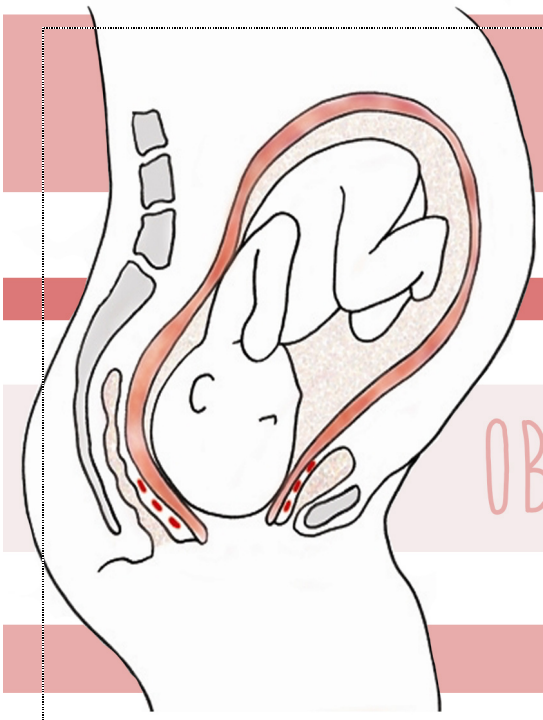


OBSTETRICS AND GYNECOLOGY

(7) PCO AND Hirsutism

Leader: Alanoud Alyousef

Sub-leader: Dana Aldubaib

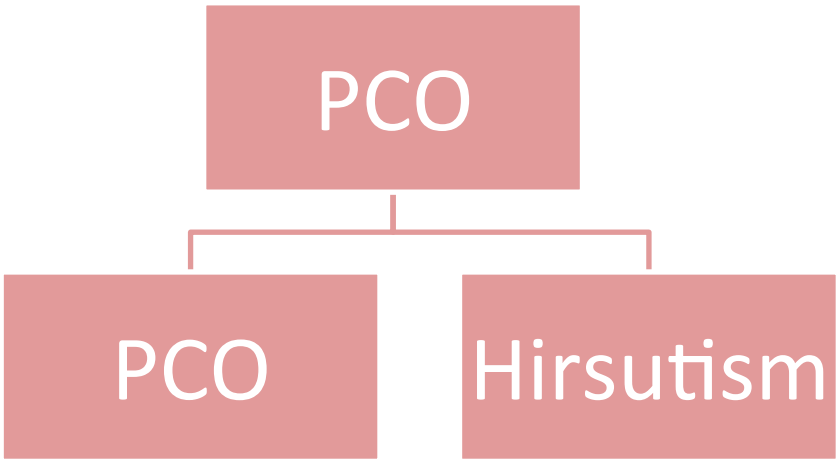
Done by: Najla Alrumaih

Revised by: Fatmah Alshehry

Doctor's note Team's note Not important Important 431 teamwork

Objectives:

Were not provided



PCOS: Defined

ACOG and NIH (1990):

Hyperandrogenism and chronic anovulation excluding other causes.

Stein and Levanthal (1935):

Association of amenorrhea with polycystic ovaries and variably: hirsutism and/or obesity.

"This syndrome is a chronic condition that has been defined as anovulation or oligo-ovulation with clinical or laboratory evidence of hyperandrogenism and without evidence of any other underlying condition. Its onset is usually at the time of puberty"

PCOS: Epidemiology

- Prevalence: 4-6% females

-Probably same worldwide

-No difference between blacks and whites

-75% of women w/ irregularity or infertility

PCOS: Pathophysiology
What we think we know

1- "Vicious cycle"

PCO leads to obesity and obesity leads to PCO, which leads to infertility

2- Abnormal gonadotropin secretion

-Excess LH and low, tonic FSH

Reversed FSH:LH ratio

You can measure that in the follicular phase (1st five days of menstruation).

