

Polycystic Ovarian Syndrome

Polycystic ovaries overview

Polycystic ovarian syndrome (PCOS) is a condition associated with irregular menstrual cycles as ovulation often fails to occur regularly. The most commonly used criteria for diagnosing PCOS are the Rotterdam Criteria which states that there must be any two of the three following factors present to diagnose PCOS:

- Ultrasound features of polycystic ovaries (more than 26 follicles of between 2-9mm, on either ovary, and ovarian volume more than 10ml)
- evidence of increase androgens (male hormone proportion in blood)
- Evidence of infrequent or irregular ovulation
- Elevated androgen levels either clinically or biochemical. This can sometimes cause excessive facial hair growth, acne, or hair thinning although this is unusual.

Many women with polycystic ovarian syndrome are overweight, although this is not invariable. They may have a higher than average risk of developing diabetes. Women with polycystic ovaries who wish to become pregnant can be treated effectively in several different ways.

Cause of PCOS

The cause of PCOS is not completely understood. It is believed in some women to have a genetic predisposition (may run in families), but it is not hereditary in the true sense. It is believed that one of the crucial abnormalities with PCOS is *insulin insensitivity*. Insulin is a peptide (small protein) hormone that controls blood sugar levels. There may be an increased level of the pituitary hormone luteinising hormone (LH) and higher levels of androgens which interfere with the normal function of the ovaries and lead to overgrowth of the ovarian stroma (the substance of the ovary, other than the oocytes themselves).

The normal menstrual cycle- important to understand

The pituitary gland, ovaries and uterus normally follow a defined sequence of events on a monthly basis. This phenomenon also occurs in higher order primates but not in all animals. This sequence helps to prepare the body for pregnancy. The cycle is initiated by an increase in follicle stimulating hormone (FSH) which causes a group of follicles (similar to small blisters) in the ovaries to grow. During the first half of the cycle FSH cause follicular growth, the follicle produces estrogen which travels through the blood stream to the uterus and causes thickening of the lining. Although the ovaries lie in proximity to the uterus they are not part of the uterus and they are not physically connected. Whether or not an egg is released by the ovaries plays no part in the process. In the middle of the month, an increase in luteinising hormone (LH) causes the final maturation of one follicle followed by release of an egg. The egg may or may not be actively picked up by one of the fallopian tubes and is carried through the fallopian tube to the uterus. In the uterus if fertilised, a day two to three embryo may begin to implant in the endometrial lining if the lining is appropriately developed.

Menstrual cycle in polycystic ovaries

In women with polycystic ovaries, there is an increased number of small follicles (tiny fluid filled spaces of between 2 and 9mm) in the ovaries and hence the term polycystic ovaries. Note that it possible to have polycystic ovaries but not polycystic ovarian syndrome. These follicles do not grow to a size that will achieve ovulation, and as a result there is a relative excess of estrogen in the cycle, but low progesterone. FSH and LH also become imbalanced with an increased level of LH. Androgens are produced by the stroma (the substance, excluding the follicles) of the ovaries.

PCOS symptoms

Because ovulation may incur infrequently or irregularly, the menstrual cycle is also irregular. Infrequent or absent ovulation may cause difficulty in conceiving although this *does not necessarily follow* and many women with PCOS are normally fertile. The increase in androgen level may cause androgenic effects such as acne, greasy skin, sometimes hair growth or hair thinning.

If ovulation does not occur the lining of the uterus does not shed uniformly and may grow excessively thick. Occasionally this can lead to precancerous change and may be manifest as heavy periods (often with passage of clots). An overgrowth of the endometrium is called *endometrial hyperplasia*.

Insulin abnormalities

Polycystic ovaries are associated with elevated levels of insulin in the blood. Insulin is normally produced by the pancreas and regulates blood glucose levels. If glucose levels do not respond to the normal levels of insulin, the pancreas produces more insulin. This is called *hyperinsulinemia*. When increased levels of insulin are required to maintain normal glucose levels a person is said to be insulin resistant. This is a common finding in polycystic ovarian syndrome. When the blood glucose levels are not completely controlled even with increased amounts of insulin, the person is said to have glucose intolerance (sometimes referred to as prediabetes). If blood glucose levels continue to rise despite increased insulin levels the person is said to have Type II (adult onset) diabetes. Diabetes is diagnosed with a blood test. Insulin resistance can occur in women who are both normal weight and overweight. Being overweight does however increase the likelihood.

