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Making sense of alphabet soup:
Polycystic ovaries and polycystic ovary syndrome explained

Unfortunately, we doctors often give diseases names which sound very threatening and then, to make matters even worse, we turn them into confusing acronyms. The term 'polycystic ovary', or PCO, is a good example of this. For good measure, let's add the word 'syndrome' and it becomes polycystic ovary syndrome, or PCOS. It sounds painful—as if the ovary is constantly full of large, painful cysts—and even hints at the threat of radical surgery. However, neither of these scenarios is true.

What is a polycystic ovary?

The possibility that a woman may have polycystic ovaries is one of the most common reasons for a GP to refer someone to my clinical practice. Many of these women arrive confused and often very

frightened. They have usually gone to their GP because their periods are irregular or because they have concerns about an excessive amount of body hair (hirsutism) and/or acne (see Chapters 4 and 5 for a more detailed discussion of these symptoms). Then they are confronted with a medical term they may not have heard about before and they dread a prognosis, sometimes linking the condition with cancer. Fortunately, it usually takes just a little accurate information to allay their fears.

The ovary is a dynamic organ, changing its shape and appearance according to its hormonal environment. We can look at a woman's ovaries through two common procedures: ultrasound scanning; and a laparoscopy, a keyhole surgical technique where a telescope is inserted into the abdominal cavity via a small cut in the navel (under a full anaesthetic). In practice, ultrasound is by far the most common way of finding polycystic ovaries. A five-year-old girl's ovaries are inactive and small, with a volume of only 1 to 2 millilitres (a teaspoon holds 5 millilitres). During a woman's reproductive years, each of her ovaries has a volume of around 4 to 6 millilitres and they have a convoluted, folded surface which looks a bit like the surface of a walnut (see Figure 1).

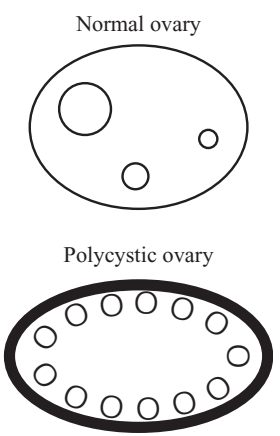

Figure 1.1 A normal ovary and a polycystic ovary

Ovulating ovaries contain fluid-filled structures called follicles, which may vary in size from 1 to 30 millimetres, depending on the phase of the menstrual cycle. Each of these follicles contains a microscopic egg, and there are usually between two and five of them scattered throughout the ovaries. In contrast, the polycystic ovary typically has more than twelve small follicles, each around 2 to 9 millimetres in diameter, which are usually arranged in a 'pearl-necklace' pattern. A polycystic ovary is also usually larger than normal, with a volume of more than 10 millilitres and has a smooth thick surface, or capsule. Often this capsule is covered in tiny blood vessels.

The name 'polycystic ovary' is an unfortunate one, as the ovary is actually not full of cysts. In medical terminology, the term 'cyst' normally refers to a fluid-filled structure more than 30 millimetres in diameter. So, strictly speaking, polycystic ovaries do not have cysts; it is the particular follicular pattern and number of follicles that defines the condition.

Myth: Polycystic ovaries are full of cysts.
Fact: The term PCO refers to a pattern of twelve or more small (2–6 millimetre) follicles arranged around the periphery of the ovary in a pearl-necklace pattern. They are not technically 'cysts', and do not need to be removed surgically.

The follicles of polycystic ovaries behave differently, in the reproductive sense, to normal follicles. If you have polycystic ovaries, you certainly do not need surgery to remove the follicles, and you are also not at increased risk of cancer of the ovaries. We will go into more detail about this later.

Myth: Women with polycystic ovaries have cysts which need to be removed through surgery.
Fact: The so-called 'cysts' are actually small follicles, each containing an egg. There is no need for surgery to remove the follicles from an ovary: they are a normal part of an ovulating ovary.

What is polycystic ovary syndrome?

