PCOS
a lifetime condition

Dr Janelle McDonald
Gynaecologist & Fertility Specialist
BMed FRANZCOG CREI
NIH Criteria (American)
Oligo-ovulation and clinical and/or biochemical signs of hyperandrogenism, and exclusion of other aetiologies

European Criteria
Two out of three of: oligo-ovulation and/or anovulation, clinical and/or biochemical signs of hyperandrogenism, or polycystic ovaries, and exclusion of other aetiologies

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Ultrasound appearance of PCO

- 12 or more follicles in each ovary (2 to 9mm)
- and/or increased ovarian volume >10mls.
- “string of pearls”
- Thickened endometrium
5 to 8% of all women
5% of lean women
28% of obese women
Case 1 KF

- 16.5 yrs primary amenorrhoea
- Thelarche, adrenarche, growth spurt at age 11-12
- Poor diet, wt 53 kgs, ht 168 cm
- FH, Mum PCOS, subfertility, grandmother diabetes
Case 1

- Thin, BMI 18.9
- Hirsutism on face, abdomen, upper thighs
- No acne
Testosterone 7.5, SHBG 17

LH 14, FSH 5, TSH 2, Prolactin normal

DHEAS 5.3, Androstendione 11.3, 17OHP 6.4

Ultrasound thin endometrium and 20 small follicles on each ovary.
Commenced 20mcg combined OCP
Had withdrawal bleed
3 months later hirsutism improved
Testosterone repeated 3.0
Synacthen test, lipids, GTT, karyotype normal.
Case 1

- Not happy with hirsutism
- BTB on OCP
- Changed to CPA OCP
- Consider other agents – spironolactone, CPA 100 mg daily 10 days/month
29 yr old with heavy irregular bleeding

Wants to conceive

Has been seeing a general O and G and has had 6 cycles of Clomiphene citrate.

Not sure if she ovulated

Feels very tired
Obese with BMI of 39
Acanthosis and skin tags on inner thighs
Bulky tender uterus, heavy bright PV loss
Heamodynamically stable.
Case 2

- HB 88, Iron 5, Ferritin 15.
- LH 27, FSH 3, Estradiol 198, Prog 3, BHCG neg.
- Fasting glucose 5.6, insulin 23
- Ultrasound endometrium 23mm, multiple follicles each ovary.
Case 2

- Hysteroscopy D and C, thick polypoid endometrium
- Histopath, Atypical endometrial hyperplasia
- Mirena
- Full GTT
- Metformin, diet and exercise.

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- Slim 21 yr old with acne and irregular periods, sexually active
- BMI 21
- US endometrium 12mm, multiple peripheral follicles
- FSH 4, LH 12, T 3.5, SHBG 20. Other hormones normal
You commence combined OCP

6 weeks later she returns with a painful swollen L leg and shortness of breath.

Venous dopples and helical CT confirm DVT and PE.
Protein s normal

AT 3 normal

Lupus anticoagulant and ACL abs neg

Activated protein C low, homozygous for the Leiden mutation.
How do we manage this woman’s reproductive health needs now and for conception, pregnancy and later life?
• 36 yr old with amenorrhoea and infertility
• BMI 29
• Insulin resistance dx by GP
• Treated with metformin 500mg tds
FSH = 6, LH = 9, E2 = 80, P4 < 5,

SHBG, Testo, TSH, PRL normal

Us reports normal uterus and ovaries but films not seen

No response 50 and 100 mg of clomiphene

What next?
AMH 0.2 (10-20)

FSH remains normal 9.0

Trial of FSH stimulation.

Produced 1 follicle after 10 days stim, HCG trigger and natural intercourse

Awaiting outcome.
Case 5 MM

- 43 yrs old on diane 35 for 12 years since completing her family
- Complains of headache and heavy withdrawal bleeds
- Moderate facial pigmentation
- BP normal, BMI 24.

How do we ix and mx this woman

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Case 5 MM

- BP 120/70
- Fasting glucose 5.1, insulin 20
- Lipids NAD
- Mirena inserted, metformin 500 mg bd
- 3 months later, Mirena removed as irreg bleeding and acne?
- What now?
Case 6  BD

- 34 yrs old with bipolar disorder
- Presents with infertility  oligoamenorrhoea,
- Wt 82 kgs, ht 165cm, BMI 31.5
- US typical PCO picture
- O/E  moderate hirsutism, mild acne
- LH 23, FSH 6, E2 130, P4 2
- TSH 2.3, PRL  normal, SHBG 23, T 2.1
- Fasting insulin 19, glucose 5.2

How do you manage this woman?
Can Na Valproate cause a PCOS picture?

