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The Disharmonious Quartet

By: James L. Holly, MD

Few things are as lovely as a harmonious performance of great performers, whether singing, or playing instruments. Voices which blend together in a melodious sound are pleasing to the ear and produce strong and positive emotions in all of us. Similarly, few things are as beautiful as the physiology and the metabolism of the human body when all elements of both are working together for health and wellness.

On the contrary, have you ever heard a quartet when one performer is “off key?” Now, you may be like me and not know exactly what it means to be “off key,” but you certainly know what it sounds like and it is not pleasant. Likewise, you may not know much about the metabolism of the human body, but you sure recognize when something isn’t working right.

A performing quartet can be made up of a tenor, a baritone, a soprano and a bass, or many other combinations of voices. Our “disharmonious quartet” is made up of four “bad actors” which together produce devastating results in the human body. Both the good news and the bad news is that something can be done about them. The good news is there is something that can be done; the bad news is ONLY you can do it.

Before identifying our quarter, let’s look at where they come from. Each member of our “strained” quartet – the strain is on the heart and arteries – comes from a condition called “insulin resistance.” This occurs when your body ceases to respond properly to insulin. But why does it do that?

Fat is actively producing hormones

We have always thought of fat on our body as a nuisance, maybe unsightly, but “no big deal.” Unfortunately, it is a “big deal.” And, the deal is that fat, far from being inactive, is producing a number of hormones call “adipokines.” But, it is not ALL fat which is doing this, just the “bad,” or “dysfunctional fat cells” which produce these harmful substances. The fat under your skin, the subcutaneous fat, is normal and healthy.

Ectopic Fat – Fat Where It Doesn’t Belong

There was a time when we thought that fatty deposits in the liver, muscle and around the waist (visceral or organ fat) were just unsightly, but they are far worse; they represent one of the great health crises of the United States. This “ectopic fat” – fat which is found where it doesn’t belong, i.e., in muscle, liver and around the organs in the abdomen – is causing many illnesses. In fact, the “adipocytokines” which are produced by these “ectopic fat” cells cause:

- Insulin resistance which leads to Diabetes Mellitus type II
- Inflammation in the arteries which leads to heart disease, heart attacks and strokes
- Hypercoagulable (increased tendency for the blood to form clots) states which leads to blood clots, strokes and heart attacks
- Abnormal cholesterol and triglycerides
- Hypertension with heart disease, kidney disease and strokes.

Disharmonious Quartet

The disharmonious quartet is made up of:

- Decreased insulin secretion b-cells – the beta cells are found in the pancreas and they produce insulin. When insulin resistance develops because of fat accumulation in the muscle, liver and around the abdomen, the pancreas produces more and more insulin in an effort to compensate for the failure of the liver, muscle and fat to respond. Eventually, the beta cells become exhausted and insulin production goes down. This is the point when insulin resistance transitions to being Diabetes Mellitus Type II.
- Decreased glucose uptake muscle -- the normal affect of insulin on the muscle is to increase glucose uptake into the muscle cell as a source of energy for the work of moving the body. When the body stops moving very much – when it becomes sedentary (couch potato) – and when fat is deposited in the muscle, liver and viscera, the muscle ignores the effect of insulin and does not absorb the glucose from the blood stream. This raises the blood sugar level which is toxic to the body and which worsens insulin insensitivity moving it gradually toward Diabetes Mellitus Type II.
- Increased hepatic glucose production – the normal affect of insulin on the liver is to decrease production of glucose by the liver. When you eat a meal, there is a Phase I release of insulin which tells the liver, “Don’t make any more sugar, we have a load coming from our friends the mouth and the stomach.” With insulin insensitivity, the liver ignores insulin, responds to all of the hormones being produced by the fat and keeps pumping our glucose (sugar). That is why the blood sugar two-hours after eating goes up in insulin resistant, pre-diabetic and diabetic patients even though the sugar from the recent meal is adequate for all energy needs. In insulin resistance and Diabetes Type II, the Phase I insulin response is absent, or decreased and the liver does not respond to insulin by stopping sugar production.
- Increased lipolysis fat cells – the normal response of fat cells to insulin is to not breakdown complex lipids and release “fatty acids” into the blood stream But, remember this is the response of subcutaneous fat – the fat under your skin which helps you maintain your body temperature and the health of your skin. But the “ectopic fat” – fat where it doesn’t belong and fat which is the result of “over nutrition” or “under activity” – doesn’t respond to insulin and keeps pumping out free fatty acids (FFA) into the blood stream. These FFA are toxic to the body; they sing a song which is not pleasant.

Free Fatty Acids (FFA)

FFAs are stored as triglycerides in fat cells (adipocytes) and FFA serve as a source of energy during fasting conditions. As mentioned above insulin inhibits the release of FFA from the fat cell. In the insulin resistant person and in Type II Diabetic, insulin's ability to inhibit lipolysis – the release of FFA from triglycerides – is markedly reduced.

Chronically, elevated plasma FFA causes insulin resistance in the muscle and liver and also causes decreased insulin secretion from the beta cell in the pancreas. Thus, the source of our disharmonious quartet:

- a. Decreased insulin secretion b-cells
- b. Decreased glucose uptake muscle
- c. Increased hepatic glucose production -- liver
- d. Increased lipolysis fat cells.

Lipotoxicity

Increased FFAs are toxic to the human body and particularly to the lining of the arteries and to the pancreas. The immediate affect of elevated FFA is to increase insulin secretion, as the body tries to rid itself of this toxic substance. However, longer term exposure to elevated FFA results in a decrease in pancreas beta cell response to increased glucose levels.

Lipotoxicity is a term which was coined to describe the negative effect of chronic FFA elevations on insulin secretion by the pancreas's beta cells. Lipotoxicity accelerates beta cell death (apoptosis) and decreases the number of beta cells by 50%. This is the point at which Diabetes Type II is usually first recognized. It is startling to realize that 50% of the pancreas's insulin secretion function has been lost before diabetes is recognized.

Fat is far from being harmless. In coming weeks, we'll talk more about the "secret life" of fat and what we can and should do about it.

Through SETMA's specialty clinics, you can receive the best, up-to-date, state-of-the-art treatment for all elements of the disharmonious quartet:

- Metabolic Syndrome with Dr. Keith Stout
- Cholesterol with Dr. Vincent Murphy
- Hypertension with Dr. Muhammad Aziz
- Weight Management with Dr. James L. Holly

Remember, it is your life and your health.