

Leptin: Chapter One

Readers Summary

1. Why is leptin the Master Hormone?
2. What labs tell you about your leptin status
3. Leptin's connection to the brain
4. Leptin's relationship to organs energy requirements
5. Obesity is an inflammatory condition caused by leptin dysregulation not insulin

Okay, so you have heard me talk a lot about **leptin**. Why is it so important? It is a hormone that controls all of energy metabolism in the body. Not only that it controls all the other hormones in the body as well. So if it is not working well you can bet that the rest of your hormones are going to show clinical problems as well. I can't tell you how many people think they have thyroid issues when all the time they have been leptin resistant. One becomes leptin resistant when the brain no longer recognizes the leptin signal sent from our fat cells. Testing leptin is easy to do but rarely done in medicine today. The easiest way is to look in the mirror. If you're way too fat or way too thin guess what? You are leptin resistant, most likely. Biochemically we can also assess it with a test called a **reverse T3** level. This is rarely ordered because many docs don't know about the test and because it is not covered by insurance. **Reverse T3** is a competitive inhibitor to **T3** and **T4**. Those are your thyroid hormones. So yes, leptin resistance completely turns off your thyroid gland! That does not allow you to burn fat in your muscles because it downregulates your basal metabolic rate. Now you know what controls your metabolism too! That process is called peripheral (muscle) leptin resistance. That is why some fat people can not burn fat with exercise. That is why your thyroid test is close to worthless clinically in leptin resistance. I bet many of you just had an epiphany!

The brain has to get information on the energy status of **20 trillion** cells in your body at all times. Due to constraints of space (your skull size), it does not monitor every single cell in the body with a nerve cell connection to complete that task. It uses the endocrine system to do that. That is the system that hormones come from. Leptin is made from your white fat cells in your body. But you first get leptin from your mother when she first breast feeds you. So if you were not breastfed you may have started life off on the wrong foot from an energy metabolism standpoint. In fact, the latest research is showing that not getting leptin from your mother's colostrum has huge implications right away for your DNA. It affects a chemical process that alters your DNA called methylation. That information is transmitted directly to your DNA and causes a change that leads to epigenetic signals. This is one way we know obesity can be transmitted across generations. There are others.

Leptin enters the brain through some complex signaling that occurs in the hypothalamus. Once it enters the brain it begins to set off a group of neurons that will modulate your energy status for the remainder of your life. This part of your brain is about the size of a pea and it sits right on your nerves that go to your eyes. Imagine a hole drilled between your eyes straight back about 5 inches. That is where all the action happens. The hypothalamus links the brain to all your endocrine system in the body. The endocrine system includes every hormone you have heard of. The hypothalamus also modulates many of the most important centers in the brain. Without energy, no animal could live or carry out any complex tasks. Think about your car for a minute. How far could you go if you never knew how much gas you had? The only way to go anywhere and feel safe is if you just filled up and went. But then again you'd never know when it was time to fill up again either would you? That is precisely what happens to a human when they are leptin resistant. The brain can't tell what the energy status is in the body. The energy status is your fat

cells. Leptin is that connection from fat to the brain. It controls everything to do with energy and information. Without energy or information, everything fails.

Some of the organ systems in the body that rely on energy the most are also tied to leptin status. Once such tissue is bone. Bone is incredibly active as it constantly remodels to stresses it is placed under. To allow a system that wide range of change it requires massive energy sources. That is why leptin is important in bone physiology. Leptin resistance always pre-dates the development of osteoporosis. Leptin also controls the ability of women to get pregnant. That is called fecundity. If a woman is leptin resistant, she will have a lot of difficulties getting pregnant. We see this in PCOS (polycystic ovarian syndrome), in anorexia, or overtraining. Having a baby requires a lot of energy for growth. Leptin is the key for that process to occur smoothly.

Leptin also controls and modulates the immune system in the brain too. It is chemically very similar to an inflammatory chemical called IL-6 (interleukin 6) and in people, with high leptin levels (fat people) we see high levels of white blood cells. It also modulates all the inflammatory cytokines associated with visceral fat. Generally, when someone is leptin resistant they also have low vitamin D levels. I also use this as a proxy to assess leptin status in working up patients. Visceral fat is the fat below your "six-pack" muscle in your abdominal cavity. This is one of the worse places to get fat because it is highly inflammatory. That is also the fat seen in type two diabetics that fills their liver cells. That is called metabolic syndrome or nonalcoholic fatty liver disease. Elevated leptin is also the first sign seen before high blood pressure shows up and causes a cascade of further physiologic problems. The reason for this is that high levels of leptin will destroy another protein secreted in the beta cells of your pancreas called amylin. The beta cells in the pancreas make insulin. So you now know why high levels of

leptin (fat) cause type 2 diabetes. The high leptin fries the amylin in the beta cells and causes them to stop making insulin eventually. If it takes a long time it can cause type two diabetes.

If that process happens fast, for example, because of an autoimmune response surrounding a pregnancy or a leaky gut then you can get autoimmune diabetes often called type 1.5 diabetes. The only difference between type 2 and type 1.5 is the time is shorter and the immune response much greater. Again, all mediated by leptin resistance. The chronic leptin elevation leads to eventual leptin resistance and usually occurs 5-7 years before someone becomes insulin resistant! (Type 2 DM) Today's medicine focuses in on insulin to treat diabetes. In my view, this is completely off target. It makes no sense to treat insulin resistance after it has occurred. It makes more sense to target leptin resistance because it occurs 5-7 years before insulin resistance occurs! It is now clear that obesity is a disease of inflammation. But we know obesity has several causes. Obesity is not a disease of excess calories. Why? Because the body has several built-in ways of dealing with calorie excess without you ever getting fat if leptin is working properly in your liver and your muscles. I promise I will get to that story too soon in a future blog. Obesity is a disease of inflammation and hormonal disruption of hormone signaling. That is why you want your physician to remain vigilant and concerned with measuring your ultra sensitive or cardiac CRP with regularity. Now you know why I do this test on all my spine patients. Leptin problems tell me degenerative disc disease and osteoporosis are going to occur in this patient unless I solve their leptin problems eventually. In my opinion, it is a test that needs to be monitored more than any other in medicine until a better one appears. It can tell us a ton about your current cellular terrain. Remember levee one in The QUILT. Whatever happens to your cells determines what will happen to you eventually. If your inflammation is elevated bad things are in your future as

you will see as the quilt expands.

Here is the key point to take home: **Leptin resistance always precedes the development of insulin resistance.** (minus traumatic pancreatic loss) Once both occurring long enough it leads to adrenal resistance. And adrenal resistance means you have a problem with CORTISOL. Don't forget this point. It's that important. When insulin and cortisol are raised simultaneously and chronically this is how cancer and chronic diseases humans occur by effecting the p53 gene (oncogenesis levee). They all start with **leptin** problems, not insulin issues.

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