It is very important to distinguish between polycystic ovaries (PCO) and polycystic ovary syndrome (PCOS). Having PCO does not necessarily mean you have PCOS. A syndrome is usually defined as a pattern of symptoms belonging to a particular disease. Medical studies using ultrasound have found that around one in four women has polycystic ovaries, but most of them have none or few of the other symptoms associated with polycystic ovary syndrome. The main features of PCOS are male hormone excess and polycystic ovaries. Some of the problems that women with PCOS may have include:

- excess hair on the body (hirsutism);
- acne and other skin problems;
- scalp hair loss;
- irregular or missing periods;
- heavy periods;
- fertility problems;
- insulin resistance;
- weight issues.

Some of these symptoms, such as excess body hair, will depend on the person's genetic makeup. For example, Asiatic people are not very hairy, so Chinese women with PCOS rarely suffer from this symptom, whereas people from the Mediterranean do have much more body hair, so excess body hair is likely to be a sign. It is the symptoms, not necessarily the realisation that they may have polycystic ovaries, that

cause women to seek medical help. As discussed, polycystic ovaries are not painful and most women do not know they have them until a symptom of the syndrome becomes a concern. During the process of treating the symptom, they discover they have PCO or PCOS.

Until 2003, there was a worldwide consensus that PCOS was diagnosed only when a woman had fewer than six menstrual cycles per year and the visual telltale sign on the ovary (twelve or more small follicles in a 'necklace' pattern) could be seen on an ultrasound. In the United States, where ultrasound is not usually performed, the diagnosis was made when an excess of the male hormone (androgen) was discovered either through the observation of excessive hair growth or via raised male hormones in a blood test, as well as fewer than six periods per year (see Chapter 2 for more details on diagnosis). While polycystic ovaries are common—with one in four women having them—only about 7 per cent of women in the reproductive age group will have PCOS—that is, PCO and fewer than six periods per year.

That all changed in 2003. A meeting of international experts resulted in a revision of the definitions. The paper they published (see Rotterdam ESHRE/ASRM-Sponsored Consensus PCOS Workshop Group, 2004) stated that: 'PCOS is a syndrome of ovarian dysfunction. Its cardinal features are hyperandrogenism and polycystic morphology.' This means that PCOS is characterised by the ovaries not working properly, an excess of male hormones (as measured on a blood test or implied by the presence of excess body hair) and a polycystic appearance of the ovaries.

It is worth noting at this point that any menstrual irregularity could be a symptom of another hormone problem such as early menopause, and excess androgen could also be caused by the adrenal gland over-producing the male hormones, rather than by PCOS. Hormonal-related symptoms therefore have to be carefully scrutinised before a diagnosis of PCOS is made to eliminate all other possible causes. We will discuss all these symptoms in greater detail later, but in order to understand PCO and PCOS it is important to go back to the basics—to understand how the female reproductive system actually works.

Myth: All women with PCO have PCOS.
Fact: PCOS is diagnosed only when two of the following three symptoms are present and other causes are excluded:

- irregular periods (usually fewer than six periods per year);
- blood tests or symptoms suggesting male hormone excess;
- polycystic ovaries.

How does the menstrual cycle work?

Menstruation is an incredibly complex process. The first period, called the *menarche*, usually occurs around the age of twelve years, but most young women notice some breast development around the age of ten, and soon after that hair starts to grow in the armpits and groin. Just before menarche, girls experience a growth spurt, initiated by *human growth hormone* (HGH), a hormone produced by the pituitary gland. Generally, growth will start to slow at the onset of the first period as a rise in levels of *oestrogen* (another female hormone) fuses the growth plates (located at the ends of the long bones in the arms and legs), turning them into bone, thus preventing further growth.

A menstrual cycle occurs roughly in a monthly pattern (typically a 28-day cycle, but usually anywhere between 21 and 35 days). In the first half of the cycle, oestrogen levels rise, causing the *endometrium* (the lining of the uterus) to thicken. *Ovulation* occurs in the middle of the cycle (about day 14), when oestrogen levels peak, and after this large amounts of a second female hormone, *progesterone*, are produced from the emptied follicle, now called the *corpus luteum*. Progesterone causes the endometrium to stop thickening and to become receptive to a possible embryo. Progesterone also

prevents menstruation if a woman becomes pregnant, and it is associated with premenstrual fluid retention and often some bowel bloating and period pain. About a week before a period is due, progesterone levels start to drop if pregnancy has not occurred. Once a period has started, oestrogen begins to rise again, starting a new cycle.

