## CASE THREE

**Short case number: 3_24_3**
**Category: Endocrine and Reproductive Systems**
**Discipline: Obstetrics & Gynaecology**
**Setting: General Practice**
**Topic: Irregular menstrual cycle & polycystic ovarian syndrome [PCOS].**

### Case

**Bronwyn Nicholson is a 38 year old woman who has had an irregular menstrual cycle for over 2 years. She states that she has been on the oral contraceptive pill [OCP] for years and her problems only commenced after coming off the pill 3 years ago. On history, you find that Bronwyn commenced menarche at the age of 13 years but that her periods were always a little irregular until she went onto the OCP to control her heavy periods at the age of 18. She had no problems with the OCP but felt that after over 15 years of "the pill", her body needed a break. Bronwyn states that she would like to know if she is normal and would like to have regular periods "just like every other woman".**

### Questions

1. Outline the clinical assessment of women presenting with an irregular menstrual cycle. What clinical features in particular would suggest PCOS?
2. Define the three main criteria of Polycystic Ovarian Syndrome (PCOS).
3. Discuss the pathophysiology of PCOS
4. Discuss the relationship between polycystic ovaries and PCOS. What are the cysts in polycystic ovaries?
5. In a table, list the symptoms and the serum endocrinology associated with PCOS.
6. What are the long-term sequelae of untreated PCOS.
7. Management of PCOS is symptom orientated. What does this mean and by using this discuss the management options for a woman diagnosed with PCOS.

**Suggested Reading**


- Abbott, J., Bowyer, L., & Finn, M. (2014). *Obstetrics and Gynaecology: an evidence-based guide (2nd ed).* Australia, Elsevier
- Dewhurst's Textbook of Obstetrics & Gynaecology, Edmonds K [editor]. Blackwell Publishing. 2007. Chapter 39, pg 377-389

## ANSWERS

**Question 1**

In a women presenting with irregular menstrual cycle history and careful examination should be carried out before investigations are instigated – in particularly looking at stature and body form, signs of endocrine disease, secondary sexual development and the external genitalia. Measurement of height and weight should be done in order to calculate the BMI. Signs of hyperandogenism (acne, hirsutism, balding (alopecia)) are suggestive of PCOS.

**Question 2**

The polycystic ovarian syndrome is a heterogenous condition which is defined by the presence of two out of the following three criteria:
Oligo and/or anovulation
Hyperandrogenism (clinical and /or biochemical)
Polycystic ovaries on ultrasound scan with the exclusion of other aetiologies (e.g. Cushings disease / adrenal disease, thyroid disease)

**Question 3**

The polycystic ovarian syndrome is a heterogenous collection of signs and symptoms that gathered together form a spectrum of a disorder with a mild presentation in some, while in others a severe disturbance of reproductive, endocrine and metabolic function.

The pathophysiology of the PCOS appears to be multifactorial and polygenic. It is believed that hypersecretion of androgens by the stromal theca cells of the polycystic ovary leads not only to the cardinal clinical manifestation of the syndrome, the hyperandrogenism but is also one of the mechanisms whereby follicular growth is inhibited with the resultant excess of immature follicles. Hypersecretion of luteinizing hormone (LH) by the pituitary – a result both of disordered ovarian – pituitary feedback and exaggerated pulses of GNRH from the hypothalamus – stimulates testosterone secretion by the ovary.

Furthermore, insulin is a potent stimulus for androgen secretion by the ovary which, by way of a different receptor for insulin, does not exhibit insulin resistance. Insulin therefore amplifies the effect of LH, and additionally magnifies the degree of hyperandrogenism by suppressing liver production of the main carrier protein sex hormone binding globulin (SHBG), thus elevating the 'free androgen index'. It is a combination of genetic abnormalities combined with environmental factors, such as nutrition and body weight, which then affect expression of the syndrome.

**Question 4**

Polycystic ovaries are commonly detected by ultrasound. The prevalence in the general population is approx 20%. The 'cysts' are not cysts in the sense they contain oocytes and indeed are follicles whose development has been arrested. The actual number of cysts may be of less relevance than the volume of ovarian stroma in the ovary itself, which has been shown to closely correlate with serum testosterone concentrations.

A recent consensus to define PCOS are the presence of 12 or more follicles measuring 2 – 9 mm in diameter, or increased ovarian volume >10ml. The presence of these findings on one ovary is enough to fulfil the ultrasound criteria for PCOS.

**Question 5**

Signs and symptoms of PCOS

Symptoms

- Hyperandrogenism (acne, hirsutism, alopecia but not virilization)
- Menstrual disturbance
- Infertility
- Obesity
- Asymptomatic

Serum Endocrinology

- Increased fasting insulin – (assays are not sensitive and it is not recommended by the most recent PCOS guidelines that insulin levels be measured (published late 2011 with the Jean Hailes Foundation)
- Increased androgens
- Increased LH to FSH ratio
- Decreased SHBG resulting in elevated 'free androgen index'
- Increased oestradiol (not usually measured)
- Increased prolactin – not always
- Remember to exclude thyroid dysfunction (TSH, T4, T3) and adrenal disorders as the cause of hyperandrogenism (170Hprogesterone, DHEAS, androstenedione)

**Question 6**

Long term sequelae of untreated PCOS

- Diabetes
- Dyslipidaemia
- Hypertension, cardiovascular disease
- Endometrial carcinoma
- Breast cancer

**Question 7**

The clinical management of a woman with PCOS should be focused on her individual problems. We are yet to elucidate the cause behind PCOS, and therefore cannot cure this condition. Women with PCOS will present with different combinations of symptoms and signs, and therefore clinical management should focus on what aspects of PCOS are troubling for the woman.

Obesity worsens both symptoms and the endocrine profile so obese women should be encouraged to lose weight. Metformin may be used if there is impaired glucose tolerance. The main side effect is gastrointestinal upset, so metformin should be increased slowly, to the dose of 500mg TDS.

Amenorrhoeic women with PCOS are not oestrogen deficient and are not at risk of osteoporosis. Indeed they are oestrogen replete and at risk of endometrial hyperplasia. The easiest way to control the menstrual cycle is the use of a low dose COCP. This will result in an artificial cycle and regular shedding of the endometrium

Hirsutism, characterized by terminal hair growth in the male pattern of distribution, including chin, upper lip, chest, arms, back, lower abdomen can be distressing. Cosmetic techniques including creams, laser may be suggested. Medical regimes including drug therapies may take 6 – 9 months before improvement may be seen. Treatment does not destroy unwanted hair that is already present, but prevents the growth of new hair. First line therapy has been traditionally a COCP which has cyproterone acetate in it such as Diane which also contains ethinylestradiol 30micrograms. Spironolactone is a weak diuretic with antiandrogen properties and may be used in some women with PCOS, in conjunction with contraception, as spironolactone is teratogenic.

Infertility can be a problem in women with PCOS. Improvement in lifestyle with a combination of exercise and diet to achieve weight reduction is important to improve the prospects of both spontaneous and drug induced ovulation.

A number of pharmacological agents have been used to amplify the physiological effect of weight loss, notably metformin. This biguanide inhibits the production of hepatic glucose and enhances the sensitivity of peripheral tissue to insulin, thereby decreasing insulin secretion. It has been shown that metformin ameliorates hyperandrogenism and abnormalities of gonadotropin secretion in women with PCOS and can restore menstrual cyclicity and fertility.