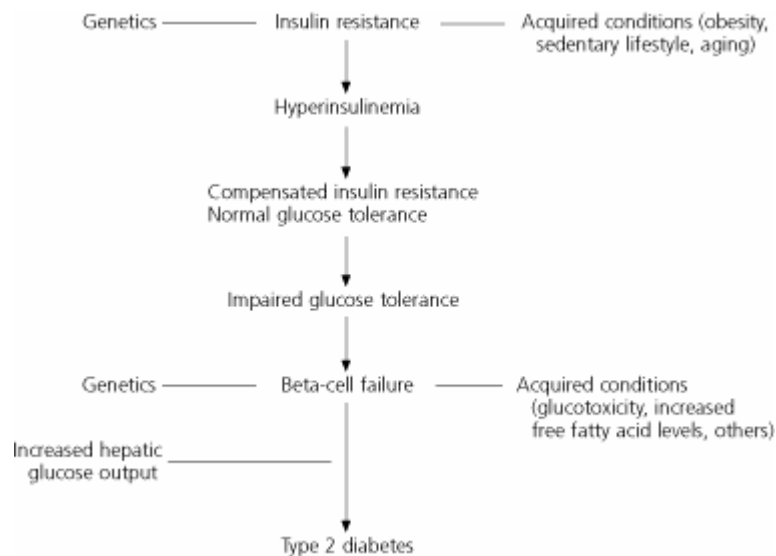


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### The Cardiometabolic Risk Syndrome Part III – Pre-Diabetes: Impaired Fasting Glucose & Impaired Glucose Tolerance By James L. Holly, MD Your Life Your Health *The Examiner* December 14, 2006

The cardiopulmonary risk syndrome is present before a patient develops full-blown diabetes. In fact, the syndrome is present at the earliest signs which predict the development of diabetes.

The sequence of events for the development of type 2 diabetes is as follows:



Before the pancreatic Beta cells, which produce insulin, fail, producing type 2 diabetes, they are put under stress by the increasing demand for more insulin produced by insulin resistance. The factors which produce insulin resistance are genetic and acquired, such as obesity, aging and a sedentary life style.

The earliest evidence of insulin resistance and of the cardiometabolic risk syndrome is found with an abnormal fasting blood glucose and/or an abnormal 2 hour glucose tolerance test. Diabetes and pre-diabetes can be detected with one of the following tests:

A **fasting glucose** test measures your blood glucose after you have gone overnight without eating. This test is most reliable when done in the morning. Fasting glucose levels of 100 to 125 mg/dL are above normal but not high enough to be called diabetes. This condition is called pre-diabetes, or “impaired fasting glucose” (IFG), and it suggests that you have probably had insulin resistance for some time. IFG is considered a pre-diabetic state, meaning that you are more likely to develop diabetes but do not have it yet.

A **glucose tolerance** test measures your blood glucose after an overnight fast and 2 hours after you drink a sweet liquid provided by the doctor or laboratory. If your blood glucose falls between 140 and 199 mg/dL 2 hours after drinking the liquid, your glucose tolerance is above normal but not high enough for diabetes. This condition, also a form of pre-diabetes, is called “impaired glucose tolerance” (IGT) and, like IFG, it points toward a history of insulin resistance and a risk for developing diabetes.

IGT and IFG predict the development of diabetes with the same specificity, but the IGT has a higher incidence which gives the test more sensitivity.

### **IFG = Impaired Fasting Glucose**

IFG is defined by a fasting serum glucose > 100 mg/dL.

- IFG is associated with insulin resistance but appears to be an independent predictor of incident diabetes.
- IFG data are easier to obtain and more reproducible.

### **IGT = Impaired Glucose Tolerance**

IGT is defined by a serum glucose between 140 and 200 mg/dL 2 hours after oral administration of a 75 gram glucose load.

- IGT represents a more severe abnormality than IFG.
- Patients with IGT have a higher degree of insulin resistance and more features of the cardiometabolic risk syndrome whether IGT occurs in association with IFG or is isolated.
- In addition, in some studies, patients with IGT have a more pronounced insulin secretory defect.

In the February, 2005 *Diabetes Care Journal* a new prediction rule was proposed for determining patients who have impaired glucose tolerance. The objective was to create a simple prediction rule that could perform as well as the 2-hour post challenge plasma glucose test to predict those at risk for diabetes. The conclusion was that the following factors could be fashioned into an equation which would produce this result:

1. Advanced age,
2. female sex,
3. Fasting Plasma Glucose and
4. triglycerides

The points allocated for each of these risk factors are:

<b><u>Risk Factor</u></b>	<b><u>Points Allocated</u></b>
Female Sex	1
Age > 70	2

Triglycerides > 150	1
Fasting Glucose	
95-104	1
105-115	2
116-125	3

### **Interpretation**

A score of 4 or higher doubled the likelihood of an abnormal post challenge glucose test result. This rule could help clinicians to better identify individuals with abnormal glucose tolerance, who should be targeted for interventions to prevent diabetes.

### **Preventing Diabetes – Pre-diabetes**

Recent reports that the incidence of diabetes can be prevented or delayed in individuals with Impaired Glucose Tolerance (IGT) by lifestyle modification has highlighted the need for identification of these high-risk individuals.