As you can see, hormones are incredibly important in the menstrual process and for many other body functions.

What are hormones?

Our body is made up of billions and billions of cells, and these cells need to communicate with each other so that everything functions in unison. The body is a bit like an orchestra, with each instrument representing an individual cell. The orchestra needs to follow the conductor to produce a beautiful piece of music. If the instruments are not coordinated, then a terrible noise results. Likewise, if the cells in our bodies are not properly coordinated, we become sick.

The body uses two main communication systems in order to keep in sync: the nervous system and hormones. The nervous system is hard-wired into the body and permits rapid commands and responses. For example, if you step onto something sharp, pain sensors in the skin of your foot rapidly let your brain know something is wrong. The brain in turn rapidly responds by activating the appropriate leg muscles to withdraw your foot—and this all happens in a split second. Hormones, on the other hand, are chemical messengers that travel from one part of the body to another to either stimulate or inhibit an 'everyday' action in the body. The effects of hormones appear more slowly and last for longer than nervous stimuli, and they are usually apparent in tissues quite remote from the gland where they originated.

Hormones are produced in the *endocrine glands*—pineal, pituitary, thyroid, parathyroid, adrenal, pancreas and ovaries or testes (see Figure 1.2). Each gland is responsible for the production of

specific hormones that control important and widely different processes such as nutrition, growth and reproduction.

The principal endocrine gland is the *pituitary*, located behind the nose at the bottom of the brain. The pituitary is responsible for controlling all the other major glands in the body, releasing a variety of hormones to control the ovaries (and testicles), the thyroid glands, the adrenals and so on. For example, the pituitary gland releases the *follicle stimulating hormone* (FSH), which stimulates the small follicles to grow in size—hence its name. FSH also stimulates the ovary to produce and release oestrogen. Oestrogen, like progesterone and androgens, is a sex hormone. Sex hormones, as the name suggests, govern our reproductive system.

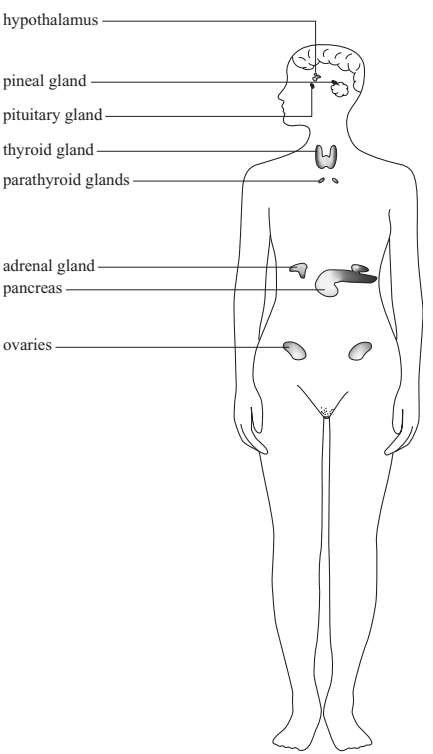

Figure 1.2 The location of the endocrine glands

How are the sex hormones produced?

There are three groups of sex hormones: the two female ones—oestrogen and progesterone—and a group of male hormones known as *androgens*. Having said that, women cannot produce any oestrogen without first making a male hormone. And men and women make both male and female hormones in order for their bodies to work correctly. It is the amounts of the particular male or female hormones within the body that differ between the genders. These three groups make up the family of sex hormones. A good analogy is musical instruments. The bassoon, oboe and clarinet are in the woodwind section of the orchestra and make a similar—but different—sound. Sex hormones are the same.

Androgen

The main male hormone or androgen is *testosterone*. The ovary produces much more testosterone than oestrogen, but then it converts some of this testosterone into oestrogen. If for some reason a woman was unable to make testosterone, then she could not produce any oestrogen. If a girl at puberty cannot produce any testosterone, then she cannot produce any oestradiol (a type of oestrogen—see below) and will remain sexually underdeveloped. Obviously men make a lot more testosterone than women, but men also make oestrogen. Interestingly, the average male produces more oestrogen than the average menopausal woman.

