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Cardiovascular Disease Risk Factors Part XII
Insulin Resistance
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As we approach the end of our extended series on cardiovascular disease risk factors, let's try to put what we have learned so far into a cohesive, comprehensible and hopefully comprehensive picture of what causes cardiovascular disease and what we can do about it as individuals. Here is what we have covered thus far:

Part I – Introduction
Part II – Sedentary Life Style Part
III – Obesity
Part IV – Smoking Part V –
Cholesterol Part VI –
Hypertension
Part VII – Combined Factors which begin in childhood Part
VIII – C-Reactive Protein
Part IX – Family History Part X –
Psychosocial Stress Part XI –
Age

(All of these articles can be reviewed on SETMA's website at www.jameslhollymd.com under the section "Your Life Your Health.")

Remember in our introduction, we identified three categories of risk factors for cardiovascular disease risk:

1. Major and independent risk factors
2. Condition risk factors
3. Contributing risk factors

Insulin Resistance

One theory which integrates our knowledge of the causative factors of cardiovascular disease is insulin resistance. To understand this condition, we must first understand what insulin does. Insulin, along with a number of other hormones such as Glucagon, Growth Hormone, Incretins, and others, maintains blood sugar levels in a "normal range," as well as helps provide glucose (sugar) to the cells of the body to produce the energy needed to breath, walk, talk, think and perform all of the other functions which are necessary for the maintenance of life.

Here is how insulin works.

When you eat a meal, some of your food is absorbed and immediately changed into a simple sugar like glucose. This causes your blood sugar to go up. When the body senses this increase in blood sugar, it insulin is immediately released from the pancreas. Insulin then signals other cells in your body – fat cells, muscles cells – to "open up" and take in the excess sugar in the blood. Interestingly, brain cells do not require insulin in order to take in glucose. The brain takes in all of the sugar it needs with or without the presence of insulin.

Insulin also signals the liver to stop making sugar. The way your blood sugar is maintained at a normal level between meals and during a fast is that your liver is constantly taking complex molecules and transforming them into glucose (a simple sugar). This process is called **gluconeogenesis** ("**gluco-**" for glucose; "**-neo-**" for new; "**- genesis**" for "to make") When you eat a meal, or a snack, insulin is produced by the pancreas. Insulin signals the liver to stop making glucose.

These two processes balance the nutritional intake of sugar and the liver's production of sugar to maintain normal blood glucose. This constant balancing act is important because while glucose is critical for life processes, excess sugar damages the kidneys, the eyes, the heart, the blood vessels, the nerves and many other parts of the body.

Insulin Resistance

In normal circumstances fat cells, muscles cells and the liver respond to insulin's signal and balance the blood sugar. However, under a variety of circumstances, the liver, the fat cells and the muscle cells do not respond to insulin. This condition is called "insulin resistance." In this condition, when insulin arrives at the liver during and after a meal, it sends it signal, "Stop making sugar (glucose), we have a truck load coming from the mouth, esophagus, stomach and intestines." However, in the case of insulin resistance, the liver ignores the signal, continues to make sugar and the blood sugar continues to rise.

The same thing happens in the fat cells and in the muscles. Insulin signals the cells to "open up" and take in the sugar in the blood and the signal is ignored. Thus the blood sugar continues to rise.

Hyperinsulinemia

At this point, the pancreas does not give up. As the blood sugar rises; as the liver continues to produce glucose out of other molecules, and as the fat cells and muscle cells fail to "absorb" the excess glucose, the pancreas produces more insulin. When the insulin levels rise to abnormal levels, this condition is called "hyperinsulinemia." In the early stages of insulin resistance, the elevated insulin level finally gets the message to the liver, fat cells and muscle cells and the blood sugar rapid returns to normal.

Eventually, however, the stress on the pancreas becomes too great and the pancreas is unable to keep producing the excess insulin and the blood sugar begins to remain abnormally elevated chronically. At first, this will be seen in an abnormal fasting

glucose; then in an abnormal blood glucose response to a Glucose Tolerance Test, and eventually Type 2 Diabetes develops.

What Causes Insulin Resistance?

Genetics apparently play a significant part in insulin resistance as everyone with the acquired conditions which are associated with insulin resistance do not develop insulin resistance, or diabetes. If you have a first, second or third degree family member (see *The Examiner*, Your Life Your Health, August 25, 2005 for an explanation of these terms, or go to www.jameslhollymd.com) with type 2 diabetes, you will be at a higher risk of developing insulin resistance. Other inherited factors which will place you at a higher risk are:

- If you have been diagnoses with cardiovascular disease, hypertension, polycystic ovarian syndrome, non-alcoholic fatty liver or acanthosis nigricans.
- If you are non-Caucasian.
- If you have a family history of hypertension or cardiovascular disease.
- If you had gestational diabetes or glucose intolerance during pregnancy.
- If you are over 40 years of age.

