

Leptin Part Deux: Liver

Readers Summary:

1. The liver is the engine of metabolism and not the thyroid
2. What does the liver do in normal metabolic conditions and in leptin resistance
3. Where does a cholesterol (LDL subtypes) fit into this leptin story?
4. How does Metabolic Syndrome commence and why does it happen.
5. Why your regular labs may be completely normal while you're slowly dying.

Many people are under the assumption that the thyroid is the real key to metabolism. I can't tell you how many meetings I have been to and heard this nonsense. It happened today while I was speaking to a dietician and nutritionist in a hospital. It's just not correct. The liver is the engine of our body's Ferrari! The thyroid is best described as the gas pedal for the engine and leptin is the electronic chip that controls the entire process. So we need to discuss some biochemistry now. Rub your head a few times before we start to increase your blood flow!

When humans eat a meal about 60% of the calories wind up in the liver to deliver energy to tissues between meals to sustain normal energy production. Another hormone, Glucagon, mediates this release of fuel. The remainder of the energy (40%) is sent packing to the peripheral tissues and the muscles where insulin allows the energy to enter the cells. If those cells are leptin sensitive they use all 40% of the calories with nothing left over. If they are leptin resistant the excess calories go directly back to the liver to be placed into fat storage (or stuck inside the liver cell) in fat cells

because of the high insulin levels. The more fat that gets deposited, the higher leptin levels go over time. If the fat gets stuck in the liver it causes a large immune reaction driving up more inflammatory chemicals. When it gets to a critical level (different body fat levels for all people) the fat begins to make the bad stuff. (IL6 and TNF alpha)

At the liver level, something new happens though. Because muscles (muscle leptin resistance) can no longer use the calories partitioned to them they return to the liver. Leptin resistance in the liver also downregulates the LDL receptor in the liver. This also changes how DHA can enter cell membranes all over the body. This allows the LDL particle to stay in the blood longer making it more susceptible to oxidation and disease. The liver responds by packaging this fuel into LDL particles to get rid of it. If the meal is high in carbs it makes small dense LDL. (**SdLDL**) If the calories are high in fat or protein the LDL is intermediate or large fluffy LDL. (IDL or VLDL) SdLDL is the particle that causes many chronic diseases when it is present in excess chronically. It correlates best with heart disease and stroke risk. This is the most important thing to take away from a lipid panel. You want this number as close to zero as possible. sdLDL also causes high blood pressure and atherosclerosis because it damages the vascular endothelium (lining of an artery) and the LDL particle is small and dense so it fits between the endothelial cells and deposited in the arterial wall to make it a lead pipe. Before it gets into the artery wall it usually becomes oxidized (rusted) because it is chemically very sensitive to chemicals that cause oxidation. (IL6, TNF alpha, and ROS are some of these) The large fluffy VLDL is not a problem because they **can not** fit in vessel walls so most go to our fat under the control of **LPL** and **hormone-sensitive lipase**. (Estrogen and testosterone levels determine where in the body this fat goes and stays!) This is the real reason why andropause and menopause cause weight gain in specific parts of your body as you age. Your sex steroid status varies with

the amount of inflammation present at the cellular level because of resonance changes in your pituitary gland. Understand that the inflammatory chemicals from the fat are what cause this to happen over time.

Having your liver make a ton of SdLDL is a huge problem for health. Eating **carbs** result in high sdLDL and not fat or protein. **Fructose** is a special carbohydrate that makes more sdLDL than another sugar nature builds because of the hydrogen it contains. The liver's physiologic function mimics the sun in many ways. Building sugars are one such example.

Therefore, the liver has to handle it differently biochemically. The large amounts of these particles cause the liver to make a ton of triglyceride particles to store all the sdLDL's for storage in the bad places like are arteries, viscera, heart or liver.

Key Point: Hepatic insulin resistance occurs when the liver decides all excess calories must be packaged and stored as fat which fuels the obesity. OK, reference point. When the liver working well and not leptin resistant what does it do? Remember the 60/40 split of calories from a meal we spoke of earlier? The liver should use the stored 60% of those calories to feed the body fuel when we are not eating like during a fast or during sleep. This is done by raising the hormone glucagon to make fuel from the energy depots in the liver. This is how the body works to supply fuel it needs when we can't eat or won't eat. The liver is a fuel bank account for use on a rainy day when we are leptin sensitive. This pathway way does not work well at all when we are leptin resistant because the liver is spewing out excess fuel for storage instead of use. It also hinders how cell membranes work all over the body because of DHA incorporation is blocked at the liver level.

When we are leptin resistant the end result is to package calories to fat in some form of LDL's. That delivery has to leave the liver because there is a physical limit to how much

fat can stay in the liver. If this process of LDL construction is chronic and overwhelms the liver, fat builds up inside the liver cell and causes extreme reactive oxygen species (ROS). Remember The Quilt's levee number seven? These are the inflammatory chemicals that insidiously kill cells and are at the heart of all chronic diseases you know of. This process is called the development of fatty liver or the **Metabolic Syndrome**. If the liver continues to be clogged with fat it physically grows and your waist size grows with it. This is why physicians are so concerned about your waist size. It also correlates with your blood test called an ultra-sensitive CRP! As your waist grows your cardiac CRP goes higher too. But if you are paying attention to the 30,000-foot view here, the growth of your waist size is a **very late** development in your disease process. If your waist is large, you have been asking your liver work like mad to store this excess fuel for a long time. The end result for the patient is a sign of a feeling of **chronic fatigue**. You also report a loss of energy if you are asked and it occurs slowly over time and nothing the doctor or you do seem to help. All your basal metabolic studies look fine. Your thyroid panel is unremarkable and you tell the doctor no matter how little you eat or as much as you exercise nothing seems to help the process. Does this sound familiar to anyone reading this? This is classic **Leptin Resistance at the liver level!**

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