Myth: Women do not have any male hormones.
Fact: Women must be able to make testosterone, a male hormone, as without it they could not produce any oestrogen.

Usually the first hormonal event of puberty for a girl is the surge in a male hormone called *hormone dehydroepiandrosterone* (DHEA), made by the adrenal glands. The adrenals sit on top of the kidneys,

one on each side. The inner part of the adrenals produces and releases adrenaline and noradrenaline, which prepare our bodies for 'flight or fight'. The outer part of the adrenals makes cortisone and DHEA, which is found in the bloodstream as DHEA sulphate (DHEAS). DHEA is itself inactive but is converted into other active hormones, such as testosterone. Rising levels of DHEA in a young girl stimulate the formation of armpit and pubic hair (called adrenarche).

In the bloodstream, a special liver-derived protein, called *sex hormone binding globulin* (SHBG), carries both testosterone and oestradiol. SHBG binds testosterone more strongly than oestradiol, so SHBG is normally saturated with testosterone rather than oestrogen. The hormone that is bound to SHBG is thought to be inactive and only the free hormone is biologically active. Many things can elevate or suppress SHBG, and this will affect free, biologically active testosterone levels (see Table 1.1). As we will discuss later, those with polycystic ovaries tend to have higher blood levels of free testosterone than those with normal ovaries, and this will make them prone to skin problems such as excess body hair and acne.

Oestrogen

As we saw earlier, oestrogen is responsible for breast development at puberty and the onset of menstruation. Oestrogen also thickens and

Table 1.1 Factors influencing levels of SHBG and free testosterone

	Effect on SHBG level	Effect on free testosterone
Oral oestrogen	Strongly increases	Lowers
Patch oestrogen	Minimal effect	No effect
Androgens	Suppresses	Increases
Insulin	Suppresses	Increases
Weight gain	Suppresses	Increases

stimulates the endometrium (the lining of the uterus). The ovaries produce most of the body's oestrogen, but many other tissues can also make this hormone, including fat, the breasts and the brain.

While most people have heard of oestrogen, the main female hormone, few realise there are three main types of oestrogen: *oestradiol*, *oestriol* and *oestrone*. Oestradiol is the most important oestrogen during a woman's reproductive years, and it is the most potent one. Oestriol is the main pregnancy oestrogen, and is produced by the placenta—which not only nourishes the baby, but is a major source of the female hormones that help maintain the pregnancy. After the menopause (the last period), when the ovaries stop working, the main oestrogen is oestrone and the main source of it is fat tissue. This is why overweight women tend to have an easier time at menopause and have stronger bones than those who are thin. The downside of this extra oestrogen from fat is that it seems to increase the risk of oestrogen-sensitive cancers such as breast and uterine cancer.

Myth: There is only one type of oestrogen.
Fact: Oestradiol is the main oestrogen of the reproductive years. During pregnancy, the most abundant oestrogen is oestriol, while after menopause oestrone is most prevalent.

Progesterone

Progesterone is mostly made after ovulation by the remains of the collapsed ovulatory follicle (the *corpus luteum*). It stops the oestrogen-induced growth of the uterus and tends to thin its lining if a woman does not conceive. (If a woman does conceive, progesterone helps maintain the pregnancy until the placenta starts producing the hormones necessary to do this job.) Progesterone also has effects on the breasts and uterus—broadly antagonising the effects of oestrogen.

Table 1.2 shows the main functions of the sex hormones.

Table 1.2 The main functions of the sex hormones

Oestrogen	Progesterone	Testosterone
Stimulates the breasts and the uterine lining	Tends to stimulate the breasts and thin the uterine lining, lightening periods	Converts into oestrogen
Maintains bone strength	May thin the vaginal skin	Stimulates hair growth in armpits and pubic area
Keeps the vaginal skin thick and moist	May have a positive effect on bone	Stimulates libido
Has an anti-depressant effect on the brain	Sedative, calming brain effect	Has a positive effect on the brain and bone

How are sex hormones regulated?

There are three main players that regulate sex hormones in both men and women: the pituitary, the hypothalamus and the testes or ovaries. In women, these three communicate with each other to fine-tune the hormones so that the body can be prepared for and carry a pregnancy.

