Women's Health Information

Polycystic ovary syndrome

Introduction
Polycystic ovary syndrome (PCOS) is a common disease affecting 3-5% of women of reproductive age. Despite the fact that it was first recognised in 1935, the exact cause of the syndrome remains elusive and there is no 'one-treatment-fits-all' answer to its management.

The following pages cover this syndrome in some detail, with the final page containing information on support groups and the published references used to compile the information, with links to the original papers where available.

What symptoms does it cause?

How is it diagnosed and what is the difference between PCO and PCOS?
Diabetes, insulin and longer-term risks
Treatment: irregular periods
Treatment: infertility
Treatment: weight loss
Treatment: hirsutism (excess hairiness)
Treatment: newer 'insulin sensitising agents'
Long term monitoring

What symptoms does it cause?
The common symptoms of PCOS are as follows:

- Period problems
- Acne, excessively oily skin or hairiness (hirsutism) due to excess male-type hormones
- Infertility
- Weight gain

Menstrual disturbance
PCOS often comes to light during puberty due to period problems, which affects around 75% of those with the disease. Infrequent, irregular or absent periods are
all common variations, many finding their periods particularly heavy when they do arrive. The period disturbance is a sign that there is a problem with regular monthly ovulation. Many teenagers use the contraceptive pill to control their periods as irregularity or heaviness is a common complaint at this time, even in the absence of PCOS. This often leads to a delay in the diagnosis of PCOS, many not presenting until the pill is stopped and finding periods cease or become irregular.

**Androgenic symptoms**

Androgens are a group of hormones, such as testosterone, found at high levels in men but present in women at much lower levels. PCOS sufferers often have higher than normal levels of androgens which most often causes excess hairiness, but some women find acne or even male-pattern hair loss a particular problem.

**Infertility**

Given that the period disruption with PCOS is due to irregular or absent ovulation it is not surprising that it is a common cause of infertility. It is not usually 100% absolute, and some women with PCOS will ovulate normally, some will ovulate less frequently (leading to a delay to pregnancy) and some will not ovulate at all, meaning that for some treatment will definitely be necessary.

**Obesity**

This is a double-edged sword for women with PCOS, around 40% of sufferers being overweight. Obesity itself will initiate the symptoms described above in some women who would not have otherwise suffered had they remained of normal weight. It will worsen the symptoms for those who do have PCOS and, unfortunately, the hormone changes associated with PCOS make weight loss more difficult.

**How is it diagnosed?**

Part of the diagnosis is finding the symptoms mentioned above. Other tests to confirm the diagnosis include:

**Ultrasound scan**

This is usually done as an internal scan, meaning a small ultrasound probe is placed just inside the vagina, giving the best views of the ovaries and pelvic organs. In PCOS, the ovaries are found to have multiple, small cysts around the edge of the ovary. These cysts are only a few millimetres in size, do not in themselves cause problems and are partially developed eggs that were not released.
Blood tests
A couple of blood tests will assist in making the diagnosis - one to check the level of androgens, such as testosterone. Another test will measure the hormones involved in egg development - in PCOS there is a characteristic rise in leutenising hormone (LH). A progesterone blood test 7 days before your expected menstrual period can check if you are ovulating.

What is the difference between PCO and PCOS?
The term 'polycystic ovaries' describes the ovaries, as seen on the ultrasound scan above. Many women have ovaries that are polycystic, but do not have any of the other symptoms or hormone findings as described previously. Overall, around 20% of women of the general population have ovaries with this appearance, and what isn’t known yet from current research is whether this is one end of a long scale including the full polycystic ovary syndrome or a sign that symptoms are more likely to develop in the future.

Diabetes, insulin & long-term risks
In recent years it has become clear that PCOS is closely related to a problem with insulin. Insulin is a hormone released from the pancreas after a meal and it allows the organs of the body to take up energy in the form of glucose. In PCOS there is a 'resistance' of cells in the body to insulin, so the pancreas makes more insulin to try and compensate. The excessively high levels of insulin have an effect on the ovary, preventing ovulation and causing a rise in androgen (testosterone) levels. One study found that 30% of slim women with PCOS have insulin resistance, however it affects as many as 75% of those who are overweight. This explains why overweight women with PCOS are more likely to suffer with excessive hairiness and infertility related to not ovulating.

Longer-term risks of PCOS
The long-term risks of PCOS are related to both the insulin problem and the high androgen levels. High levels of insulin are associated with an increased risk of developing type II diabetes which, if it develops, generally means strict diet control or possibly tablet medication. 25-35% of overweight PCOS women show signs of this by their 30’s and it probably becomes more common in the 40’s and beyond.
The hormone changes described increase the chance of developing high blood pressure and high cholesterol levels, both of which can lead to a greater risk of heart disease.