How could we clarify if this is a primary or secondary problem?

Who else should we involve in the management of this patient?
Sodium Valproate

- Children exposed to Valproate in utero had lower scores on cognitive function tests than children exposed to Lamotrigine, Carbamazepine, or phenytoin.
- Lithium is contraindicated in pregnancy as well.
Insulin resistance leads to androgen excess by stimulating androgen production in the theca cell and by suppressing SHBG production in the liver.

High androgens associated with disordered follicular development, low E2, high T in follicular fluid. Follicular development is arrested at 5 to 8 mm. Increased follicular atresia.
Abnormal gonadotrophin secretion is common, high LH common but not always found.

FSH:LH ratio not diagnostic
Metabolic issues

- Most are insulin resistant regardless of weight but is more severe in the obese women.
- ?? insulin regulatory locus on chromosome 11.
- Increased LDL cholesterol in women with PCOS (OR 1.53, CI 1.39-1.68) after adjusting for BMI

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Metabolic issues

- Nurses health study, hx of irreg cycles associated with a risk of non fatal and fatal CHD (RR 1.25 and 1.67)

- Fatty liver is increased in PCOS (up to 30%) have elevated ALT.
Teenagers with PCOS

- Menarche may be delayed
- Girls are most concerned by acne and hirsutism
- Mothers are most concerned by their daughters irregular cycles, occasionally increased rather than decreased bleeding
Mood disturbance is common

Caution must be used if advising weight loss

Focus on healthy lifestyle and exercise rather than diet
20 to 40 year old women

- Management depends on when they want to start a family
- Mood disturbance is common
- Acne, hirsutism, alopecia
- Oligoamenorrhaoea
- Infertility

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Women over 40

- High risk of endometrial hyperplasia
- Oligoamenorrhoea and dysfunctional uterine bleeding can be misinterpreted as the perimenopause
- Insulin resistance or diabetes increase with age
- Dyslipidaemias increase with age
- Hypertension is common in obese women
Women over 40

- Don’t forget about contraception
- Cycle length shortens with age and may result in improved fertility in the 40s
- If contraindications to the combined OCP, consider progesterone only contraceptives
Women over 40

- Mirena will provide contraception and protect from endometrial hyperplasia.
- Progesterone only pill does not have a high enough dose to protect the endometrium and provide cycle control.

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Management summary

Genetics

Androgens

Hirsuitism/acne

Lifestyle

Ovarian follicles/anovulation

Critical

Menstrual disturbances

Insulin

Diabetes

Metformin

Cardiovascular disease

Lifestyle/MF/0CP/+-Clomiphene

Lifestyle/MF monitoring

0CP – oral contraceptive pill

anti-A – anti-androgens

MF – metformin

Teede et al
- All combined OCPs will reduce androgens by increasing SHBG and reducing ovarian production.
- Cost can be an issue.
- OK to try standard 30ug COCP 1st.
- Lower dose E2 pills may be useful in the young and the old.
- Cyproterone acetate pills improve skin by action on T receptors.

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Lifestyle change

Cosmetic; laser, electolysis better than waxing.

Cyproterone acetate for 10 days each month with OCP if severe problem.

Spironolactone 50 - 100 mg twice daily (monitor potassium)

Metformin, no evidence that it improves hirsutism

Eflornithine cream
Treatment of Infertility

- Depends on age
- Lifestyle change, good evidence that diet and exercise improve chances of pregnancy
- Metformin (no increased risk of multiple preg)
- Clomiphene citrate* (risk of multiple pregnancy)
Treatment of Infertility

- FSH ovulation induction* (risk of multiple preg)
- IVF; if pregnancy not achieved by above methods or if male factor infertility
- Metformin reduces risk of serious side effects in IVF
Laparoscopic Ovarian Drilling

- Improved chance of pregnancy after surgery but benefit is short term only
- Risk of peri-ovarian adhesions
- Obese patients have increased surgical risks
- No increase in multiple pregnancy

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AMH may become a diagnostic test for PCOS

Controversies?

- Should we use the COCP in young women with PCOS?
- Does the OCP make the metabolic syndrome worse?
• Teede et al, Polycystic ovary syndrome; a complex condition with psychological, reproductive and metabolic manifestations that impacts on health across the lifespan. BMC Medicine 2010;8.41.

• Teede et al, Assessment and management of Polycystic Ovary Syndrome: Summary of an Evidence based Guideline S66 MJA 195 (6) · 19 September 2011

Questions?