Lothian Guideline for the Diagnosis of Polycystic Ovary Syndrome (PCOS) in Primary Care

Summary

A diagnosis of PCOS requires at least 2 of the following 3 criteria:-

- Oligomenorrhoea or amenorrhoea
- Clinical and / or biochemical signs of excessive androgen secretion, ie hirsutism, acne, raised total testosterone or a raised Free Androgen Index (FAI). *Although raised LH, with a normal FSH, may be found in PCOS, gonadotrophin results no longer form part of the diagnostic criteria.*
- Presence of at least 12 follicles measuring 2-9 mm in diameter, an ovarian volume > 10ml, or both.

Lothian guidance is that a scan for suspected PCOS is not required unless there are other indications eg pelvic symptoms. THEREFORE THE DIAGNOSIS IS PRIMARILY MADE ON CLINICAL AND BIOHCEMICAL FEATURES.

Other possible causes of presenting features should be considered and excluded: congenital adrenal hyperplasia (CAH), androgen secreting tumour, Cushing's syndrome, thyroid dysfunction, hyperprolactinaemia and perimenopause etc. These generally are excluded with basic blood tests and clinical features. The most important pointer to the possibility of CAH, androgen secreting tumour or Cushing's syndrome is Testosterone >4nmol/l*

Laboratory investigation of patients with suspected PCOS

Sample Timing

Unless the patient is amenorrhoeic, the sample should be taken on days 1-5 of the menstrual cycle (since misleading increases in testosterone may occur later in the cycle).

Clinical details

- State the LMP
- If there is amenorrhoea, state this on the request form.
- Provide clinical details eg hirsutism, irregular periods etc: these are crucial as the laboratory may add additional tests.

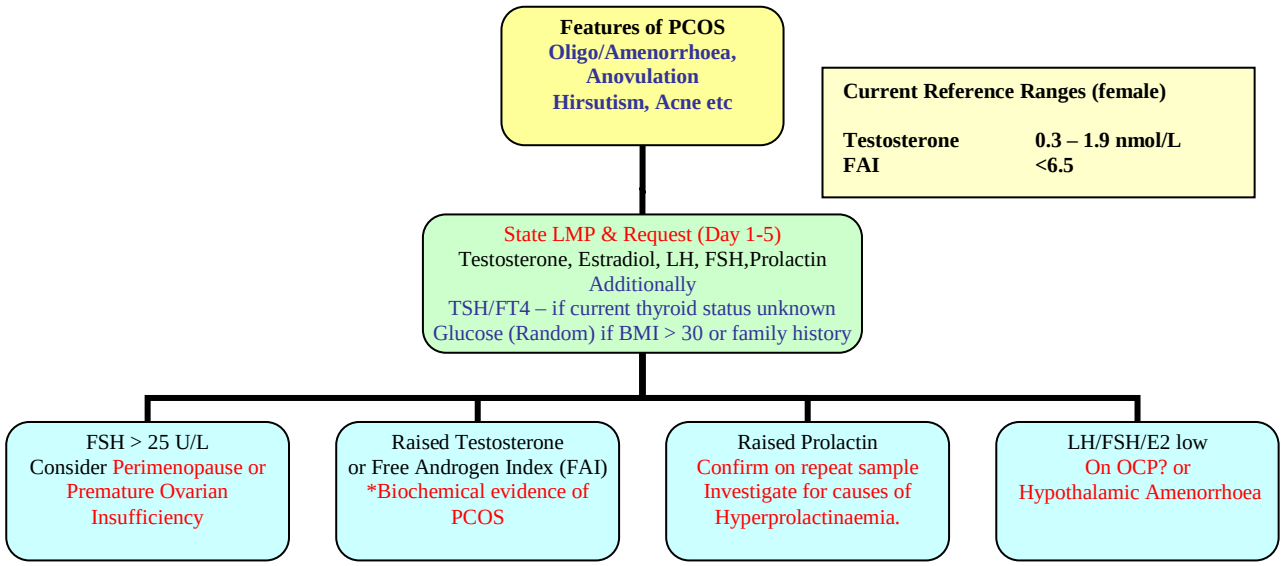
Test requests

- **LH, FSH, Estradiol, Testosterone & Prolactin as first line**
- **TFTs if thyroid status unknown**
- **random glucose (if BMI is > 30 or family history of diabetes)**

The laboratory will add any necessary additional tests (eg free androgen index (FAI), Dehydroepiandrosterone sulphate (DHEAS), 17 hydroxyprogesterone, androstenedione) in the light of the results and the clinical details provided. To facilitate the selection of further appropriate tests **it is crucial to provide all relevant clinical details.**

Reports

All results are scrutinised by the Duty Endocrine Biochemist who will issue an interpretative comment - if adequate clinical details have been provided – and indicate what additional action regarding further sampling etc is advised. Provision of full clinical details is important to ensure appropriate interpretation can be given. **The Endocrine Duty Biochemist can be contacted on 0131 242 6880**



*** It is unusual for PCOS to present with a testosterone of >4 nmol/L: in such patients the test should be repeated as soon as possible. If confirmed on repeat sampling, the patient should be referred for an endocrine opinion.**

Lothian PCOS : additional information

Background

PCOS is very common, with a prevalence in women of child-bearing age of 5-10%, and may be higher in women of South Asian origin. Clinical manifestations include infrequent or absent menses, anovulatory infertility, signs of androgen excess (hirsutism, acne or seborrhoea). Many women with the condition are overweight or obese. Biochemical abnormalities include raised testosterone and / or free androgen index. However, the gonadotrophins - LH and FSH - are often normal.

