

Osteoporosis Part 1

Readers Summary

1. Is osteoporosis tied to leptin biochemistry?
2. Does your spine surgeon know what really causes bad bone?
3. What dietary factors are tied to osteoporotic risk?
4. Does your gut control your bone mass?
5. What little known hormones control your bone mass?

In my day job as a neurosurgeon, I operate on a lot of diseased spines. In the last 12 years, I have repaired over 1000 vertebral fractures from osteoporosis. If you remember back to my podcast with Jimmy Moore, I mentioned in the talk that the changes I had seen in osteoporosis incidence and prevalence is what made me look for the underlying cause. This ultimately led me to leptin and our diet. Many people think since bones are hard and used for support that they are not an active tissue. Bone is a very active tissue in the body that is constantly turned over. We constantly lay down new bone to stressors and resorb bone from areas that are not stressed. Since bone is so active, it uses massive amounts of energy. Energy is usually tied to a strong source of electrons. This is where leptin comes in because it is our electron accountant in the brain. Any tissue that requires a ton of energy is coupled to leptin biochemistry. The story on bones and osteoporosis, however, is a very complicated one. I am going to give you a flavor of just how complicated. This osteoporosis series will have many twists and turns. Most seasoned spine surgeons won't know much of what you are going to learn here about bone. Most don't know that osteoporosis is caused by leptin resistance. Just ask one and see if I am correct. Most will tell you to take Calcium, Vitamin D, and exercise a bit to treat osteoporosis. They may mention a Rx for a bisphosphonate class of drugs too. I don't use these

drugs at all. If you do just that, you can bet you won't cure a thing and you might even make the problem worse. Spine surgeons are taught a law called Wolff's law in reference to bone metabolism. It says the more stressed a bone is, the more bone is laid down and the stronger the bone is. This law is why most spine surgeons don't think that obese folks will have osteoporosis when they come to see us, much less test for it. These are the people who are experiencing a silent epidemic of this condition. Their numbers have exploded over the last thirty years. I mentioned that in my career I have seen a tremendous increase in this disease. In medical school, I think I had a one hour lecture on this disease. Now it is involved in close to 80% of the cases I see in my clinic. Few spine surgeons expect to see osteoporosis in our younger patients because most think this is predominantly a disease of old women with low estrogen levels. We are not taught to look for it in its correct biologic context, so it is often missed as a diagnosis, but often found on MRI imaging as loss of mineral content and more fat present in the marrow space. Spine surgeons must be more vigilant about this disease, because if it's tied to the leptin hormone, it points to the fuels we are putting in our Ferrari's! I will show you why diet is a huge factor in the development of metabolic bone disease that you should consider. This is why I treat osteopenia and osteoporosis a lot differently than conventional wisdom you will hear from other sources.

Here are some random dietary facts about osteoporosis in humans: When your diet has a lot of...

- **Total protein: risk reduction of fractures is 3.6 times**
- **Animal protein: risk reduction of fracture's is 4.5 times**
- **Vegetable protein: risk INCREASE of fracture's is 2.9 times**

▪ **Carbohydrate: risk INCREASE for fracture's is 4.9 times**

These basic facts point out why your spine surgeon or PCP needs to understand what you eat puts you at risk for your bones disappearing, no matter what age you are or what sex you are. Diet affects the two main cells that are involved in bone metabolism. **Osteoblasts** lay bone down, and **osteoclasts** resorb bone. Most of the bisphosphonate drugs only work on osteoclasts to stop them from resorbing the bone. They are only two drugs that use anabolic mechanisms on making new bone. One is a human cloned hormone that does this and that is PTH, the other drug is Forteo. Forteo is a very risky drug with many side effects. Osteoporosis can be caused both by poor bone apposition, or by resorption of the bone or a combination of both. These bone cells are controlled by hormones. Leptin, testosterone, estrogen, progesterone and cortisol are some of the ones but there are many more major players as you will soon find out.

