Diagnosis and treatment of polycystic ovarian syndrome

**AUTHOR** Ann Elaine Jones, BSc, RGN, is tutor in clinical skills, University of Wales Swansea, School of Health Science, Carmarthen.


Polycystic ovarian syndrome is a hormonal disturbance that results in a collection of symptoms and has wide-ranging health implications. There is evidence that it may run in families, and it is associated with the development of type 2 diabetes and recurrent miscarriage. Diagnosis involves eliminating other potential conditions, while treatment aims to manage individual symptoms rather than provide a cure.

Polycystic ovarian syndrome (PCOS) is a complex hormonal disturbance with numerous implications for general health and well-being (McKittrick, 2002). It is the most common endocrine gland disorder in women of reproductive age (Lockwood, 1997) and has a prevalence of 5–10 per cent in this group (Hill, 2003). However, many women remain undiagnosed or are misdiagnosed as having other conditions such as premenstrual syndrome (Harris and Carey, 2000; Raisbeck, 1999).

**Normal physiology**

According to Poisson et al (1998), although about 20 per cent of all women are found to have polycystic ovaries on ultrasound, only 10–20 per cent of these develop full PCOS. The two conditions are occasionally referred to collectively as PCO/S (Harris and Carey, 2000).

To appreciate the complexity of PCOS, it is important to understand the menstrual cycle and the hormones involved. A normal 28-day cycle commences with the onset of menstruation, coinciding with the development of a dominant cyst (a follicle) within the ovary (Kelley, 2003). During the cycle’s first (follicular) phase, the hypothalamus sends gonadotrophin-releasing hormone (GnRH) to the pituitary gland, triggering it to release low levels of follicle-stimulating hormone (FSH).

To produce oestrogen, follicles require a small amount of luteinising hormone (LH). This causes the thecal cells (ovary cells directly surrounding the follicle) to manufacture testosterone, which is transported to the cells on the inside of the follicle (granulosa cells) (Harris and Carey, 2000). There, an enzyme called aromatase converts testosterone into oestrogen, and as the follicle increases in size stimulated by FSH, oestrogen production increases (Harris and Carey, 2000). This rise in oestrogen levels, especially late in the follicular phase, boosts the release of LH and FSH from the anterior pituitary in a positive feedback loop. As a result, LH and FSH secretion increases rapidly prior to ovulation (Seeley et al, 2003).

The sharp rise in LH secretion is not only due to the direct effect of oestrogen on the anterior pituitary but also to the increase in secretion of GnRH by the hypothalamus (Tortora and Anagnostakos, 1990). On the 14th day of the cycle, ovulation is initiated by this LH surge, causing the ovulated follicle to become the corpus luteum.

Shortly after ovulation, in the luteal phase of the cycle, oestrogen production decreases and progesterone increases as the granulosa cells change to corpus luteum cells (Seeley et al, 2003). Progesterone prepares the endometrium for implantation of the ovum in the event of fertilisation (Kelley, 2003).

The increase in progesterone has a negative feedback effect on GnRH release from the hypothalamus, resulting in a decrease in LH and FSH release from the anterior pituitary (Seeley et al, 2003). On day 24 or 25, before the end of the cycle on day 28, the corpus luteum regresses, leading to a fall in progesterone levels and a deterioration of the endometrial lining, which results in menstruation.

**The condition**

PCOS is a complex, heterogeneous disorder involving a combination of abnormalities associated with PCO (Aherne, 2004). However, there remains a degree of uncertainty about its aetiology (Hopkinson et al, 1998). There is some evidence to suggest autosomal genetic transmission, with strong familial clustering (Hopkinson et al, 1998). McKittrick (2002) asserts that women with PCOS often have both male and female relatives with adult-onset diabetes, obesity, elevated blood triglycerides and high blood pressure, and female relatives with infertility, hirsutism and menstrual problems.
PCOS is the product of a metabolic state of insulin resistance having polycystic ovaries (Harris and Carey, 2000). Presenting with recurrent miscarriage are recognised as the ovary results in anovulation, multiple cysts and excess androgen output (Kelley, 2003). Harris and Carey (2000) maintain that an elevated level of LH can be a constant stimulation of LH (McKittrick, 2002). This constant stimulation of the ovary results in anovulation, multiple cysts and excess androgen output (Kelley, 2003). Harris and Carey (2000) maintain that an elevated level of LH can be a useful marker for predicting women who are at risk of miscarriage. Regan (1990) demonstrated that 67 per cent of women with an elevated LH miscarried, compared with seven per cent of those with a normal level of LH. Following on from this, over 80 per cent of women presenting with recurrent miscarriage are recognised as having polycystic ovaries (Harris and Carey, 2000).

It has been suggested that primarily insulin-dependent PCOS is the product of a metabolic state of insulin resistance in which it is difficult to transfer glucose into the cells (Kelley, 2003). This results in increased blood glucose, which signals for further secretion of insulin, leading to hyperinsulinaemia. Insulin, in combination with LH, stimulates an increase in the manufacture of testosterone by the ovaries and decreases the level of sex hormone-binding globulin (SHBG), resulting in more free testosterone and a potential exacerbation of symptoms (Harris and Carey, 2000).