The American Diabetes Association adopted the term of “pre-diabetes” to identify persons with IGT (2-hour post challenge plasma glucose between 140-200, or Impaired Fasting Glucose (IFG, plasma glucose between 100-125 after a 12 hour fast. This study found that adding age, sex and triglycerides to elevated FPG results increased the predictive accuracy for diabetes.

### **Diagnosing Insulin Resistance:**

These tests however give only indirect evidence of 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 determines the diabetes risk on all patients seen and if a patient is at how risk for developing diabetes determines if the patient has pre-diabetes, either with impaired fasting glucose or impaired glucose tolerance. SETMA also computes the HOMA-IR on all patients who have a fasting glucose and a fasting insulin level done. If the HOMA-IR is above 2, then the patient has a high probability of being insulin resistant.

### **Reversing Insulin Resistance and preventing diabetes**

The Diabetes Prevention Program showed that the diabetes drug metformin, a biguanide, reduced the risk of diabetes in those with pre-diabetes but was much less successful than losing weight and increasing activity. In another study, treatment with troglitazone, a thiazolidinedione later withdrawn from the market following reports of liver toxicity,

delayed or prevented type 2 diabetes in Hispanic women with a history of gestational diabetes. Acarbose, an alpha-glucosidase inhibitor, has been effective in delaying development of type 2 diabetes. Additional studies using other diabetes medicines and some types of blood pressure medicines to prevent diabetes are under way. No drug has been approved by the Food and Drug Administration (FDA) specifically for insulin resistance or pre-diabetes.

Research indicates that low fat diets may aggravate the effect of insulin resistance on blood lipids. Therefore, for individuals who are insulin resistant, a diet low in saturated fat (less than 10 percent of total calories) and more moderate in total fat content (40% of total calories) may be beneficial. This recommendation is different from the low-fat, high-carbohydrate diet that many health organizations recommend to help prevent heart disease. Specifically, they recommend decreasing fat intake to less than 30 percent of calories. Some groups recommend even lower levels of dietary fat.

It is also beneficial to maintain an appropriate body weight because obesity can aggravate insulin resistance. To maintain an appropriate weight, regulate caloric intake and maintain a physically active lifestyle. A registered dietitian can assist with developing a proper diet plan for people with insulin resistance, or a family history of type 2 diabetes.

Scientists have established some numbers to help people set goals that will reduce their risk of developing glucose metabolism problems.

- **Weight.** Body mass index (BMI) is a measure used to evaluate body weight relative to height. You can use BMI to find out whether you are underweight, normal weight, overweight, or obese. SETMA determines the BMI for every patient seen in our clinic.
- **Blood pressure.** Blood pressure is expressed as two numbers that represent pressure in your blood vessels when your heart is beating (systolic pressure) and when it is resting (diastolic pressure). The numbers are usually written with a slash—for example, 140/90, which is expressed as "140 over 90." For the general population, blood pressure below 130/85 is considered normal, although people whose blood pressure is slightly elevated and who have no additional risk factors for heart disease may be advised to make lifestyle changes—that is, diet and exercise—rather than take blood pressure medicines. People who have diabetes, however, should take whatever steps necessary, including lifestyle changes and medicine, to reach a blood pressure goal of below 130/80.
- **Cholesterol.** Your cholesterol is usually reported with three values: low density lipoprotein (LDL) cholesterol, high density lipoprotein (HDL) cholesterol, and total cholesterol. LDL cholesterol is sometimes called "bad" cholesterol, while HDL cholesterol is called "good" cholesterol. To lower your risk of cardiovascular problems if you have diabetes, you should try to keep your LDL cholesterol below 100 and your total cholesterol below 200.

If you have the cardiometabolic risk syndrome, your doctor will recommend weight loss with diet and exercise, as well as possibly recommending medication to lower your cholesterol and blood pressure levels.

### **Stop Smoking**

In addition to increasing your risk of cancer and cardiovascular disease, smoking contributes to insulin resistance. Quitting smoking is not easy, but it could be the single smartest thing you can do to improve your health. You will reduce your risk for respiratory problems, lung cancer, and diabetes.

Two classes of drugs can improve response to insulin and are used by prescription for type 2 diabetes—biguanides and thiazolidinediones. Other medicines used for diabetes act by other mechanisms. Alpha-glucosidase inhibitors restrict or delay the absorption of carbohydrates after eating, resulting in a slower rise of blood glucose levels. Sulfonylureas and meglitinides increase insulin production.

### **Be Active and Eat Well**

Physical activity helps your muscle cells use blood glucose because they need it for energy. Exercise makes those cells more sensitive to insulin.

The Diabetes Prevention Program (DPP) confirmed that people who follow a low-fat, low-calorie diet and who increase activities such as walking briskly or riding a bike for 30 minutes, five times a week, have a far smaller risk of developing diabetes than people who do not exercise regularly. The DPP also reinforced the importance of a low-calorie, low-fat diet. Following a low-calorie, low-fat diet can provide two benefits. If you are overweight, one benefit is that limiting your calorie and fat intake can help you lose weight. DPP participants who lost weight were far less likely to develop diabetes than others in the study who remained at an unhealthy weight. Increasing your activity and following a low-calorie, low-fat diet can also improve your blood pressure and cholesterol levels and has many other health benefits.

Remember, it is your life and it is your health.