Women with PCOS have an increased risk of insulin resistance which, with the high prevalence of obesity, is a powerful risk factor for progression to Type 2 diabetes. They also have an increased long-term risk of endometrial hyperplasia/cancer. There does not seem to be an increased risk of breast cancer or ovarian cancer. Currently, despite having a number of risk factors for cardiovascular disease, it is unclear whether the actual risk is increased. Investigation of glucose tolerance (initially by a random glucose) should be considered in women with PCOS with relevant *additional* risk factors such as obesity and a family history.

LH and PCOS

Although increases in LH and the LH/FSH ratio occur in many women with PCOS, it is generally established that a serum LH is not required for the diagnosis. LH is often normal in PCOS, and a raised LH and LH/FSH ratio commonly found in women who do not have the syndrome, reflecting the pulsatile nature of LH secretion (or blood sampling shortly before ovulation). However, measurement of LH (and FSH) can be useful in identifying *other* causes of amenorrhoea eg the low gonadotrophins and estradiol found in 'functional' or 'hypothalamic' amenorrhoea associated with weight loss, stress and excess exercise. In the conditions with low gonadotrophins LH is initially more affected than FSH and FSH concentrations can be normal.

Testosterone and free androgen index (FAI) and PCOS

A large proportion of circulating testosterone is bound to a protein called sex hormone binding globulin (SHBG). SHBG-bound testosterone is biologically inactive, in contrast to the unbound or 'free' form of the hormone. The concentration of serum SHBG is decreased (and therefore active testosterone increased) in: PCOS, insulin resistance, obesity, hyperprolactinaemia, hypothyroidism and when there are high serum androgens. Conversely serum SHBG is increased (and active testosterone reduced) by: oestrogen, pregnancy, hyperthyroidism, excess alcohol, liver disease and anticonvulsants.

The free androgen index (FAI) is a simple method of estimating the circulating free testosterone in women but may be unreliable in situations where there are extreme abnormalities in the concentration of SHBG. It is calculated as:

$$\text{FAI} = \frac{[\text{total testosterone}] \times 100}{[\text{SHBG}]}$$

The FAI is more sensitive at detecting hyperandrogenism than total testosterone, and may be helpful in assessing androgen status in some women who have a total testosterone in the upper half of the reference range. At the other end of the scale, if the total testosterone is in the lower part of the reference range, FAI is generally not raised. As SHBG production is regulated by factors relevant in PCOS; obesity and insulin resistance are associated with reduced SHBG levels, therefore tending to increase the FAI (ie *active, free* hormone), while *total* testosterone can remain normal.

Testosterone production increases approximately two-fold outside the early follicular phase of the menstrual cycle and may rise above the upper reference limit of 1.9 nmol/L. If a patient is having periods, a sample taken during/shortly after menses (day 1-5 of cycle) is the most suitable for diagnosis of PCOS: a sample taken later in the cycle may give a misleadingly-high testosterone result.

Prolactin and PCOS

Prolactin can be increased in the presence of pituitary adenomas. However, there are non-adenoma causes for increased prolactin eg stress, drug treatment (dopamine antagonists), hypothyroidism and unopposed estrogen. As women with PCOS are more likely to have unopposed estrogen they are likely to have higher prolactin concentrations. Up to 40% of women with PCOS will have mildly elevated prolactin, although the values are generally <750 mIU/l. One rule of thumb is that in these cases the LH will always be higher than the FSH unlike true hyperprolactinaemia where the LH concentrations are lower than the FSH concentrations (and estradiol concentration may also be low).

Referral of PCOS to secondary care

Most women with PCOS are successfully managed symptomatically in primary care. However, when there are specific concerns about the diagnosis or questions around information provision or more specialised management strategies, (such as for hirsutism or where the COCP is not suitable) in the short or long term the most appropriate place for referral is the specialised Reproductive Endocrine clinics based in EFREC at the Royal Infirmary of Edinburgh. Women with PCOS and anovulation looking for fertility should be referred immediately without the one-year requirement.

Guideline compiled September 2010 and reviewed in 2018 in collaboration with Primary Care Laboratories Interface Group

Dr Geoff Beckett
Consultant Clinical Biochemist
Honorary Reader in Clinical Biochemistry
Clinical Biochemistry
Royal Infirmary of Edinburgh

Professor Richard Anderson
Honorary Consultant Gynaecologist
Royal Infirmary of Edinburgh
Professor of Clinical Reproductive Science
University of Edinburgh

Prof Rebecca Reynolds
Honorary Consultant Endocrinologist
Royal Infirmary of Edinburgh
Professor in Endocrinology and Diabetes
University of Edinburgh

Prof Colin Duncan
Honorary Consultant in Reproductive Medicine
Royal Infirmary of Edinburgh
Professor of Reproductive Medicine and Science
University of Edinburgh