

## **POLYCYSTIC OVARIAN SYNDROME and INSULIN RESISTANCE**

Many women do not ovulate or ovulate very irregularly. Many of these women have infertility problems. There is a special category of ovulation problems called the polycystic ovarian syndrome (PCOS or PCO). This used to be called polycystic ovarian disease, but syndrome is really a much more appropriate medical term. Syndrome in medicine refers to a condition that has a number of features, but not every individual will show every feature. So, for PCOS, the features include the following:

1. Irregular menstrual periods or total lack of periods
2. Sometimes extremely heavy periods when they do occur
3. Infertility
4. Hirsutism (unwanted hair in the male pattern)
5. Stout build or chunky physique
6. Characteristic ovarian appearance on ultrasound showing many small cysts
7. Abnormal hormone blood levels

Polycystic ovarian syndrome has been described since the 1940's and was initially called the Stein-Leventhal Syndrome. The treatment was totally dependent on whether the patient wanted to achieve pregnancy or not. If she was hoping to achieve pregnancy, then ovulation medications were used. If she did not wish to become pregnant, then the standard of care was to begin birth control pills as this frequently decreases unwanted hair growth and results in more regular and lighter menstrual periods.

Polycystic ovarian syndrome is estimated to affect 8-10 percent of all women of reproductive age, so the total number of women affected is massive. It's the most frequent hormonal abnormality of women, exceeding even diabetes and thyroid disease for this age group. We have recently begun to understand this disorder in much greater detail with new information that involves an unlikely hormone, **insulin**.

### **INSULIN RESISTANCE**

In the last 10 years it has become increasingly clear that the story of polycystic ovarian syndrome is really the story of insulin resistance. As most people know, insulin is the hormone made by the pancreas to control blood sugar. When the pancreas stops making insulin completely, often times in childhood, this is juvenile onset diabetes or Type I Diabetes. When the pancreas slowly decreases the production of insulin, more often in adults and more often associated with weight gain, this is Type II or adult onset diabetes.

In order to really understand insulin resistance, I need to briefly describe how hormones work, so hang with me through this paragraph. Every hormone is a

molecule that is produced by some organ and floats through the blood stream until it attaches to a receptor in the target tissue. These receptors are glycoprotein molecules that are on the cell surface membrane. So insulin is produced by cells in the pancreas, in response to eating food. The insulin molecules go through the bloodstream and attach to their respective insulin receptors on cell membranes, especially muscle cells, liver cells, and fat cells. The main action is to cause these cells to pull nutrients, especially the sugar glucose, into the cells to be used for metabolism and energy production, or if in excess to be stored away as fat. People who have insulin resistance will have insulin receptors that are defective and very inefficient in responding to the insulin molecule. However, in these individuals, the pancreas will simply make a much larger amount of insulin and this will force the inefficient receptors to get the job done and prevent the individual from being diabetic. Eventually the pancreas may wear out and be unable to continue making the excessive amounts of insulin. When this happens, the insulin levels will begin to fall and blood sugar levels will begin to rise, and that individual will now be in the early stages of adult onset diabetes.

## **AN AMERICAN EPIDEMIC**

Many people are aware of how obesity in America has dramatically increased over the last 50 years. This is despite low fat diets preached by dieticians, physicians, and government sources such as the National Institute of Health. This is despite efforts to educate and to encourage exercise. This is despite many other diet fads. This is despite weight loss programs including several national paid programs such as Jenny Craig, Weight Watchers, NutriSystem, LA Weight Loss, etc. This is even despite recent emphasis on surgeries such as gastric bypass or laparoscopic band surgery.

