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The Cardiometabolic Risk Syndrome Part II – Insulin Resistance By James L. Holly, MD Your Life Your Health *The* Examiner December 7, 2006

Points to Remember as you learn more about The Cardiometabolic Risk Syndrome

- Glucose is the simple sugar that is the main source of energy for the body's cells.
- Insulin helps cells take in blood glucose and convert it to energy.
- If you have insulin resistance, your body's cells do not respond well to insulin.
- Insulin resistance is a stepping-stone to type 2 diabetes.
- Lack of exercise and excess weight contribute to insulin resistance.
- Engaging in moderate physical activity and maintaining proper weight can help prevent insulin resistance.
- Insulin resistance plays a role in the development of cardiovascular disease, which damages the heart and blood vessels.
- Controlling blood pressure and LDL cholesterol and not smoking can also help prevent cardiovascular problems.
- The Diabetes Prevention Program confirmed that exercise and a low-calorie, low-fat diet are the best ways to prevent type 2 diabetes.

Insulin helps the cells of the body use sugar (glucose) as fuel. Insulin is a hormone secreted by the pancreas. It helps the body utilize blood glucose (blood sugar) by binding with receptors on cells like a key would fit into a lock. Once the key -- insulin -- has unlocked the door – the cell wall -- glucose can pass from the blood into the cell. Inside the cell, glucose is either used for energy, or stored for future use in the form of glycogen in liver or muscle cells. Interestingly, the brain can absorb sugar without the need for insulin which protects the brain from the damage which would be caused by the brain's sugar levels dropping too low.

Insulin resistance occurs when the cells no longer respond well to insulin. Muscle cells don't "open up" to sugar and liver cells don't stop making sugar. Therefore, the cells don't get the fuel they need, the liver keeps making more glucose and the body keeps making more insulin in an effort to lower blood glucose levels. Insulin resistance may be a key component of cardiometabolic risk, and may cause other problems to develop.

The ability of insulin to transport glucose varies more than 600% in the population at large. The one-third of people with the most insulin resistance are sufficiently insulin resistant as to be at greatly increased risk to develop a number of abnormalities and clinical syndromes.

Type 2 diabetes develops when your pancreas can't keep up with your body's demand for insulin. This is generally because your cells become resistant to insulin. If your body

becomes resistant to the action of insulin, glucose processing is impaired. Your body reacts by churning out more and more insulin in an effort to help glucose enter your cells. This extra insulin helps maintain normal glucose levels in your blood for a while, but eventually your pancreas is unable to overcome insulin resistance. As a result, glucose accumulates in your body, ultimately leading to type 2 diabetes, which is the most common form of diabetes. It formerly was called non-insulin-dependent diabetes, or adult-onset diabetes. These terms were unsatisfactory because sometimes people with Type 2 diabetes need insulin to treat their diabetes effectively, i.e., they become insulin dependent even with type 2 diabetes, and more and more children are developing type 2 diabetes.

Another important function of insulin is to signal the liver to stop making sugar. One of the many functions of the liver is to take the complex carbohydrates which you eat and process them into simple sugars which can be used by your body. After a meal or snack, when sugar levels go up, insulin levels also go up. This signals the liver to stop producing sugar. However, when the body becomes resistant to the effects of insulin, the liver ignores the insulin and continues to produce sugar even when the blood sugar level is high. The cardiometabolic syndrome occurs before the point when the muscles cells fail to respond to insulin, when the muscle cells don't absorb as much sugar and when the liver fails to respond to insulin, and when the liver continues to produce sugar in the face of elevated blood sugar levels.

Elevated sugar in your blood is toxic to a number of organs, including your eyes, your heart, your arteries, your kidneys and others – even when your glucose levels are not high enough to classify you as diabetic. Before you are classified as diabetic, the excess insulin in your system puts you at risk for many health consequences. The levels of cholesterol and triglycerides – another blood fat — in your bloodstream may increase, causing damage to your coronary arteries. And, excessively high insulin levels may interfere with your kidneys' ability to process salt, which can raise your blood pressure.