The pituitary gland

The pituitary gland (see Figure 1.3) is situated behind the nose, at the bottom of the brain, suspended from the hypothalamus. It is very small, about the size of a thumbnail. It is the master gland that controls the development and functioning of important organs and systems throughout the body. It has two lobes, and it is the front part or 'anterior pituitary' that releases the hormones that regulate other glands in the body, including the thyroid, the adrenals and the ovaries in women, and the testes in men.

The hypothalamus

On top of the pituitary is a small area of the brain called the hypothalamus, which regulates many of the automatic functions of the

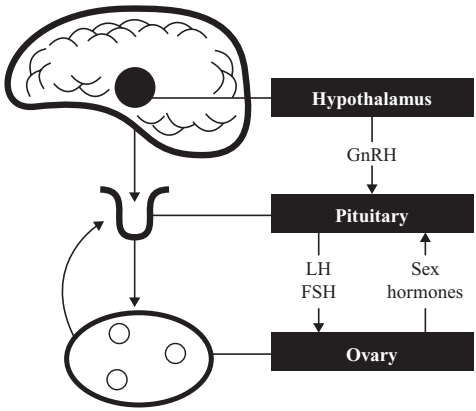

Figure 1.3 The hypothalamic–pituitary–ovarian axis

body such as temperature control. Within the hypothalamus is the *cyclic centre*, or *arcuate nucleus*, which regulates the pituitary's control of the ovaries. During the reproductive years, the cyclic centre fires a pulse of a hormone called *gonadotropin releasing hormone* (GnRH) every 90 minutes or so to stimulate the pituitary to release the two hormones that regulate the ovaries: *luteinising hormone* (LH) and *follicle stimulating hormone* (FSH). These two then act on the ovary to produce androgens and oestrogens and to stimulate ovulation. Other hormones such as activin can alter the action of FSH on the ovary. Activin stimulates pituitary FSH secretion, acts on the ovary to promote follicular growth and also affects insulin secretion.

The ovaries

Most of the fine-tuning of the menstrual cycle involves a dialogue between the ovaries and the pituitary. Using a 28-day cycle as an example (remember, a menstrual cycle ranges from 21 to 35 days), this is what usually happens:

Day 1 This is the first day of menstrual bleeding. The pituitary gland starts to release LH and FSH into the bloodstream to stimulate the ovaries. LH will act on the ovary to

produce androgens, which will then convert into oestrogens under the influence of FSH. FSH will also cause the ovarian follicles to grow.

Day 7 A cluster of follicles on an ovary (usually only on one of the ovaries) can be seen using ultrasound scanning. A dominant follicle produces increasing amounts of oestrogen and another hormone called inhibin. The rising blood levels of these two hormones suppress FSH levels. LH levels are not affected as much as FSH.

Day 10 Blood FSH levels have dropped and, while these falling levels don't seem to affect the dominant follicle, the smaller follicles start to disappear.

Day 13 The dominant follicle has grown to about 20 millimetres in diameter (see Figure 1.4) and it signals the pituitary that it is ready to ovulate. This signal involves two hormones—very rapidly rising levels of oestradiol and progesterone. Either alone won't do it: both are needed. The pituitary then releases all its stored LH and FSH. Because FSH has been selectively suppressed for the days leading up to this time,

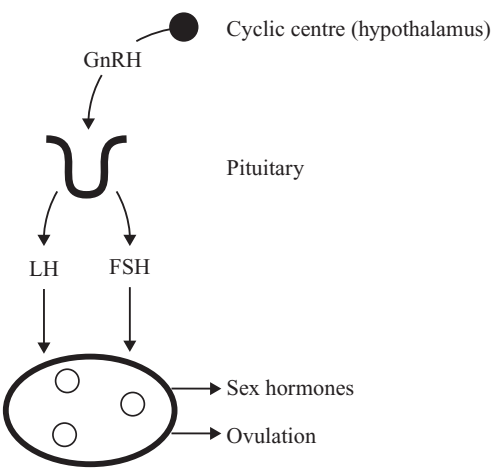

Figure 1.4 Control of follicular growth in the ovary

much more LH is released compared with FSH. This spike in blood levels of LH is called the *LH surge*. The LH surge does two things to the dominant follicle: it induces ovulation; and it switches on the egg to make it receptive to sperm.