Irregular or infrequent periods over a long period of time lead to an increased risk of cancer of the lining of the uterus (endometrial cancer). This is, in part, due to high levels of the hormone oestrogen, which over-stimulates the lining of the uterus. Absence of ovulation, and the resulting progesterone deficiency, also contributes to this risk.

**Control of irregular periods**

As mentioned previously, irregular and heavy periods can occur due to problems with ovulation. Whilst it would seem that restarting ovulation would be the best treatment, this is generally reserved for when a pregnancy is desired. The ovarian stimulation drugs to do this have other side effects, making their long-term use inappropriate.

Excess weight is a cause of menstrual problems in both women with and those without PCOS. Extra oestrogen is made in fat tissues and this interferes with ovulation and leads to over-stimulation of the lining of the uterus and heavier periods. Weight reduction will improve cycle control and reduce the heaviness of menstrual flow.

Periods may be controlled by the use of the contraceptive pill, which is most suitable for women under the age of 35 who also require a good form of contraception. The other type of drug used is a progesterone-like hormone. Progesterone is the main hormone of the second half of the menstrual cycle, maintaining its length and helping reduce the heaviness. Progestagens are taken as tablets in a cyclical way, for example between days 12-26, the exact type and timing depending upon the woman's individual cycle problem.

Some women have no periods at all, and either the contraceptive pill or cyclical progestagens are advisable to avoid the risk of endometrial cancer. Around 6 periods per year is adequate to protect against this.

**Infertility treatment**

Polycystic ovary syndrome is found in around 70% of women who have ovulation difficulties leading to infertility. This is more common in women who are overweight, and as a first-line treatment, weight reduction can be very successful in restarting spontaneous ovulation. The amount that needs to be lost is less than
most women might expect - around 5% of the current weight is associated with an increased number of ovulatory cycles.

**Clomiphene**

Clomifene citrate is the most commonly used drug to stimulation ovulation. It is taken in the early days of the cycle (usually days 2-6) and results in ovulation in around 80% of women overall, and a 6 month successful pregnancy rate of 45-50%.

**Ovarian stimulation**

When clomifene is unsuccessful, there are two main approaches. The first is to use injectable hormones to stimulate the ovary to produce eggs. This is known as ovarian stimulation and, where there is an additional sperm problem, is combined with insemination of sperms through the cervix around the time of ovulation (intrauterine insemination, or IUI). The hormone treatment must be monitored by blood tests and ultrasound scans to avoid over-stimulation. Live birth rates after ovarian stimulation following failed clomifene treatment reach 54% after 6 months and 62% after 12 cycles.

Multiple pregnancy is always a risk with this type of treatment, but especially so for women with PCOS, whose ovaries are particularly sensitive to the hormones. If ovarian stimulation is unsuccessful, many women resort to in vitro fertilisation (IVF), success rates of which depend very much upon individual characteristics such as age, length of infertility and weight.

Neither IVF nor ovarian stimulation is likely to be successful if a woman is overweight (body mass index greater than 30 kg/m2). This is why most hospitals restrict these treatments until a woman's weight is within the normal range.

**Laparoscopic ovarian diathermy**

The alternative to ovarian stimulation is an operation called laparoscopic ovarian diathermy (LOD), also known as 'ovarian drilling'. This involves a day case operation, a short general anaesthetic, and a telescope look into the abdomen. The ovaries are identified and several small holes made in each ovary, either with a fine hot diathermy probe or via laser. It is not actually known how this works, but it can restore regular ovulation, or make the ovary more sensitive to clomifene.

By 12 months after LOD the average pregnancy rate is around 60-80%, the greatest success rates being in women with a shorter length of infertility (less than 3 years) and a higher level of the hormone LH (>10 iu/l). Advantages of LOD include the fact that it may improve other symptoms of PCOS, such as menstrual disturbance, as well as avoiding the need for stimulatory drugs and their increased risk of over-stimulation and multiple pregnancy.
Weight loss
This is a very difficult area for women who are constantly told by their care providers that they must lose weight. The very disease that is worsened by the excess weight conspires against them in this quest, making weight loss more difficult than usual. There is no one-shot, sure fire answer and the key is a combination of strict calorie reduction combined with aerobic exercise as part of a supervised programme.

Weight loss will regulate periods, lead to more ovulatory cycles, improve hairiness, reduce the risk of heart disease and lower insulin levels. GP's can often arrange a referral to a dietician to discuss the optimum diet, which is particularly important considering the tendency toward high cholesterol and unhealthy blood lipids that comes with PCOS. Getting weight into the normal range and maintaining it there should considered a lifelong process, rather than a short-term fix. This will help ensure that you maintain the weight you lose and the healthy lifestyle that helped you achieve it.

