



## **Polycystic Ovarian Syndrome (PCOS)**

PCOS is an ovulatory disorder that women are born with. Women with PCOS often report irregular or absent periods, abnormal hair growth (hirsutism), acne, infertility and difficulty losing weight, although these symptoms are not present in all PCOS patients. There is a genetic component to the syndrome and it affects up to 12 % of the patients seen by reproductive endocrinologists. The treatment varies depending on whether or not you are attempting to conceive.

How is the diagnosis made? The diagnosis begins with a menstrual history. Women with PCOS may have periods as frequently as every 35-40 days or as infrequently as once per year. The diagnosis is confirmed by excluding other problems. Your gynecological history is very helpful. Thyroid, prolactin, and 17 hydroxyprogesterone levels may be checked to confirm normalcy. A morning serum cortisol level may be obtained to rule out Cushing's syndrome, a group of symptoms produced by excess free cortisol. An ultrasound would likely show that your ovaries have many small follicles or cysts in the periphery of the ovary, hence the name given to the syndrome. Each of these small follicles contains an egg (oocyte). In normal ovulatory cycles, one of these eggs matures each month and is released for fertilization. In PCOS, however, many small follicles may grow to moderate size, but no single egg develops to maturity, therefore, ovulation of an egg does not occur. Since each follicle does make estrogen, however, the endometrium thickens in PCOS patients and menstruation occurs when the endometrial lining becomes disorganized. This often confuses women, causing them conclude that they must have ovulated since they had a period. PCOS is also referred to as "estrogenized anovulation". The small cysts rarely grow significantly in size and rarely rupture spontaneously.

Another feature of PCOS is insulin resistance. Insulin is a hormone that controls how your body uses sugar. Many women with PCOS make excessive amounts of insulin. This contributes to problems with weight gain and difficulty losing weight. Since insulin resistance is a major component of PCOS we may perform insulin resistance screening. This involves checking a fasting insulin and glucose, and then repeating the testing one and/or two hours later after a 75 gram glucose load (a sweet tasting drink). Based on your insulin screening, your doctor may recommend the addition of oral medications to help you body use insulin more effectively.

Another feature of PCOS is androgen excess. Androgens (testosterone and androstenedione) are hormones that are made by the ovaries in women and are likely elevated. The levels are not indicative of the severity of your hirsutism or response to therapy. Hence we may not even check these hormone values.

What is the treatment? If you do not want to conceive then our first mode of therapy is oral contraceptives. The "pill", a combination of estrogen and progestins will promote cycle regularity in most women after 3 months of use. The estrogen will have beneficial effects on acne and unwanted hair growth.

Weight gain is usually not a problem with the new pills. Some are thought to promote weight loss.

Spironolactone, a diuretic, blocks the action of testosterone at the hair follicle, thereby decreasing hair growth. Vaniqa is a facial cream that is very effective in reducing the appearance of unwanted hair. The latter two should not be taken without birth control pills as exposure to a fetus may be harmful. It may take up to 3 months to see early beneficial changes.

If you do want to conceive then the approach to treatment is different. If you have been determined to have insulin resistance then an insulin sensitizer may be the first drug of choice if Letrozole or Clomid are not used. (In the past, insulin sensitizers were considered the first line therapy for PCOS, but in 2008 the pendulum started to swing back to using Clomid or Letrozole for treatment.) Features of insulin resistance can include high levels of insulin on your screening tests, weight gain at your waist as opposed to your buttocks, a strong family history for adult onset diabetes and a darkening of the skin around your neck or other skin in body folds (acanthosis nigricans). Glucophage is the current choice of insulin sensitizing agents. Glucophage is prescribed in various manners. Occasionally you will receive a dose as low as 500 mg daily. Commonly you will be prescribed an 850 mg dose daily for 10 to 14 days. Then you will be asked to increase to twice daily for 10 to 14 days and then up to three times a day. Glucophage is best taken with meals, especially higher protein meals. The main side effect is GI (gastrointestinal) intolerance, especially diarrhea. If this occurs, skip pills or fall back to a lower dose. Usually patients experience new levels of energy and are willing to tolerate the minimal side effects experienced with Glucophage. The medicine should be stopped if you become dehydrated and on the day before any surgery. It may be continued during pregnancy.

Actos is a very effective insulin sensitizer. It works by making the fat and muscle cells more sensitive to your insulin. It is associated with few side effects (sometimes ankle swelling). We check liver function tests three months after initiation of treatment and currently ask women to discontinue the medication once they conceive.

Weight loss and in turn improvement in your insulin resistance may be gained by the use of Xenical (Orlistat). Xenical, unlike Glucophage, is not absorbed through the digestive tract. A tablet should be taken with each meal in which a proportion of the meal will consist of fat. No more than three 120 mg tabs should be taken daily. Since Xenical blocks the absorption of fat, fat soluble vitamins crucial to proper nutrition may become deficient. It is essential that you take your multivitamin 2 or more hours before or after your Xenical (typically upon retiring for the night). The combination of Glucophage and Xenical is often not tolerated well by patients due to increased gastrointestinal side effects. If taken together, the extended release form of Glucophage is best taken with one of the meals and Xenical with the other two meals.