Many people with insulin resistance will experience some degree of hypoglycemia. This occurs a couple of hours after having eaten a sugar load, when the pancreas over responds with a high level of insulin. Basically the insulin level overshoots and causes a delayed but much lower than normal level of blood sugar (glucose). Now the person will have different symptoms, mental dullness, jitteriness, headaches and then an intense craving for sugary or starchy foods. It is not hard to see why people with these symptoms will tend to steadily gain weight. They have hypoglycemia followed by craving and eating, followed by hypoglycemia then craving and eating, again and again. The excess carbohydrate is being stored away as fat. The typical low fat diet will be miserably unsuccessful because if the person is eating low fat (and low protein), then they will be eating high carbohydrates. I believe it ultimately will be shown that low fat dieting is the wrong type of diet for most Americans.

After years and years of high carbs, often associated with minimal or no daily exercise, Americans are usually becoming ill with a complex of diseases all together

called Syndrome X or the Metabolic Syndrome. This syndrome involves abnormal blood lipid levels (high cholesterol and/or high triglycerides), obesity, high blood pressure, adult onset diabetes, coronary heart disease, and strokes. Obviously, these are all old age problems that none of us would ever wish to have.

## **PCOS**

As I stated previously, it has now become increasingly clear that the story of PCOS is really the story of insulin resistance. High insulin levels in women causes a disruption in ovarian ovulation function. Worse yet, the ovaries now secrete a higher than normal amount of male hormones (called androgens), including testosterone and androstenedione. These high male hormone levels result in the excessive hair growth that is quite distressing to young women, involving the face (upper lip, chin, sideburns), neck, central chest, and lower abdomen.

Most women with severe PCOS have the onset of these symptoms when they are between 10-15 years of age, right at the time that they should be beginning normal menstrual cycles. Often times they have physical features that are very distressing to them such as being shorter and quite chunky, bothersome facial hair along with acne and oily skin. Frequently they have a family history of diabetes and sometimes other women who have the PCO syndrome as well.

It is now very apparent to me that whether a doctor diagnoses somebody, as PCOS is not the real issue, but whether that patient has insulin resistance or not. The diagnosis of insulin resistance must be made through appropriate blood tests for glucose and insulin (fasting and then repeated after a glucose challenge). While even this testing is not perfect, it will diagnose the vast majority of individuals with insulin resistance. I am doing this testing nearly everyday for women with infertility and ovulation problems, and others who are experiencing problems with difficulty losing weight, or fatigue, and sometimes in men who have sperm deficiencies. I believe that if young girls could be diagnosed in their early adolescence, treatment could then be instituted that would greatly moderate the degree of distressing hair growth, weight gain, and menstrual bleeding problems. So it is certainly not necessary to be an infertility patient in order to be seen for diagnosis and treatment.

Besides those severe PCOS cases, there are many other women who do not have an inherited deficiency of insulin receptors, but who gradually develop acquired insulin resistance through over eating, wrong eating (high carb diet, fast food), and lack of exercise and activity. Therefore it is not uncommon to see women who had regular menstrual cycles and were fertile when they were younger, who then begin to have irregular menstrual cycles and are no longer fertile later in life when they have gained considerable weight.

## INFERTILITY TREATMENT

The good news is that women who have ovulation problems as a cause for their infertility can be treated with medications and have good success. If they have insulin resistance, the treatment will include the use of the medication called Metformin (brand name Glucophage). This is an insulin sensitizer which makes our cells much more responsive to the insulin molecule. Therefore, the amount of insulin in the woman's blood stream will fall down to more normal levels and stop causing adverse ovarian function. This sometimes will be enough to allow her to ovulate without any other medications. This also may diminish the amount of male hormones and diminish hair growth. Very often, other ovulation medications will need to be used as well, such as Clomiphene (Clomid, Serophene), Letrozole (Femara), or injectable medications. The end result is that almost all of these women will be able to achieve successful pregnancies.

If the woman has insulin resistance and is on Metformin in order to achieve pregnancy, I keep her on the Metformin until at least 8-10 weeks into the pregnancy, as this has been clearly shown to decrease miscarriages. Some of these women may be kept on Metformin throughout the whole pregnancy or have it restarted later in the pregnancy if they show signs of gestational diabetes.



*"I'm going to order a broiled, skinless chicken breast, but I want you to bring me lasagna and garlic bread by mistake."*