So if diet is so critical to osteoporosis, maybe we should start this journey in the gastrointestinal tract. This month, an article showed up in the GI literature that gave more credence to my thoughts on how osteoporosis should be treated. In this paper, from Gastroenterology, we have the evidence that food absorption from the GI tract can directly influence bone mass. That evidence came from the study of ATF4, a transcription factor found in osteoblasts, the bone forming cells. ATF4 is required for osteoblasts terminal differentiation and to function to make new bone. ATF4 affects all known activities of the osteoblasts. It affects bone formation, including extracellular matrix synthesis, osteoclast differentiation, and energy metabolism that is overseen by leptin function. ATF4 is needed also for amino acid import into cells. Experiments in mice and humans have also shown that high animal protein and fat diets tend to overcome the lowered ATF4 levels in the gut. High fat diets are also protective of the bones, because fats are required to

make the hormones that protect the bone namely the sex steroid hormones and vitamin D all are derived from LDL cholesterol. This is another major reason I'm completely against the use of statins in humans.

The most important dietary issue in osteoporosis is that it appears high carbohydrate low fat and low protein diets cause osteoporosis. This is precisely the diet outlined in the USDA pyramid or plate. This clinically fits with my clinical findings over the last 15 years in my spine practice as well. I found once I left residency and began a private practice that fat people have really bad bone. This was not what I was taught to expect in medical school or my spine training. I was taught about an axiomatic bone metabolism doctrine called Wolff's law. Wolff's law says that a stressed bone placed under a load should be made stronger over time. Based upon Wolff's law, I learned in medical school fat people should have great bones. After all conventional wisdom says, the heavier one is the more stress is placed upon the bones. Well, as a clinician within one year of being in practice, I was overwhelmed with many patients who had osteoporosis at all ages and many different body types. I learned that if one is leptin resistant, Wolff's law is null and void. This is rule number one of my osteoporosis Rx and everything flows from this rule.

Hormones you did not know were involved but are

Recently Gerard Karsenty, MD, PhD, and colleagues at Columbia University Medical Center discovered that osteoblasts (bone-forming cells) secrete a hormone that regulates insulin production and enhances insulin sensitivity. This hormone is called osteocalcin. If you remember my recent top ten paleo supplements post we talked about osteocalcin briefly when I mentioned Vitamin K2. What does osteocalcin do? The latest

data from Columbia shows it regulates insulin release to protect our bone stores while also increasing our testosterone levels. Testosterone levels increase our bone density in both men and women. It is a hormone only secreted by the osteoblasts, and it is vital in forming bone and directing calcium ion homeostasis in bone, dentin and the arteries of our body. Remember in the teeth blog we spoke of the hypothalamic pituitary axis and how it controlled flow in the dentinal tubules used to mineralize teeth. Vitamin K2 and osteocalcin are also key factors in saliva and help maintain optimal dental health. In essence, osteocalcin directs the calcium we absorb in guts from our diet to go to the correct tissues in our body. In humans, osteocalcin has to be **carboxylated to be active**. When someone is IR or has T2D they have a lot of uncarboxylated osteocalcin, and this won't allow calcium into the bone collagen matrix. Instead, it gets placed in tissues it should not be in like the heart valves and in many different arteries of our body. This can be measured with a calcium index score. A high calcium index score is not a good sign for your long term health. This is particularly true for your heart.

So what carboxylates osteocalcin to make it active in humans? Vitamin K2 carboxylates osteocalcin to make it an active hormone to direct which tissue the absorbed calcium should go to. When K2 levels are low, we see calcification in places it should not be, like in your arteries in spine x-rays ,or in your mouth as tartar build up on your lingual surface of the bottom incisors.

All diabetics are very deficient in Vitamin K2. Most people who eat a SAD also are quite Vitamin K2 deficient too. Because osteocalcin helps modulate insulin release, vitamin K2 can also be used to treat T2D as well. In this country it is not used often for any reason. Most physicians and health providers do not know what it is much less what it does. If you go into most pharmacies or supplement stores you will be

hard pressed to find Vitamin K2. I use Vitamin K2 a lot in my practice and this is why it's in my top ten paleo supplement list. Most vascular surgeons don't even know what Vitamin K2 is. Sadly, neither do most healthcare practitioners who take care of the patients with the highest risk of being K2 depleted. The next time you go visit your doc ask them about K2 to see if I am right or wrong about this. I use osteocalcin to quantify how much a patient's diet is depleted in Vitamin K2. Most of our endogenous Vitamin K is made from our gut bacteria when we are healthy. Humans also have a very slick way of recycling Vitamin K too in our guts. So if one has a leaky gut or gut dysbiosis you might not be able to recapture your Vitamin K2 and need a bigger dietary source constantly. I believe this is the major reason we have a pandemic in Vitamin K2 losses. I also think it is why cardiovascular disease is so prevalent these days on a SAD. I think a SAD selects for a gut microflora that ensures Vitamin K2 depletion.

