

A Practical Approach to the Diagnosis and Management of Polycystic Ovary Syndrome

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Introduction

Polycystic ovary syndrome (PCOS) is a clinical diagnosis. It occurs in 7% of reproductive aged women (newer criteria have it at 10%), making it the most common disorder (endocrinopathy related or otherwise) in reproductive aged women. The associated metabolic components continue after menopause. It has been recognized throughout history.¹ There may have been survival advantages during the hunter and gatherer stages,¹ but it now persists as the common combined genetic-environment/lifestyle disorder we recognize today.

Pathophysiology

This is likely multifactorial, both from genetic alterations and abnormalities in follicular growth. The normal menstrual cycle is complex, designed to have a single ovulation once a month. This can be disrupted by various changes noted in women with PCOS. These include the growth of too many follicles, follicles being more mature, and granulosa cell dysfunction, but the most consistent abnormality is theca cell dysfunction.² The theca cells from PCOS secrete more androgen than theca cells from normal follicles, and this is further aggravated if there is concomitant insulin resistance. The net effect is anovulation (but occasional

Victoria's Case

Victoria is a 22-year-old university student with complaints of irregular periods and unwanted body hair. Menarche was at age 15, and her periods have never been regular. They would occur from two weeks to five months apart and vary in intensity from light spotting for a few days to very heavy flow for two to three weeks. Midline, dark, coarse hair over the lip, chin, upper chest, and lower abdomen began at age 17 and has been slowly progressing ever since. She weighs 60 kg, which is appropriate for her height of 165 cm, but her weight has gone up by 5 kg since high school. She does not use contraception, as she considers her periods to be abnormal. There is no evidence of depression or sleep apnea. Family history finds that her mother complained of having excessive hair, and she now has type 2 diabetes while her only sister has irregular periods but no noticeably increased hair. There is no history of CVD. Clinical exam finds normal vital signs, euthyroid, and hirsutism, but no virilization, skin is thicker than normal (3 mm), no signs of Cushing syndrome, nor acanthosis nigricans.

normal ovulation), resulting in unopposed estrogen, which cause breakthrough menses at erratic times and of variable amount and subfertility. Excessive androgen secretion results in hirsutism, acne, and scalp alopecia. These symptoms can occur from the time of menarche or begin at a later time, especially after weight gain, which can aggravate insulin resistance and



Table 1
Criteria for Diagnosis of PCOS

NIH	Eshre 2003 (two new phenotypes)
1. Chronic estrogenized ovulation	1. Chronic estrogenized anovulation (occasionally do ovulate)
2. Hyperandrogenism (clinical or biochemical)	2. Hyperandrogenism
3. Exclusion of other causes of irregular menses and hirsutism	3. Polycystic ovaries on ultrasound <ul style="list-style-type: none">• two of three of the above
	4. Exclusion of other causes of irregular menses and hirsutism (some have regular ovulatory cycles, and some have no hirsutism)

enhance theca cell androgen secretion; subclinical PCOS may now be clinically evident PCOS. Primary insulin resistance (twice normal incidence) and obesity (twice normal incidence) are not the primary factors but, rather, are aggravating factors for the clinical and metabolic manifestations of PCOS.

How to diagnose PCOS

Diagnosis comes from the pathophysiology and the resulting clinical presentation of anovulation and hyperandrogenism. Standard androgen assays are problematic in women, so the clinical definition of hyperandrogenism is accepted. Diagnosis is by National Institutes of Health (NIH) criteria or European Society of Human Reproduction and Embryology (ESHRE) criteria using ultrasonography (see Table 1).

Personally, I do not use ultrasonography for clinical diagnosis. It is neither sufficiently sensitive nor specific, as normal women, and some women with other ovulatory disorders may have polycystic ovaries found on ultrasound. Table 2 shows the investigation for diagnosis and associated complications. The diabetic and lipid

Table 2
Investigation for Diagnosis of PCOS and Associated Problems

Diagnose PCOS	Screen for Associated Problems
<ul style="list-style-type: none">• Serum follicle-stimulating hormone (rule out ovarian failure)• Serum prolactin (rule out hyperprolactinemia)• Pregnancy test• AM serum 17 hydroxyprogesterone (screen for adult onset congenital adrenal hyperplasia)	<ul style="list-style-type: none">• Fasting serum glucose (oral glucose tolerance test is more sensitive)• Fasting lipids• Liver enzymes (consider ultrasound of liver)

screens may need to be repeated every few years and certainly before a planned pregnancy. The strong genetic component of PCOS dictates that first-degree relatives are at risk, including men, and they should be screened for associated metabolic problems.³ Exclusion of the rare Cushing's syndrome is done clinically or by screening tests (overnight dexamethasone suppression test, or 24-hour urinary free cortisol), and the rare androgen-secreting tumours can be excluded by a history of slow onset and symptom progression. It may be best not to over investigate. Many blood tests and ultrasonography are usually not needed, and they may be confusing.

