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# Polycystic ovary syndrome

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Polycystic ovary syndrome (PCOS), a highly prevalent endocrine disorder, is the commonest cause both of hirsutism and of anovulatory infertility. In addition, it is now known to be associated with a typical metabolic disturbance which predisposes to a high risk of non-insulin-dependent diabetes mellitus (NIDDM) in later life. The aetiology of PCOS is unknown but there is evidence that it is a complex trait involving the interaction of a small number of key susceptibility genes with environmental factors.

## Definition and presentation

The most widely accepted definition of PCOS is the association of hyperandrogenism with chronic anovulation in the absence of specific underlying disorders of the pituitary or adrenals. With the aid of high-resolution ultrasonography of the ovaries, it has become apparent in recent years that PCOS is a heterogeneous condition with a spectrum of clinical and biochemical features. This spectrum encompasses anovulatory subjects without hirsutism or acne but who usually have elevated serum levels of testosterone, and, conversely, hirsute women with regular ovulatory menses. Obesity is common, although still occurring only in a minority (35–40%) of subjects with PCOS. The *syndrome* of polycystic ovaries is therefore best defined as the presence of symptoms of anovulation (oestrogen-replete amenorrhoea, irregular menses) and/or symptoms of hyperandrogenism (hirsutism, acne, androgenic alopecia) in women with polycystic ovaries.

The typical biochemical features of PCOS are elevation of serum testosterone (mean 3.2 nmol/l [range 1.3–7.0] in our series; normal 1.7 [0.9–3.0]) and luteinising hormone (LH) levels but with normal serum follicle-stimulating hormone (FSH) concentrations. However, as with the clinical presentation, there is considerable heterogeneity in the endocrine indices, which has implications for the diagnostic application of hormone measurements.

## Metabolic abnormalities

Hyperinsulinaemia and peripheral insulin resistance are the central features of the metabolic disorder now recognised to be typical of PCOS. There is an associated dyslipidaemia, and it has been suggested that women with PCOS are at increased risk of cardiovascular disease – although there is no direct evidence for this as yet. It is, however, clear that women with PCOS are at increased risk of NIDDM. Impaired glucose tolerance is present in 10–30% of obese young women with the 'classic' syndrome (ie hyperandrogenism and anovulation), and it is estimated that

## Key Points

▶ **Hypersecretion of androgens associated with polycystic ovaries is the commonest cause of hirsutism, even in women with regular menses**

▶ **Polycystic ovary syndrome (PCOS) is the commonest cause of menstrual disturbances**

▶ **The typical, but not invariable, biochemical features of PCOS include elevated serum levels of luteinising hormone and testosterone**

▶ **PCOS is associated with metabolic abnormalities characterised by hyperinsulinaemia, insulin resistance and dyslipidaemia**

▶ **The risk of developing non-insulin-dependent diabetes mellitus in later life in women with PCOS is 6–7 times that in the appropriate control population**

▶ **The diagnosis of the syndrome is made primarily on a clinical basis, supported by ultrasound and biochemical tests**

▶ **Selection of investigations and decisions about management are made according to clinical presentation**

**Table 1. Endocrine investigation of polycystic ovary syndrome.**

| Presentation | Tests |
| --- | --- |
| Hirsutism/acne/alopecia | Serum testosterone |
| Oligomenorrhoea/amenorrhoea | Follicle-stimulating hormone<br>Luteinising hormone<br>Prolactin<br>Assessment of oestrogen production |
| Obesity | Fasting glucose<br>(Lipid profile) |

women with PCOS are 6–7 times more likely than weight-matched controls to develop NIDDM in later life.

## Diagnosis

The diagnosis of PCOS is primarily clinical. A patient presenting with irregular menses, oligomenorrhoea or amenorrhoea and who has signs of hyperandrogenism is very likely to have PCOS. Even in the absence of hirsutism, PCOS is the most likely cause of these menstrual symptoms, accounting for about 30% of cases of amenorrhoea overall and about 90% of amenorrhoeic women with normal oestrogen levels.

The majority of patients presenting with hirsutism have polycystic ovaries, irrespective of menstrual history. Much rarer, but more serious, causes of hirsutism and menstrual disturbances include Cushing's disease, acromegaly, hyperprolactinaemia and tumours of the adrenal or ovary. In such cases, however, there are usually other clues to the diagnosis, both clinical and biochemical, for example, a short history of increasing hirsutism and significantly raised serum testosterone (>5 nmol/l). For this reason, serum testosterone should be measured in all hirsute patients as a screening test to exclude more serious causes of hyperandrogenism.