Polycystic ovaries and infertility

Because many women with PCOS do not ovulate regularly, it may take longer to fall pregnant. Note that *most women with PCOS will successfully fall pregnant without difficulty*, using medication, occasionally injections (+/- IVF) or in some cases, surgery. There may be a very slight increased chance of miscarriage.

PCOS diagnosis

There is no single test for diagnosing polycystic ovarian syndrome and often combinations of the above mentioned criteria are used. Occasionally, a woman acts as if she has polycystic ovarian syndrome even though the tests may not agree. Blood tests and an ultrasound are usually recommended to diagnose PCOS and they may also be conducted to exclude other possible causes of diabetes or irregular periods. If PCOS is confirmed on the above criteria, an oral glucose tolerance testing and fasting lipid levels are usually requested. This is to obtain a baseline estimation of sugar and lipid control and to diagnose any pre-existing problems.

Treatments

Oral contraceptives

The combined oral contraceptive pill (OCP) (estrogen plus progesterone) is generally recommended to regulate periods, if a woman with PCOS does not immediately wish to fall pregnant. Unfortunately there is no way of "getting rid of" PCOS rather the symptoms are treated with agents that either regulate the cycle, or control blood glucose.

The combined OCP is important as it prevents overgrowth of lining and regulates periods which are often important. The oral contraceptives also decrease the body's production of androgens, decrease the amount of free androgen in the blood stream and therefore may improve skin changes such as acne and hair growth. This is not simply "covering up" the symptoms of PCOS, but represents the current best practice in managing PCOS in these women. Occasionally the combined OCP cannot be taken; in which case regular progesterone induced withdrawal bleed may be prescribed to prevent endometrial hyperplasia. Note that a progesterone only pill (POP, or mini pill) is not sufficient to control endometrial growth or regulate the cycle.

Weight Loss

Weight loss is also important for managing polycystic ovarian syndrome. Weight loss is associated with increased insulin sensitivity, decreased fasting blood glucose levels, decreased lipids and general increase in general health. Many women with PCOS who lose 5 to 10% of their body weight resume regular ovulation (regular periods). Weight loss can often be achieved with a combination of diet, exercise and oral hypoglycaemic agents (for example Metformin). Weight loss is certainly important in women who have a body mass index of >35, prior to considering a pregnancy as all complications of pregnancy are increased with a BMI of over 35.

Metformin

Metformin is a medication that improves the effectiveness of insulin in the body. It was developed as a treatment for Type II diabetes, but is also often used for polycystic ovarian syndrome. Using it on its own will often result in an increase in regular ovulation and regular periods however it is not as effective at producing a pregnancy as agents which cause ovulation (for example clomiphene citrate, Clomid, or letrozole, Femara). A combination of these is often used. Metformin may assist in reducing the metabolic consequences of polycystic ovarian syndrome for example impaired glucose tolerance and increased effects. (PCOS and infertility) PCOS is one of the most common causes of infertility. I will generally commence my thorough evaluation, checking complications of polycystic ovarian syndrome and confirming a diagnosis. This would consist of a blood test and an ultrasound. Following that, if your BMI is raised, losing weight is very important. If everything else is optimal, including your partners semen analysis, then I will generally recommend commencing with an ovulation induction agent such as clomiphene citrate, or letrozole.

Clomiphene citrate, but not letrozole, is given in an adjusted dose (increasing dose) according to effectiveness. If a maximum dose is reached without regular ovulation a laparoscopy is often indicated. Addition of Metformin may also help to sensitise the body to clomiphene citrate and produce ovulation. If these measures do not work, I often trial letrozole ovulation induction or proceed to laparoscopy if other indications exist. At laparoscopy, ovarian golf balling (also called ovarian drilling or ovarian diathermy) is used. Interestingly golf balling causes a very slight injury to the ovarian stroma, reversing the hormonal signature of polycystic ovarian syndrome and often resulting in resumption of spontaneous ovulation. It has similar effectiveness to clomiphene citrate. At laparoscopy a full assessment of the pelvis including dye hydrotubation and hysteroscopy and curettage is also undertaken along with excision of any endometriosis that may be found.

Long term treatment

In those with polycystic ovarian syndrome not seeking to fall pregnant, long term monitoring is indicated. This will consist in roughly second to third yearly hormone profiles, glucose tolerance test, lipid profile and if required, attention to weight loss. *I will have to emphasise again that commencing the combined OCP is an important part of management in order to eliminate the chance of endometrial hyperplasia.*

Further reading: See www.reproductivefacts.org, the consumer web site of the American Society of Reproductive Medicine.

