with severe PAD, CAD or restless leg syndrome. Mg glycinate is helpful if one has a leaky gut or autoimmune disease like type 1.5 diabetes. Epson salts (Mg sulfate) can be used topically or orally but when they are used orally one must be careful because of the dose of Mg one gets from this salt. I teaspoon has 100 times the RDA of Mg at 3.5 grams. Magnesium sulfate contains only 10 percent magnesium available for absorption. (MgCl) magnesium chloride has approximately 12 percent magnesium available for absorption and is useful in mild Mg deficiency cases. Most doctors check ionic Mg blood levels which are not all that accurate and gives many docs a false sense of security. I find this is the most inaccurate test in my own lab. You need better testing and equipment to diagnose Mg deficiency. I good

history and physical is best both those seem to be relics of the past these days. Serum Mg levels are 90{a7b724a0454d92c70890dedf5ec22a026af4df067c7b55aa6009b4d34d5da3c6} false positives in my own practice. That is a function of how bad our clinical testing is. I prefer the EXATest which measures direct Mg bioavailability on red cells in cases with high risk patients with neuropathy, osteoporosis, migraine, and high cortisol levels. We can also use a direct Mg challenge test but it is not often done because it is a pain in the ass to perform and most hospitals are not set up to do it. I asked for it last week and got the most empty look you could imagine. It requires two separate 24 hour urine collections and two IV infusions of Mg salt. In fact in medical school we learned about Chvostek's and Trousseau's sign for calcium deficiency but they actually also tell us more about Mg deficiency. I use these tests in osteoporosis and migraine patients daily. I see these more commonly in diabetics today than any other sign. I wonder why you might be asking Dr. Kruse? Its coming trust me.

What exactly does Magnesium do to keep us optimal, Doc?

Magnesium is vital to human biochemistry. All life is tied to the production of ATP because ATP = energy. As I laid out in my mitochondrial series, foods provide electrons to our mitochondria to make energy in the form of ATP. ATP (adenosine triphosphate), the main source of energy in cells, and must be bound to a magnesium ion in order to be biologically active. What is called ATP is often actually Mg-ATP molecule. That is just how important Mg is. Without it we call the human a cadaver! Mg is also vital for chemical stabilization of our DNA and RNA. Nucleic acids have an important range of interactions with Mg2+. The binding of Mg2+ to DNA and RNA stabilizes its structure. Additionally, ribosomes contain large amounts of Mg2+ and the stabilization provided is essential to the complexation of this ribo-protein. A large number of enzymes involved in the biochemistry of nucleic

acids bind Mg2+ for activity, using the ion for both activation and catalysis. Finally, the autocatalysis of many ribozymes (enzymes containing only RNA) is also Mg2+ dependent. Most of the biologic enzymes that catalyze the stress response in humans are also catalyzed using Magnesium. This is true as well in the sleep hormone cascade of optimal sleep.
Both Mg2+ and Ca2+ regularly stabilize membranes by the cross-linking of carboxylated and phosphorylated head groups of lipids. This allows for cohesive architecture of cells but also allows for optimal cellular communication. When Mg levels are low it can cause bad signaling between cells and allow the cellular terroir to be more prone to cancer. After all, cancer is a disease of genetic chaos and bad signaling. To make this clear…..Mg is the major co factor in most key critical enzymatic steps activating proteins in our cells. The transport of Mg2+ between intracellular compartments may be a major part of regulating enzyme activity. The interaction of Mg2+ with proteins must also be considered for the transport of the ion across biological membranes as well. So if magnesium concentration or transport are altered you can bet your ass bad things are going to follow.

Speaking of bad things lets talk about the disease where intracellular magnesium is totally disordered. Let’s talk diabetes. High levels of insulin make cells store excess Mg, but if you become insulin resistant you can no longer store Mg and begin to lose it at high concentrations in your urine. So all diabetics are seriously deficient in Mg. This is why they all have neolithic diseases. It directly affects their energy production, their DNA and RNA is more susceptible to cancer, and they develop sleep apnea quickly because they ruin the coupling of energy and sleep metabolism signaling of their hormone cascade.

***Doc, where do you weigh in on the Guyenet, Lustig, Taubes and now Eenfeldt arguments on obesity?***

Muscle become affected because Mg helps relax muscles and blood vessels. If you're deficient you have more muscle cramps and higher rates of peripheral artery disease (PAD). Can you say hello to fibromyalgia, restless leg syndrome and arterial disease all seen in T2DM? Connecting the dots yet? Moreover, when your intracellular Mg level drops your vessels tighten and your BP goes up too. And to make matters worse for T2 DM patients Mg is also a co factor the action of insulin production and manufacture and release! I have seen in the recent blog comments of Stephan Guyenet, Kurt Harris and Andreas Eenfledt and many people comment we don't know what initially causes insulin resistance. I completely disagree with that statement. My answer is Oh…..yes we do! Its low intracellular magnesium levels that causes the genesis of insulin resistance peripherally. And we have known it for a long time but have done little in clinical medicine to treat it. This is why so few people know about it. Peripheral leptin and insulin resistance (at muscles and fat cells) occurs first for this to happen but the **depletion of Magnesium always predates insulin resistance**. So when blood insulin rises, you lose intracellular Mg and this feedback loop makes the peripheral cells even more insulin resistant because we can't make insulin or let it act properly on target cells. Simultaneously, arteries constrict decreasing blood flow and glucose and insulin to the target tissues. This worsens the magnesium deficits going forward. This feedback loop continues daily in all diabetics until the brain becomes leptin resistant at the hypocretin neurons. Once this occurs, epigenetic switches are thrown in the hypocretin neurons for leptin and insulin signaling at the brain level…again this occurs because of the poor magnesium concentration at these cells and our DNA/RNA then become "hard wired" for a diabetic metabolism at the brain level. This allows for the human brain to become exquisitely sensitive to the dopamine reward of foods. The reward of foods are important when the brain is already LR because this is an outflow only tract of the hypocretin neurons in the hypothalamus. This is why I have