Day 14 Ovulation takes place. A red bubble called a *stigma* forms on the surface of the follicle, which breaks down, allowing the egg to escape. It is then drawn into the nearby fallopian tube. The activated egg usually survives only a day or so and if it is not fertilised it will die. The remains of the follicle are converted into the corpus luteum, or 'yellow body'. The corpus luteum starts to produce large amounts of oestrogen and progesterone. As oestrogen and progesterone are essential for the maintenance of a pregnancy, the corpus luteum will continue to produce these essential hormones until the placenta takes over that job from about the eighth week of the pregnancy.

Day 21 If pregnancy does not occur, then the corpus luteum will start to die, and blood levels of oestrogen and progesterone will begin to fall.

Day 28 The top layer of the uterine lining needs oestrogen and progesterone to function. If these two fall to very low levels, then the endometrium dies and starts to slough off.

Day 1 Menstruation occurs. Most of the menstrual loss during the first two menstrual days is tissue from the endometrium; after that, most of the loss is bleeding from damaged uterine blood vessels.

Summary

Hormones play an important role in body function. Going back to the orchestra metaphor, think of hormones as the notes of the music. They need to be released by finely tuned glands (the instruments) so your body (the orchestra) can perform harmoniously. There are

many types of hormones, including 'male' and 'female' ones. But note that both men and women must make both male and female hormones. Women need male hormones such as testosterone for their menstrual cycle to function normally. In fact, the ovaries produce more testosterone than oestrogen, although they convert some of this into oestrogen.

Problems occur when too much of a particular hormone is produced. For example, when testosterone is in the bloodstream, it is mostly attached to a carrier protein called SHBG. A small percentage of testosterone, however, is free. This is dissolved in blood, and is biologically active.

Excess free testosterone is like too many wrong notes being played. It can cause someone who is prone to develop skin problems such as excess body hair and acne to do so. As we will discuss later, those with PCOS tend to have higher blood levels of free testosterone than those with normal ovaries.

It is very important to distinguish between polycystic ovaries (PCO) and polycystic ovary syndrome (PCOS). It is thought that about one in four women, or 25 per cent, will be found to have PCO if they are screened on an ultrasound. If you are scanned and found to have PCO but have no symptoms, then you should consider yourself normal. As I will discuss in later chapters, problems such as irregular periods, acne and excess body hair that generally start around puberty are usually managed quite easily.

Around 5–7 per cent of all women will have PCOS, meaning they have two out of three of the following problems: polycystic ovaries; fewer than six periods per year; and/or blood or cosmetic evidence of excess male hormone production. As we will see later, long-term issues such as diabetes are more common for those with PCOS than for those who simply have polycystic ovaries and no symptoms. It is therefore vital that a correct diagnosis of PCOS is made, as this will determine how much—if any—treatment is required to manage symptoms.

Frequently asked questions

What's the difference between having PCO and PCOS?

It is quite likely that one in four women will be found to have PCO (polycystic ovaries) if their ovaries are scanned on an ultrasound. Most of these women, however, will have menstrual cycles every three to eight weeks. Women with PCOS (polycystic ovary syndrome) have polycystic ovaries and symptoms such as irregular periods and excess body hair. Those with PCOS are more likely to be at greater risk of more serious medical conditions, such as diabetes. All of these symptoms will be discussed in greater detail in Chapters 4 and 5.

Are women with PCO infertile?

No. Women with PCO whose menstrual cycles occur every three to eight weeks usually have little trouble conceiving. If they are having problems conceiving then they should have other fertility factors checked, such as the health of their fallopian tubes and their partner's sperm count.

What is a hormone?

Hormones are simply chemical messengers that coordinate bodily functions. They are produced in the glands of the body and are sent to other parts of the body to stimulate or inhibit a reaction. For example, the pituitary gland sends FSH to the ovaries to stimulate follicles to grow larger.

Do women make male hormones too?

Yes, it is essential for women to make male hormones. The ovaries produce testosterone, which is then converted into oestrogen. Thus

a woman who can't make testosterone cannot make any oestrogen at all. Men produce both testosterone and oestrogen too, but men make a lot more testosterone than women do.