Late-onset ('non-classical') congenital adrenal hyperplasia due to 21-hydroxylase deficiency may be difficult to distinguish clinically from PCOS, but it is debatable whether this makes much practical difference to the management of symptoms. Thus, in our clinic, where the prevalence of non-classical 21-hydroxylase deficiency is less than 5%, measurement of 17α-hydroxyprogesterone, the biochemical marker of 21-hydroxylase deficiency, is not performed routinely.
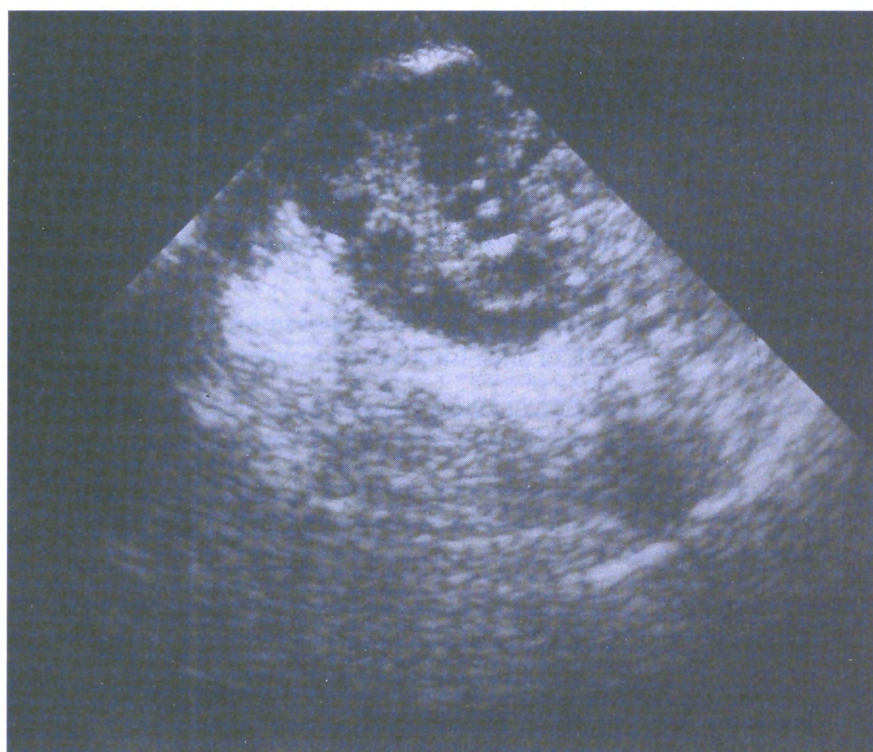
### Diagnostic tests

No single test is diagnostic of the syndrome and the choice of investigations should be tailored to the clinical presentation (Table 1):

- *Serum LH levels* are typically elevated in PCOS, but up to 50% of women with all other clinical and biochemical features of the syndrome may have normal serum LH. Measurement of LH is therefore of limited diagnostic value. Although quite specific, in that raised LH levels with normal FSH essentially occur only in PCOS, it is not very sensitive.

- *Pelvic ultrasonography* will define the polycystic ovarian morphology (Fig 1), but accurate assessment of the ovaries by ultrasound is a particular skill and false negative results are not uncommon.

Conversely, the presence of polycystic ovaries does not *necessarily* mean that the patient has polycystic ovary *syndrome*. Polycystic ovaries may be found coincidentally in women who have, for example, hypothalamic, oestrogen-deficient amenorrhoea. Thus, investigation of women with PCO and



**Figure 1.** Ultrasound image of a typical polycystic ovary, showing multiple follicles and increased stroma.

amenorrhoea should also include measurement of serum prolactin and assessment of oestrogen production.

In summary, pelvic ultrasonography and measurements of LH, FSH and testosterone may be of some diagnostic value when set in the appropriate clinical context (Table 1). By contrast, routine measurements of adrenal androgens are not indicated, and measurement of sex hormone-binding globulin (primarily an index of body weight) is not helpful. It is recommended that obese women with PCOS should have a fasting glucose measurement at least once a year because of the increased risk of NIDDM and, in view of the associated dyslipidaemia, there may also be some merit in checking the lipid and lipoprotein profile at the same time.

## Management

The physiological basis of PCOS is unknown, so treatment is largely symptomatic. Patients with anovulation may require induction of ovulation. The anti-oestrogen, clomiphene, is usually effective, but even this 'simple' treatment should be monitored at a specialist centre because of the risk of ovarian hyperstimulation and multiple pregnancy. For those not concerned about fertility, menstrual regulation by means of oral contraceptives or cyclical progestogens should be considered. Non-androgenic progestogens (eg medroxyprogesterone acetate, desogestrel, gestodene) are obviously preferable to norgestrel and norethisterone in women who may already have symptoms of androgen excess.

Symptoms of hyperandrogenism can be managed by anti-androgens such as cyproterone acetate. In women with acne and/or mild or moderate hirsutism, this can usually be given in the form of Dianette (cyproterone acetate, 2 mg + ethinyloestradiol, 35 mg). Cosmetic advice about removal of hair should not be forgotten, whether or not anti-androgens are given. Obese subjects with PCOS require particular attention. Calorie restriction greatly improves the chances of ovulation and reduces the risk of NIDDM.

## Further reading

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# New treatments for acromegaly

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Acromegaly is a clinical diagnosis, occasionally helped by consulting old photos to look for bony and facial changes. Men and women of all ages are equally affected, with a peak age of diagnosis between 30 and 50 years[1]. With increasing awareness, the diagnosis is made earlier now: in the 1930s, 30% of patients presented with visual field defects due to their pituitary tumour, whereas now the figure is nearer 10%[2].

Patients most frequently notice increasing hand and foot sizes (*akron* = extremity, *megas* = great), headaches, and excessive perspiration (Table 1). The diagnosis is often made by chance at a medical encounter for another reason or at presentation to a diabetic, neurology or urology clinic.

## Aetiology

In over 99% of patients acromegaly is caused by a pituitary adenoma secreting either growth hormone alone or both growth hormone and prolactin (35% of cases); very rarely, the pituitary adenoma may secrete thyroid stimulating hormone (TSH) as well as growth hormone, in which case there is hyper-

## Key Points

▶ In over 99% of patients acromegaly is caused by a growth hormone-secreting pituitary adenoma

▶ Acromegaly is associated with increased mortality due to cardiovascular and respiratory disease and probably malignant disease

▶ The aims of treatment are to decrease or remove tumour mass, reverse symptoms and normalise growth hormone hypersecretion

▶ Surgical cure may be achieved by an experienced surgeon in acromegalic patients with a microadenoma. The majority of patients are left with growth hormone hypersecretion

▶ Somatostatin analogues offer the most effective medical treatment for acromegaly, resulting in symptomatic improvement and a fall in growth hormone levels in the majority