In the follicular phase you'd expect all the hormones are back to the base line, in PCO the LH is higher in that state **and FSH is either lower or normal because of the suppressed effects of increased estrogen levels which results from the conversion of androgenic hormones in the peripheries.**

"Patients with PCOS exhibit increased LH pulse frequency, usually resulting in higher circulating levels of LH. It is likely that these patients exhibit increased LH levels because of increased GnRH secretion from the hypothalamus and increased pituitary sensitivity .to GnRH"(1)

3- Hypersecretion of androgens

-Disrupts follicle maturation. That's why you can see small cysts at the periphery of ovaries the don't mature into a follicle and rupture

"The increased LH level promotes androgen secretion from ovarian theca cells, leading to elevated levels of ovarian-derived androstenedione and testosterone. This then leads to atresia of many developing follicles and interferes with the normal development of a dominant or preovulatory ovarian follicle much of the time"

-Substrate for peripheral aromatization **and it converts into estrogen.**

4- Negative feedback on pituitary

- Decreased FSH secretion OR normal **results from the increased levels of estrogen.**

5- Insulin resistance, Elevated insulin levels

Either because of obesity or hormonal disturbance

PCOS

Polycystic ovary

-Usually in obese woman

FSH: LH ratio, in the proliferative phase of the cycle will be reversed

-↑ Oestrogen

Without ovulation there's no corpus luteam to produce progesterone, without progesterone there's unopposed estrogen.

'The unopposed estrogens in women with PCOS may cause hyperplasia of the endometrium and occasionally endometrial carcinoma."

-Hirsutism

Not all cases of hirsutism have PCO but some cases of PCO have hirsutism

"Elevated androgen and insulin levels in PCOS reduce the hepatic production and secretion of SHBG sex hormone binding globulin. When SHBG production is suppressed, the amount of free testosterone may be dramatically increased, even though the overall increase in total testosterone is moderate or small. Thus, the physical manifestations of hyperandrogenism in PCOS may seem dramatic in relation to the level of total .testosterone"

-Raised level of circulating insulin

"In women with PCOS there is an association between abnormal androgen production and insulin resistance with hyperinsulinism. In about 60% to 70% of patients with PCOS, insulin sensitivity is decreased, leading to insulin hypersecretion. This hyperinsulinemia results from direct insulin stimulation of theca cells resulting in androgen secretion" which leads to decreased insulin sensitivity leading to insulin hypersecretion

-Raised blood sugar

In the long term, the insulin resistance associated with PCOS may lead to an increased risk for metabolic syndrome (diabetes and heart disease)

DIAGNOSIS

1- History

- Irregular cycle

- Oligonorrhoea

- Infertility

- Galactorrhoea

- Recurrent abortions

2- Examination

- Usually obese but it can happen in thin patients

- Hirsutism

- Acanthosis nigricans (not common)

"The degree of hirsutism , acne, or androgenic alopecia should be assessed and the thyroid palpated for enlargement *why to examine thyroid? Because hypothyroidism is one of the causes of oligorroea and must be ruled out*. Patients should be expressly asked about excess facial hair because they may conceal their hirsutism by waxing or electrolysis and be too embarrassed to volunteer the information. Evidence of cushingoid features should be noted *central obesity, moon face, buffalo hump, abdominal striae, weakness, and muscle wasting.* Acanthosis nigricans is a frequent marker of insulin resistance and hyperinsulinemia. A bimanual pelvic examination may identify ovarian enlargement. Asymmetric ovarian enlargement associated with the rapid onset of virilization can indicate a rare androgen producing .tumor"

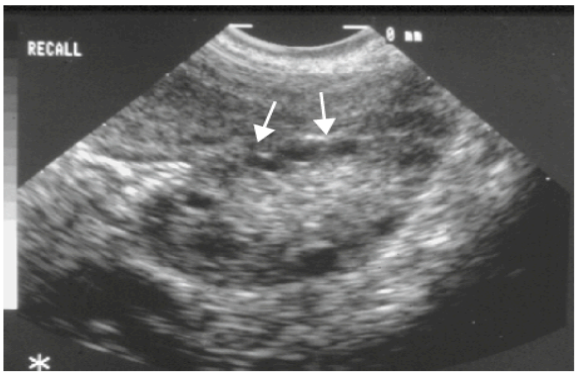


FIGURE 32-3 Transvaginal ultrasound in a woman with polycystic ovarian disease. The multiple subcapsular cysts, with their "string of pearls" appearance (*arrows*), are common in this syndrome.

3- Investigation:

- ↑ LH

- FSH may be normal

- ↑ Oestrogen

- Free testosterone may be ↑ or normal

- Ultrasound - multiple small cysts at the periphery of the ovary looks like necklace.

-Laparoscopy – thick, enlarged non-active ovaries Not usually done

TREATMENT:

- Weight reduction 1st line
- Induction of ovulation (clomid)
- Metformin decrease insulin resistance
- Laparoscopic ovarian diathermy (used in severe cases).
- IVF (if induction of ovulation doesn't work)

some oral contraceptive pills (Diane) can help with hirsutism and induce regular withdrawal bleeding. These agents include estrogen *Estrogen component in the OCP ↑ SHBG; SHBG binds androgens; free androgen levels are then ↓*. , progesterone and small dose of Cypreterone acetate (anti-androgen) which will help reduce access hair

PCOS: Associated Disorders

- Diabetes
- Hyperlidpidemia (LDL, Triglycerides)
- Obesity
- Hypertension
- CAD?