So if one has LR or has a leaky gut (dysbiosis), we should expect a major problem with osteocalcin and K2. I always look at the patient's HDL level to see if the gut maybe leaky. If the patient is on coumadin, the problem is even bigger. Why you ask? Coumadin's mechanism of action is to deplete our cells of vitamin K by blocking our ability to recycle Vitamin K. By blocking vitamin K epoxide reductase, this lowers the Vitamin K dependent clotting factors made in our liver to clot our blood. Vitamin K2 is not only important to diabetics, patients with heart disease, and patients with peripheral artery disease from atherosclerosis, but it is critical in those with osteopenia or osteoporosis too. Vitamin K2 is used as a first line treatment of osteoporosis in Japan in doses up to 45 mgs a day. Unlike the SAD, the Japanese diet, however, has a major source of Vitamin K2 in natto. The best source of Vitamin K2 in the SAD, is pastured butter which most physicians advise their patients not to use ironically.

Dysbiosis is the major cause of osteocalcin problems in clinical medicine, because most of the Vitamin K2 a human gets is from our gut bacteria. If the gut microbiotic is not optimal, we lose our ability to recycle our endogenous Vitamin K. This creates an overall depletion of Vitamin K, that must be made up in our diet. In America, our diets have been stripped of Vitamin K2 because the process of pasteurization robs dairy products of its Vitamin K content. Raw dairy products contain a lot of vitamin K2. This is why I tell my osteopenic patients to seek raw milk, and raw milk cheeses from other countries. Our government wont let us have access to raw dairy either. It makes you wonder why? That is a topic for another blog. Vitamin K is also found in many green leafy plants but with newer farming techniques and with the advent of many pesticides in use the Vitamin K levels have dropped in most non organic foods that contain Vitamin K.

If we cant recycle our vitamin K2 and we have poor dietary sources, it means that the proteins that depend upon K2 are not going to work optimally in us. When this happens, we see the effects in the heart, arteries, and in our bones. So people who are deficient in K2 cannot activate osteocalcin. Moreover, the data from the labs at Columbia University, made it clear that osteocalcin tells our beta cells in the pancreas to produce more insulin and our pituitary gland to make more testosterone. These two maneuvers help us form bone. Osteocalcin also has another function. Osteocalcin also instructs fat cells to release adiponectin, a hormone that increases our insulin sensitivity. Adiponectin is inversely correlated with body weight. It is highest in thin patients. This hormone plays a role in the metabolic derangements that result in T2D, obesity, atherosclerosis, and fatty liver disease. There is also a sexual dimorphism with adiponectin in that women have higher levels than men. Women also display a sexual dimorphism in leptin too. They have higher levels than men do. When adiponectin is released from fat cells so is leptin.

Where does leptin fit into the Osteoporosis story?

You all should be leptin experts now. But now we need to add some more detailed biochemical knowledge to your leptin foundation. Leptin is a hormone secreted by fat cells, and leptin inactivates osteocalcin via the sympathetic nervous system, according to research by E. Hinoi et al. Leptin also is released from fat cells when inflammation levels are high. Leptin is very similar in structure to IL-6 the main inflammatory cytokine behind all neolithic diseases. When a person has high levels of leptin, it eventually drives cortisol higher and this stimulates even more inflammatory cytokines from cells. As this occurs LR develops all over the body. Cortisol is one of the major hormones involved in the sympathetic nervous system. When cortisol is chronically high, as I told you in the Hormone 101 blog, it's bad news. When someone is leptin resistant, they block osteocalcin's main function and this causes osteoporosis. This is one major reason why fat people lose their bone. It also definitely proves that Wolff's law is null and void when you are LR. The law is true when we are dealing with healthy conditions. When cortisol is chronically elevated with insulin, you get major neolithic diseases that are deadly. This is why leptin resistance leads to insulin resistance and then eventually to cortisol excess. When I make the diagnosis of osteoporosis or osteopenia, this is a sign to me that a person is dying slowly biochemically. Leptin it turns out is the "Ferrari brake" that keeps osteocalcin and circulating insulin levels from becoming too high. People who are LR (fat) have high leptin levels and this causes a rise in JNK (mitogen activated protein kinase). JNK's do many things in our bodies. One major function is to respond to inflammatory cytokines like IL-6 and to leptin. Remember from my first leptin blog I told you that leptin and IL-6 look chemically quite similar to one another. In our GI tract, JNK directly inhibits ATF4 in the