Increased risk (5- to 10-fold) of associated problems⁴ include sleep apnea, hepatic steatosis (associated with, but independent of, obesity and insulin resistance), depression, and endometrial carcinoma. The increased incidence of insulin resistance, even after compensating for obesity, does greatly increase the premenopausal risk of type 2 diabetes, metabolic syndrome, presence of surrogate markers and risk factors for CVD, and possibly CVD later in life. Evidence for increased CVD is minimal and is not seen in premenopausal women,⁵ but it has been suggested to be increased after

Table 3
Treatment Options for PCOS Clinical Problems

Menstrual chaos	Hirsutism	Subfertility
<ul style="list-style-type: none"> • Oral contraceptive • Regular progestin-induced bleeds • Progesterone-only (Oral, BCP, im, intrauterine) • Weight loss 	<ul style="list-style-type: none"> • Oral contraceptive • Antiandrogen • Weight loss • Cosmetic depilation • Topical eflornithine • Combinations 	<ul style="list-style-type: none"> • Weight loss • Clomiphene • Gonadotropins • Ovarian electrocautery

menopause.⁶ Pregnancy in a woman with PCOS is accompanied by increased risks of gestational diabetes, hypertension, premature labour, obstetrical intervention, and perinatal complications. Ovulation induction increases the risk of multiple pregnancy.

Treatment of various aspects of PCOS

At any time of her reproductive life, patient concerns and clinical objectives will vary. If obesity is present, weight loss (even 5%) will generally improve most clinical problems in PCOS.^{7,8} Lifestyle and CV risk management is always addressed. Treatment is individualized, monitored, and altered as the clinical objectives change (see Table 3).

The most common treatment of hirsutism/acne is either spironolactone alone, birth control pill alone, or both in combination with each other. Menstrual regulation is best achieved by birth control pill or regular progestin challenges. Ovulation induction is achieved by clomiphene; failure to ovulate dictates referral to a specialist experienced with using gonadotropins.

Antiandrogens include mainly spironolactone, but also cyproterone, flutamide, and finasteride. The longest experience is with spironolactone, but the others are good alternatives. At this time, it is premature to consider aromatase inhibitors

Frequently Asked Questions

1. Is obesity part of PCOS diagnosis?

No, it is twice as common (60%), but not part of the diagnosis; normal BMI should not deter the diagnosis.

2. Do I treat CV risk factors in premenopausal women?

Put them in context of the total picture; preventative measure should be considered, such as smoking, BP, glucose intolerance.

3. When do I worry about an androgen-secreting neoplasm?

Less than 0.1% of hirsute women; rapid onset and progression is the clinical clue; do serum testosterone/DHEAS and abdominal ultrasonography

4. What is the role of routine ovarian ultrasonography?

If she has clinical PCOS, a positive ultrasound adds little, and a negative one does not change the diagnosis.

5. Can these women get pregnant without intervention?

Yes, later than normal and more spread out; thus, the need for contraception, and ovulation induction is only indicated after an unsuccessful trial.



Back to Victoria

Other causes of oligomenorrhea were excluded by a normal serum FSH and serum prolactin; the pregnancy test was negative. Fasting glucose (4.1 mmol/L) and lipids, liver enzymes, and 17-hydroxyprogesterone were all normal. Polycystic ovary syndrome was diagnosed by the presence of chronic anovulation with hyperandrogenism and with the exclusion of other causes. Because she was hesitant to use the birth control pill, Victoria started on monthly progestin-induced bleeding (prometrium 200 mg at bedtime for 10 days), and spironolactone 100 mg a day, all for a six-month trial. Follow-up serum electrolytes and creatinine were done after one month. The normal need for contraception was discussed.

for ovulation induction. Metformin has not been shown to be effective or superior to any of the treatments listed and is not recommended by most scientific bodies and Cochrane reviews.

Summary

PCOS presents with many clinical problems that vary over a woman's lifetime. It is important to identify and address the problems and individualize a clinical and therapeutic approach for the present and near and distant future. It is important to educate the patient and involve her in the treatment choices, and screen first-degree relatives for similar disorders. Lifestyle management, if needed, is always the initial choice, followed by symptomatic therapy.

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Take-home Message

1. PCOS is a common, clinical condition that presents with multiple problems over a woman's lifetime.
2. PCOS is diagnosed clinically after confounding conditions are ruled out by a clinical evaluation and a focused cost-effective investigation.
3. The identified problems are treated as long as they are clinically indicated, and they will vary over time in their priority.

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Resource

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