The other factors which promote insulin resistance are:

- Sedentary Lifestyle – being a couch potato
- Obesity and particular abdominal obesity

How Does Obesity contribute to or Produce Insulin Resistance?

It has long been popularly thought that fat cells are just unsightly, inactive cells which add weight and bulges to the torso. Unfortunately, fat cells are actually little "endocrine" glands which produce a variety of hormones, almost all of which are harmful to the body. One of these is a substance "Resistin," which causes insulin resistance. Another is "Angiotensinogen," which increases the levels of Antiotensin II which has been implicated in the development of atherosclcerosis. Fat cells also produce Plasminogen activator inhibitor-1 (PAI-1) which favors the formation of blood clots and accelerates the atherosclerotic process.

Is there a relationship between Insulin Resistance and Cardiovascular Disease?

There is a very strong association among insulin resistance, hypertension and accelerated cardiovascular heart disease. In 2003, the American College of Endocrinology (ACE) published a "Position Statement on Insulin Resistance." In part, the ACE said: "While the majority of insulin resistant individuals do not become frankly diabetic, they remain at increased risk to develop cardiovascular disease…".

The keynote address in May, 2005 at the 4th Working Group on Insulin Resistance was entitled "Insulin Resistance and Vascular Disease." The following relationships were identified. Genetic and environmental factors (obesity and sedentary lifestyle) produce insulin

resistance, which in turn, by means of the following"

- Hyperglycemia (Impaired Glucose Tolerance)
- Dyslipidemia
- Hypertension
- Endothelial Dysfunction (Microalbuminuria)
- Hypofibrinolysis
- Inflammation produces

vascular disease

Endothelial Dysfunction and Insulin Resistance

The lining of arteries is called "endothelium." It was once thought, as it was of fat cells, that the endothelial cells were passive conduits for blood flowing through the arteries.
We now know that endothelial cells are highly active and that when they don't function properly, arterial disease – cardiovascular heart disease, cerebrovascular disease and peripheral vascular disease – develop. "Endothelial dysfunction" is an early event in atherosclerosis and endothelial dysfunction is closely associated with insulin resistance.

Improvement in the following, all of which are associated with insulin resistance:

- Hyperglycemia – high blood sugar
- Hypertension – high blood pressure
- Microalbuminuria – protein in the urine
- Endothelial Dysfunction – failure of the artery lining to function properly
- Dyslipidemia – high cholesterol
- Hypofibrinolysis – increased clotting of the blood
- Inflammation – infection and/or inflammation of the lining of the arteries

prevents, delays or decreases vascular disease.

What Can You Do?

1. **Control Your Insulin Levels** – you can decrease the demands on your pancreas by decreasing the total amount of food you eat and by changing the kind of food you eat. The total calories are important, as all foods, whether protein, carbohydrate or fat, will be processed into sugar by the liver. The type of calories is important because some foods are absorbed much more rapidly than others and therefore raise your blood sugar much more rapidly and higher.

   We call these foods "high glycemic" – foods that raise your glycemic level. Mashed potatoes for instance are absorbed very rapidly and cause your blood sugar levels to go up very high very fast. This makes your pancreas work harder to produce insulin to get the blood sugar down to a normal level. Proteins and fats on the other hand slow the absorption of foods and allowing your blood sugar to rise slowly making it easier on

your pancreas. You can read more about the glycemic index and the glycemic load at www.jameslhollymd.com.

2. **Lose Weight** – decreasing the fat around your abdomen will decrease the secretion of the harmful hormones by the fat cells in your body.
3. **Exercise** – regular exercise not only will help you decrease and control your weight, but also will help your body maintain a normal blood sugar and therefore decrease the demand on your pancreas for more insulin production.

In its Position Statement on the Insulin Resistance Syndrome, the ACE also said, "The most powerful modulators of insulin action are differences in degree of obesity and physical activity…Finally, it should be emphasized that obesity and physical inactivity are variables that not only significantly increase the likelihood of an individual being insulin resistant, but also represent predictors of the Insulin Resistance Syndrome."

Do you want to decrease your risk of cardiovascular disease? Of course, you do. How? Lose weight, exercise, change what you eat, stop smoking…. These are simple and inexpensive measures, but they require the currency which is in short supply in America today: self discipline, self control and delayed gratification. Don't ever forget, and always remember, it is your life and it is your health..