gut effectively turning off all osteoblastic formation! So we cannot make anymore bone, even if our diet is loaded with good foods! You all know that LR also leads to high cortisol levels, and these high levels also cause us to resorb bone in far greater amounts at the osteoclast footplate further worsening the osteopenia to osteoporosis. Most people know that excessive steroid use can cause osteoporosis too. Chronically elevated cortisol levels also does this to overweight people as well.

Obese individuals with diabetes often exhibit high blood levels of both leptin and insulin. Researchers are trying to understand the interaction among leptin, osteocalcin, and beta cells in the hope of developing new treatments for diabetes. Anyone I see with this disease gets placed on vitamin K2 and now you can see why. I also think anyone with T2D must consider taking Vitamin K2 as well as their other needs. I don't think we need to wait for more research on this issue. We have 60 million T2D in the USA and 150 million who likely have it but don't meet our current guidelines to diagnose the disease. Ten years ago, the Vitamin D council was talking up D3 and telling us how important it was and why we need to be on it. Dr. K is now telling you that Vitamin K depletion is likely a bigger deal than Vitamin D deficiency because no one, including most primal folks, recycle enough of K2 or replace it in their diets in this country. If you doubt me, go get your osteocalcin checked if you eat a lot of carbs or PUFA's. Population studies have been done on K2 and it backs up what I found in my clinic over the last 12 years. We have a major K2 deficiency problem, and it's a lot more significant than the current D3 issue that is finally being addressed. Why? When we are depleted of K2, we tend to calcify our coronary arteries. These plaques are the ones that kill us suddenly. Last I checked, heart disease remains the number one cause of death for men and women in the USA. The Jupiter trial data also showed that calcium index scores are probably the best clinical marker we have for silent heart disease. Peter, over

at Hyperlipid, wrote about this topic on his site that you should read.

What about carbs?

Here is one of the twists and turns I told ya was coming. On our bone forming cells we have a special LDL receptor. The surface molecule Lrp5 (LDL receptor related protein 5) is a gene of great interest to bone biology. When Lrp5 is inactivated, we see the worst cases of osteoporosis in humans. Surprisingly, the gene most highly expressed in micro arrays studies when Lrp5 is absent is Tph1, which encodes tryptophan hydroxylase 1. This is the rate-limiting and initial enzyme in the synthesis of serotonin in enterochromaffin (EC) cells of the GI tract! It turns out serotonin is not just a neurotransmitter. Remember we make most of our serotonin from dietary carbohydrates and not protein. I went over this in my neurotransmitter blog. Here is a quick reminder. Remember tryptophan is the least common AA in our diets. This also complicates serotonin biochemistry. Tryptophan is found in fish, poultry, and dairy products, but eating these products does not necessarily increase serotonin levels. The reason for this paradox is because other foods compete with tryptophan for absorption in the gut! It has to compete with other AA. In fact, another paradox of serotonin production is that is eating carbohydrates raises its level in the body faster than does eating a protein diet! The reason for this is that carbs stimulate insulin release, and this insulin spike favors the absorption of tryptophan in the gut over other amino acids. Most serotonin is stored in the enterochromaffin cells of the gut lining (60{a7b724a0454d92c70890dedf5ec22a026af4df067c7b55aa6009b4d34d5da3c6}), and the balance is stored in the pineal gland of the brain.

Serotonin is now also **categorized as a gut hormone that inhibits osteoblastic bone formation!** Yes, you read that

right. The gut hormonally regulates bone formation! When I realized this, I finally put together why I was seeing so much osteoporosis. It was the SAD and Leptin resistance at work directing our gut not to form any new bone. The more of a SAD you eat, the worse your gut microflora becomes and the more Vitamin K2 you can't recycle. This requires a much higher K2 requirement from the diet. In the US food supply Vitamin K2 is horrifically deficient. The end result is you get depleted of K2 and you never can activate your osteocalcin by carboxylating it.