**Diagnosis**

Hill (2003) asserts that a diagnosis of PCOS should be considered when women present with symptoms such as menstrual cycle dysfunction, infertility and hirsutism. Due to the syndrome’s heterogeneous nature the development of a diagnostic criterion has proven difficult (Hill, 2003), but Marantides (1997) maintains that diagnosis should commence with a detailed history and physical examination, focusing on the elimination of other possible differential diagnoses.

**History**

Initially, a brief review of symptoms should be completed, establishing any contributory chronic illnesses, abnormalities and medication history (Marantides, 1997). If one of the more common symptoms of PCOS is absent or menstrual flow is decreased, a thorough menstrual history is vital. This should include information on age of menarche, if and at what age periods regulated, duration of menstrual cycle, flow volume and duration, and any change apparent over time (Miller, 2002). An accurate menstrual history can be obtained by asking the patient to keep a diary noting commencement of menstruation and quantity of flow each day. Further information regarding reproductive history is important, including contraception, number of pregnancies, miscarriages and terminations (Miller, 2002). Symptoms of excess androgens, such as abnormal hair growth and distribution, voice changes, frontal balding and clitoromegaly should be explored (Marantides, 1997). The hirsutism of PCOS is characterised by coarse hair on the upper lip, chin, sideburn area, periareolar area, chest, lower abdomen in the midline and inner thighs (Miller, 2002). A careful medical history is vital, as many drugs have been associated with hirsutism including antiepileptics such as phenytoin and sodium valproate (Hill, 2003).

Acanthosis nigricans (a skin disorder that causes light-brown-to-black, velvety, rough areas or increased skin markings) mainly in the axilla and other body folds is an indication of PCOS and suggestive of significant insulin resistance. Screening should be undertaken for diabetes, including excessive thirst, hunger, urination, along with information regarding fertility and any history of weight gain or acne (Miller, 2002).

Enquiries into family history are also vital: a woman whose mother or sister has PCOS is at highest risk. Family history of hypertension, diabetes, obesity and early coronary artery disease should also be explored, as these may be the only available historical clues (Miller, 2002).

**Metabolic disturbances:**

- Dyslipidaemia;
- Cardiovascular risk;
- Hyperinsulinaemia;
- Insulin resistance and risk of diabetes.

It may be that a gene or series of genes renders the ovaries susceptible to the insulin-mediated stimulation of androgen secretion, while blocking maturation of the follicles. This genetic predisposition may be expressed as premature balding in men (Hopkinson et al, 1998).

Kelley (2003) maintains that PCOS is a much more complex disorder, and that there may be two types: one primarily LH dependent and the other primarily insulin dependent. In LH-dependent PCOS, normal ovarian function is dependent on appropriate signals from the FSH and LH secreted from the pituitary gland (McKittrick, 2002).

PCOS is characterised by hyperstimulation of the pituitary by LH (McKittrick, 2002). This constant stimulation of the ovary results in anovulation, multiple cysts and excess androgen output (Kelley, 2003). Harris and Carey (2000) maintain that an elevated level of LH can be a useful marker for predicting women who are at risk of miscarriage. Regan (1990) demonstrated that 67 per cent of women with an elevated LH miscarried, compared with seven per cent of those with a normal level of LH. Following on from this, over 80 per cent of women presenting with recurrent miscarriage are recognised as having polycystic ovaries (Harris and Carey, 2000).

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Pelvic and physical examination
A physical examination measuring blood pressure, weight and height should be completed. A routine pelvic and general physical examination should also be conducted, noting the presence of secondary sex characteristics, along with palpation of the thyroid gland for masses or enlargement. The ovaries and adnexae should be palpated for signs of enlargement and the presence of any tumours or cysts, both of which suggest PCOS (Marantides, 1997).

Kelley (2003) maintains PCOS is a diagnosis of exclusion, requiring the presence of hirsutism, evidence of ovarian dysfunction and obesity. These features usually appear at adolescence and deteriorate over time.

Laboratory studies
Further diagnostic information can be obtained through laboratory measurement of FSH, LH, thyroid-stimulating hormone, prolactin, dehydroepiandrosterone and testosterone levels to ascertain the exact hormonal imbalance (Munson, 2002). Total cholesterol and high-density lipoprotein cholesterol levels should also be obtained as a baseline (Campbell and Poirier, 2000).

However, establishing a diagnosis of PCOS insulin resistance is more problematic and can only be gauged from clinical signs of PCOS and impaired glucose metabolism, which is demonstrated in the laboratory by a fasting glucose level of 110–125mg/dL, impaired two-hour glucose tolerance test (GTT) of 140–199mg/dL, and fasting insulin ratio of <4.5 (Kelley, 2003).

Ultrasonography
Ultrasonography can be helpful in establishing the diagnosis of PCOS. A finding of eight or more discrete ovarian follicles smaller than 10mm in diameter is suggestive of the syndrome (Miller, 2002). Follicles are usually on the periphery of the ovary, arrayed around an enlarged hyperoestrogenic ovarian stroma (Miller, 2002). Diagnosis of PCOS is therefore preferable when there are the associated symptoms, namely irregularity of the menstrual cycle, hyperandrogenisation, obesity or raised serum LH and testosterone in addition to ultrasound findings of polycystic ovaries (Balen, 1995).