said many times I don’t agree that SG position of reward being the dominant cause of obesity is correct. Do I think he has more correct than the rest of the crew? Yes, I do. The real issue is what is happening to the main nucleus in the brain that controls all energy balance as insulin wrecks the periphery and the liver. That nucleus is the hypocretin neurons. That is where I separate myself from SG views. Obesity is a brain disorder. It also fully explains why no macronutrient is the major cause of obesity. And it ironically, shows why carbs appear to be the major macronutient that causes obesity. Its because of insulin’s affect on Magnesium directly. I fully understand why we have the Kitavins and the Taubian view of obesity. It’s called an incomplete our of context story that can be fully understood by biochemistry.

Doc, how do you explain the central affects of leptin and insulin and the contrary data on their signaling?

If this disease process goes on long enough we will eventually see hypocretin neuron death and the numbers of these neurons then become less. Humans only have 50,000 hypocretin neurons and they cannot be restored as we can other neurons. This makes the brain blind to leptin on a more permanent basis when their numbers are decreased permanently. We learned this from the Amgen trials on synthetic leptin…… the morbidly obese became dependent upon the synthetic leptin because their signaling at the blood brain barrier was destroyed. So the receptor had to be flooded with leptin to get the hypocretin neurons to react to it. This is precisely what goes on when someone is really fat and making a ton of leptin. To be clear from the trial data, not everyone gets to this point. When a patient gets to this point they will not be able to control their weight unless they severely carb restrict and monitor their calories diligently. The reason? The master control nucleus…the hypocretin neurons absolute numbers were lowered. This is an event that changes how calories will be partitioned

by hormones. Increasing the synthetic leptin is the only way to turn these cells off at this point. Leptin, is not as Dr. Lustig says, just a starvation hormone. LR is clinically evident in the morbidly obese and anorexic by both patients having high reverse T3 levels. A high reverse T3 is a biochemical marker for leptin resistance. I have several blog posts dedicated to this on my site. These two types of patients have completely opposite phenotypes, but have the same biochemical problem. So Dr. Lustig's theory is only partially correct in my view. He must consider this biologic fact and when he does he will get to the seat of the problem. The hypocretin neurons! And yes, when that gets published in the Journal of Pediatrics next week, we will see if they take my question on it. Anorexics and some of the morbidly obese, "french fried" their hypocretin neurons by different paths but they both destroyed how the brain senses energy balance. The problem is a leptin problem now and not an insulin one. Insulin is an anabolic only hormone with local affects. When it is injected into CSF it actually causes weight loss. When you understand this post you will understand fully why Taubes and Eenfledt beliefs are also only partially correct too. It does begins as an insulin problem peripherally in the liver and muscles, and the major initial player is the intracellular loss of Magnesium. I think these guys really need to rethink their positions. This is precisely why a T1DM patient long term, looks exactly like an anorexia nervosa patient. They can't keep any weight on at all because they have damaged their hypothalamus. To a degree they are all correct in part…but they are missing the forest view because they have allowed their biases to fog their excellent minds. Obesity is an inflammatory brain disease that has numerous causes. But how carbs start the process is known…it just does not appear to be well known, based upon their own comments lately in the blogosphere. Insulin is merely the initial trigger that starts the cascade in on pathway to obesity and loss of hypocretin neurons can be the last step in all pathways. There are other ways to obesity and LR too…see the omega six pathway with a

heavy preponderance of trans- omega six fats. Obesity is a disease with an allostatic load. It depends upon stimulus and intensity and duration of the inflammatory cytokines affect at the brain level. If it is large and sustain and colored by an emotional stressor the obesity is more likely to damage the hypothalamus. If it is due to heavy fructose and PUFA intake it is likely reversible with a leptin reset protocol. Each one of these paths turns on different epigenetic switches and alters our genes. The result is measured in our hormonal response to foods. This is why so many people react differently to dietary macronutrients. The obesity epidemic spans the spectrum in between these two opposite positions and is why we see so many incongruent details that confuse the players. That is my view.

And J. Stanton…thanks for asking for the Magnesium blog at AHS…the subsequent "SG vs GT squabble" got me motivated to post it. Go check out Gnolls.org. It rocks! And I think you need to go read the comments in SG latest blog. Passion mixed with emotion. Scientific gravity will bring it all back to the brain, the ultimate judge.

CITES:
1. The Miracle of Magnesium by Carol Deans
2.
http://bcs.whfreeman.com/lehninger/default.asp?s=&n=&i=&v=&o=&ns=0&t=&uid=0&rau=0