Serotonin begins with the AA tryptophan. It requires B6, Mg, B12 and folate as co factors in production. So high levels of serotonin block our ability to lay down new bone. The data in the literature on this are pretty deep. I am still amazed that few people in my world of spine surgery talk much about this at all. I'm also puzzled that our orthopedic sports medicine folks and the general orthopedists never mention this at all to patients. In fact, they often tell people to carb load before and after exercise. This completely is counterproductive to healing any bone!

So how does this all work? Your head is getting ready to hurt. Gut-derived serotonin regulates bone mass accrual in humans. LDL receptor related protein 5 (Lrp5) favors bone formation by inhibiting tryptophan hydroxylase 1 (Tph1) expression in enterochromaffin cells of the duodenum. The gut-derived serotonin, following its binding to Htr1B on the osteoblast cell, and this inhibits CREB expression, which results in a decrease in cyclin expression and leads to osteoblast proliferation and lots of new bone formation. Most of my patients get told what they should eat pre and post op because of this science I read about. I rarely go into the biochemistry of why this happens, but here it is for all of you to read about. I have them eat a ton of pastured butter, raw dairy, coconut oil, eggs and grass fed meat and limit their carbs to less than 50 grams a day. All these things

support optimal bone function.

The implications of the new experimental news on Lrp5 is that inhibition of serotonin biosynthesis in EC cells may actually provide an anabolic treatment for osteoporosis! This also explains why we see so much osteopenia and osteoporosis in our vegan and vegetarian friends. The effects of serotonin are remarkable for another reason. One experiment suggested a broader clinical implication for enteric serotonergic regulation of bone mass. In mice that totally lack Tph1, researchers found virtually no detectable circulating plasma serotonin and a high bone mass phenotype because of an increase in bone formation parameters. This was shocking. Remarkably, even gonadectomized (ovaries removed) female Tph1 mice did not develop osteoporosis because their increase in bone formation parameters outperformed the increase in bone resorption caused by the gonadectomy. **This means that menopause may not mean automatic bone loss if we can get ladies to change their diets.** Remember this could have major implications for post menopausal women if the same effect is found in humans. So far the data seem to be pointing us in that direction. Because of this, I advocate this dietary advice for patients with this disease. This observation is potentially important clinically for humans, because the therapeutic drugs some use against osteoporosis that is currently in use, is mostly geared toward inhibiting bone resorption and not adding new bone. Forteo and PTH are the only two substances used today that are anabolic treatments for osteoporosis. Both have major side effects. Using diet to do the same thing is a lot safer in my view and this is how I currently treat osteoporosis.

Does meal timing of the Leptin Rx play a role here too?

The short answer is yes it does. I told you in the blog about

how the Leptin Rx works that meal timing is more critical than even food choices. Lets talk a bit about what happens at meals. We eat and the food in our gut is sensed by the vagus nerve and also by the EC cells of the gut. When food enters parts of the gut, it creates a intraluminal pressure. This pressure is what causes our gut to release serotonin from our EC cells to stimulate bone formation. Remember that diabetics are also prone to gut stasis, and this decreases serotonin release and is another cause of osteoporosis in diabetics. Experiments by Edith Balbring and her colleagues have confirmed that EC cells secrete serotonin in response to increases in intraluminal pressure. My morning 50 to 70 grams of protein creates a bigger intraluminal pressure because of the shear volume of food that enters your gut, and is also why we want to eat this large a portion in the AM for breakfast. The big ass breakfast (BAB) also stimulates peristaltic waves in the gut and this further releases more serotonin from the gut that might hinder bone formation. This is offset by the fat and protein loads in the BAB. Another major effect of the BAB is that it is a big stimulus to the secretion of testosterone and growth hormone in the body when this occurs. Both of these hormones are anabolic to bone and to muscle. This is also why the BAB helps body composition when it is applied over long periods of time. This can be followed with lab testing of testosterone levels and IGF-1 levels. Intraluminal pressure also releases gut bile acids and some other hormones like NYY, CCK, and pancreatic enzymes too that are critical in creating the proper satiety signal in the brain to stop eating.

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- Hormones 101: Clinical thoughts revealed
- Leptin: Chapter One
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- My Leptin Prescription
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