Signs and symptoms
Aherne (2004) states that the major clinical features pertaining to PCOS can be divided into three components:

- Hyperandrogenism – characterised by elevated levels of serum androgen;
- Anovulation;
- Metabolic disturbances (Box 1, p41).

Edwards (1999) found that 75 per cent of female volunteers with PCOS had irregular menstrual cycles. Chronic anovulation can result in difficult conception and increased risk of miscarriage (Aherne, 2004).

Kelley (2003) states that obesity associated with PCOS presents primarily in the abdomen. Obesity is associated with numerous conditions including hypertension, diabetes, dyslipidaemia and heart disease, but for women with PCOS it produces further complications, with the hyperoestrogenic environment converting ovarian and adrenal androgens to oestrone peripheral fat cells (Kelley, 2003).

Management and treatment
Treatment for PCOS is complex and is limited to addressing symptoms rather than providing a cure (Raisbeck, 1999). It should be based on the patient’s wishes and concerns regarding symptom management (Marantides, 1997).

Hill (2003) says the goals of treatment include suppression of hyperandrogenism to improve acne and hirsutism, resumption of reproductive function for desired fertility, endometrium protection and the reduction of the long-term risks of type 2 diabetes and cardiovascular disease. No single therapy treats all aspects of PCOS and some will treat one symptom but exacerbate another, and so are mutually exclusive (Hill, 2003).

There are two types of therapy for hirsutism – cosmetic hair removal and pharmacotherapy. Cosmetic removal includes temporary measures such as tweezing, shaving, waxing and depilatories, while electrolysis and laser treatment will remove hair permanently (Hill, 2003). These treatments should not be attempted until six months after the start of medical therapy, or there will be regrowth of coarse hair (Campbell and Poirier, 2000).

The pharmacological treatment of hirsutism slows growth of new hair but does not affect established hair (Rosevear, 2002). Reduction of testosterone to normal levels can be accomplished by ovarian suppression with 100–200mg spironolactone daily (Campbell and Poirier, 2000). This is a diuretic as well as having an antiandrogenic effect. Improvements take 6–12 months to appear (Raisbeck, 1999). Side-effects include menstrual irregularities, which occur in 50 per cent of patients, and it is recommended the drug is used in combination with a combined oral contraceptive (COC) (Hill, 2003). The COC has also been found effective in treating hirsutism by suppressing LH secretion and therefore LH-mediated androgen secretion by the ovary (Rosevear, 2002).

Flutamide, a proposed alternative to spironolactone, acts by inhibiting the androgen receptor. Liver function monitoring is essential as hepatotoxicity has been

Guided reflection
Use the following points to write a reflection for your PREP portfolio:

- Outline your area of expertise and why you read this article;
- Explain the implications of PCOS for the health and well-being of women;
- Summarise the symptoms of PCOS and the diagnostic process;
- Summarise the treatment available;
- Explain how the information in this article will help you in your future practice.
Women with anovulatory infertility and oligomenorrhea (infrequent menstruation) need ovulation induction, for which clomiphene citrate is the drug of choice (Rosevear, 2002). However, this increases the risk of multiple pregnancy, and it is recommended that treatment lasts no longer than six months due to the increased risk of ovarian cancer (Hopkinson et al, 1998).

Laparoscopic ovarian surgery – most commonly ovarian diathermy and laser – has replaced ovarian wedge resection as the surgical treatment for clomiphene-resistant women with PCOS (Balen, 2000). However, while surgery is effective in treating ovulation and regulating menses, the effects are short term (Hopkinson et al, 1998).

Implications for nursing practice
Due to the complex nature of PCOS and the wide range of possible symptoms, health care professionals need an in-depth understanding of the condition, its pathophysiology, diagnostic measures and symptom management. Women presenting with menstrual irregularities should be encouraged to monitor their symptoms as this will help in the diagnosis of possible PCOS. Once diagnosis has been confirmed, nurses need to ensure patients receive adequate written information, such as leaflets, to clarify issues discussed on initial diagnosis.

As a diet regimen is one of the main treatments for PCOS, a referral to a dietitian should be discussed once diagnosis has been confirmed. A suitable exercise regimen should also be discussed, and the importance of both diet and exercise should be explained to the patient. Psychological support is vital, particularly on initial diagnosis. Nurses should be aware of the various agencies that offer further advice and support. Counselling and follow-up should also be made available to all women with PCOS (Lockwood, 1997).

FURTHER INFORMATION/SUPPORT
www.kathies-pain.com/pcos.htm
www.womens-health.co.uk/pcos.asp
www.pcos-support.org (US)
www.netdoctor.co.uk/womenshealth/facts/pcos.htm
www.ihr.com/infertility (Infertility Resources for Consumers)
www.infertilitynetworkuk.com
www.pcovitaline.com (personal healthy eating plans, caring support)
www.verity-pcos.org.uk (UK self-help group)
www.m2w3.com/acne (acne support group)