Hirsutism (hairiness)
This is usually due to above average levels of androgens, the male hormones that are normally present in women at low levels. Some women do not find the excess hair a problem, particularly if it does not affect their face, or it is blonde in colour. Sometimes excess hairiness is not abnormal and is a racial or genetic variation.

Initial treatments include bleaching and electrolysis. If these do not produce an acceptable result, drugs may be used to reduce the high androgen levels, if that is the cause.

The contraceptive pill contains oestrogen, which reduces androgen levels and will improve hirsutism. A formulation is available which includes a specific drug to reduce these further, known as 'Dianette'. The other component of Dianette is called cyproterone acetate, and this is the next drug to try if hirsutism persists. It is used in a higher dose than contained in the Dianette pill, but must be combined with adequate contraception, as it can cause fetal abnormality if taken during early pregnancy. Spironolactone is another alternative, but this frequently causes erratic periods, so is often given with a low dose contraceptive pill. A newer drug is called flutamide, which appears promising, though its safety profile is less clear. Side effects of the anti-androgens include tiredness, mood changes and reduced sex drive. Both flutamide and higher dose cyproterone acetate have a rare but serious side effect of causing problems with liver function, and so regular blood tests are advised.
All hirsutism treatments must be continued for 8-18 months before a response can be expected, due to the slow rate of hair growth. At that time, electrolysis can be performed to remove the unwanted hairs already present, and less return growth can be expected.

**Insulin-sensitising drugs - metformin**

PCOS can lead to a resistance to insulin, leading to the body producing excessively high levels in an attempt to compensate. This higher level of insulin is known to cause abnormal cholesterol and lipid levels, obesity, irregular periods, higher levels of androgens, infertility due to disturbance of ovulation and an increased likelihood of diabetes. *Metformin* is a type of drug known as an 'insulin-sensitising agent', which lowers the blood sugar level, in turn reducing the excessively high insulin.

There are actually very few studies that have been carried out and published concerning the use of insulin sensitising drugs as a treatment for PCOS. These suggest that it may well be useful in several areas: helping weight reduction, improving irregular periods (70%), normalising blood cholesterol and leading to ovulation. One study looking at ovulation in particular found that compared to no treatment, 34% of women ovulated taking metformin (compared to 4% who did not receive it) and when this was combined with clomifene it was as high as 90% (as compared to 8% in those who only received clomifene). These studies contained overweight women with PCOS - its role in treating women of normal weight has not been investigated. The most common side effects during treatment are diarrhoea, nausea, vomiting and abdominal bloating.

*Early studies*

The studies that are available concerning the insulin-sensitising drugs are very exciting and will hopefully pave the way for a longer-term treatment for this disease, which can affect many different areas of a woman’s life. It is important to realise that the investigation is still at a very early stage. Long-term effects are not known - the longest follow up so far is for around 6 months of use. Considering its use as a treatment for infertility, the studies are small compared to more traditional treatments, containing only up to 35 patients receiving metformin. Most studies are not comparative, in that they did not compare 'treatment' with 'no treatment', an extremely important point. The outcome of the studies has looked at the effect on ovulation rather than actual pregnancy or birth rates. We know from clomifene that only half of women who ovulate actually get pregnant - what is the figure for these newer drugs?
Because of the lack of research using these drugs, many doctors are awaiting further studies to confirm their initial apparent success and identify potential side effects before jumping in and prescribing them. This is a safe and sensible approach. There may be specific cases when their use is considered appropriate at this stage, and this is something for an individual doctor to decide with the patient's full understanding of the present situation.

**Long term monitoring**

Given the longer term risks that have been identified, particularly in women who are overweight, such as high blood pressure, high cholesterol, the increased risks of diabetes, heart disease and cancer of the lining of the uterus, it is important for the GP to keep an eye on these and provide appropriate counselling to reduce the risks as much as possible. The extra risks of smoking should be made clear, and diet advice given regarding excess fatty foods & weight control. Blood tests for cholesterol levels and diabetes should be considered, perhaps every one or two years from age 35 and even earlier if there is a family history.

**Useful addresses**

**WOMEN'S HEALTH**

A resource and information centre
52, Featherstone street, London EC1Y 8RT
Tel: 0207 251 6580
Health enquiry line: Mon-Fri 9.30 am -1.30pm
E mail: Health@womenshealthlondon.org.uk
Website: www.womenshealthlondon.org.uk

**NATIONAL ENDOMETRIOSIS SOCIETY**

50, Westminster Palace Gardens
1-7 Artillery Row, London SW1P 1RL
Helpline 0808 808 2227
Website: www.endo.org.uk
www.womens-health.co.uk/endo1.htm

**PCOS**

Websites of interest

www.womens-health.co.uk/pcos.htm
www.pcos-support.org/what.htm
www.verity-pcos.org.uk
www.netdoctor.co.uk/womenshealth/facts/pcos.htm