Diagnosing Insulin Resistance

The test that most accurately measures insulin resistance is too complicated and expensive to use as a screening tool in most doctors' offices. However, there are two tests which give excellent information about the presence or absence of insulin resistance. One is the **Triglyceride/HDL ratio**. If the ratio is above 2.0, then you are probably insulin resistance. The other is the **Homeostasis Model Assessment of Insulin Resistance**, also called **HOMA-IR**. This is a complex formula based on the fasting glucose and fasting insulin levels. SETMA computes the HOMA-IR on all patients who have a fasting glucose and a fasting insulin level done.

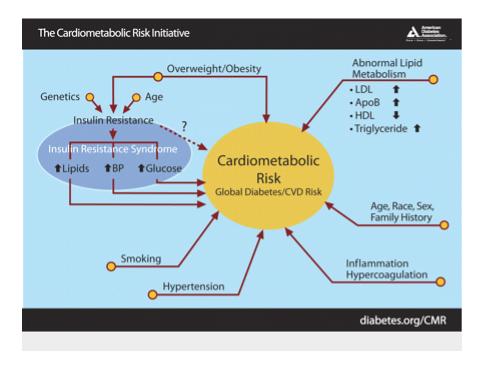
Causes of Insulin Resistance

The cause of insulin resistance isn't well understood, but it probably involves a variety of genetic and environmental factors. Doctors believe that some people are genetically predisposed to insulin resistance, and the tendency may be partly inherited. But being overweight and inactive are major contributors.

Insulin resistance and pre-diabetes usually have no symptoms. You may have one or both conditions for several years without noticing anything. If you have a severe form of insulin resistance, you may get dark patches of skin, usually on the back of your neck. Sometimes people get a dark ring around their neck. Other possible sites for these dark patches include elbows, knees, knuckles, and armpits. This condition is called acanthosis nigricans.

If you have a mild or moderate form of insulin resistance, blood tests may show normal or high blood glucose and high levels of insulin at the same time.

The following chart helps explain some of the interaction of the elements of the Cardiometabolic Risk Syndrome – Insulin Resistance – and the other elements of this condition which we will be discussing in coming weeks. As you can see, there are genetic (hereditary) factors some of which include ethnicity and gender (sex). There are environmental factors and habits such as smoking, diet and exercise.



Clinically, the ultimate manifestation of insulin resistance is the onset of type 2 diabetes. Anyone 45 years or older should consider getting tested for diabetes. If you are overweight and aged 45 or older, it is strongly recommended that you get tested. You should consider getting tested if you are younger than 45, overweight, and have one or more of the following risk factors:

- family history of diabetes
- low HDL cholesterol and high triglycerides
- high blood pressure

- history of gestational diabetes (diabetes during pregnancy) or gave birth to a baby weighing more than 9 pounds
- minority group background (African American, American Indian, Hispanic American/Latino, or Asian American/Pacific Islander)

Can you reverse insulin resistance?

Yes. Physical activity and weight loss make the body respond better to insulin. By losing weight and being more physically active, you may avoid developing type 2 diabetes. In fact, a major study has verified the benefits of healthy lifestyle changes and weight loss. In 2001, the National Institutes of Health completed the Diabetes Prevention Program (DPP), a clinical trial designed to find the most effective ways of preventing type 2 diabetes in overweight people with pre-diabetes. The researchers found that lifestyle changes reduced the risk of diabetes by 58 percent. Also, many people with pre-diabetes returned to normal blood glucose levels.

The main goal in treating insulin resistance and pre-diabetes is to help your body relearn to use insulin normally. During this series of articles on the cardiometabolic risk syndrome you will learn more about what to do but SETMA's **LESS Initiative** is a good start: **L**ose weight, **E**xercise, **S**top **S**moking. Remember, it is your life and it is your health.