Incr in Risk Factors, but not mortality

- Endometrial CA
- Ovarian CA?
- +/- Breast CA
- NO increase in Osteoporosis because of high estrogen
- Eating disorders

PCO → high insulin level →stimulate hunger →eating problem

- Psychiatric dz

HIRSUITISM:

Pathological

PCO
adrenal cortex trauma
cushing syndrome

-Constitutional

This topic is clearly and simply covered in the first aid for the obstetric and gynecology clerkship third edition , chapter 18.

SITE:

Fecal.
Chest.
Anterior abdominal wall.
The rest of the body is not considered hirsutism e.g. legs

INVESTIGATION:

Free testosterone level
ACTH Cushing Syndrome
FSH, LH PCO

TREATMENT:

Difficult and needs reassurance
- Treat the underlying cause
-Hair removal by different methods
Diane
- Cypreterone acetate – anti-androgen (teratogenic)
-Treatment will take long time

Summary

❖ PCO:

- Hyperandrogenism + chronic anovulation.
- Usually in obese woman.
- **Dx:** Irregular cycles and infertility, ↑ LH, FSH may be normal, ↑ Estrogen; free testosterone may be ↑ or normal ± Hirsutism.
- Ultrasound - multiple small cysts at the periphery of the ovary looks like necklace (Nucleus appearance).
- **Rx:** Weight reduction, Metformin, Clomid for ovulation induction

❖ Hirsutism:

- Site: Face, chest, and anterior abdominal wall

Rx: Very difficult, Diane (MUST GIVE CONTRACEPTIVE PILLS WITH IT because it can cause teratogenicity

(1)All texts in purple are from our recommended book

MCQ's :

1) A 16 year old presented with irregular cycles, increased facial hair and obesity. What is the diagnosis?

a) Dysfunctional uterine bleeding
b) Polycystic ovarian syndrome
c) Hyperprolactemia
d) Hyperthyroidism

2) Polycystic Ovarian Syndrome (PCOS) which is FALSE :

A. common endocrine disorders in reproductive women
B. known as Stein-Leventhal syndrome
C. associated with high BP and BMI > 30
D. associated with hyperandrogenism and insulin resistance
E. None of the above

3) Your patient is a 23-year-old woman with primary infertility. She is 5 4 in tall and weighs 210 lb. She has had periods every 2 to 3 months since starting her period at age 12. She has a problem with acne and hair growth on her chin. Her mother had the same problem at her age and now has adult-onset diabetes. On physical examination of the patient, you notice a few coarse, dark hairs on her chin and around her nipples. She has a normal-appearing clitoris. Her ovaries and uterus are normal to palpation. Which of the following blood tests has no role in the evaluation of this patient?

A. Total testosterone

B. 17 α-hydroxyprogesterone

C. DHEAS

D. Estrone

E. TSH

4) You have just diagnosed a 21-year-old infertile woman with polycystic ovarian syndrome. The remainder of the infertility evaluation, including the patient's hysterosalpingogram and her husband's semen analysis, were normal. Her periods are very unpredictable, usually every 3 to 6 months. She would like your advice on the best way to conceive now that you have made a diagnosis. Which of the following treatment options is the most appropriate first step in treating this patient?

A. Dexamethasone

B. Gonadotropins

C. Artificial insemination

D. Metformin

E. In vitro fertilization

5) A 22-year-old woman consults you for treatment of hirsutism. She is obese and has facial acne and hirsutism on her face and periareolar regions and a male escutcheon. Serum LH level is 35 mIU/mL and FSH is 9 mIU/mL. Androstenedione and testosterone levels are mildly elevated, but serum DHAS is normal. The patient does not wish to conceive at this me. Which of the following single agents is the most appropriate treatment of her condition?

A. Oral contraceptives

B. Corticosteroids

C. GnRH

D. Parlodel

E. Eflornithine hydrochlorid

Answers:

1) B
2) E
3) D
4) D
5) A

Questions 3,4, and 5 where from Obstetric and Gynecology PreTest Self-Assessment and Review and here there explanations:

3) Thyroid dysfunction and hyperprolactinemia can both be associated with hirsutism, and therefore it is important to check levels of TSH and prolactin. In order to rule out congenital adrenal hyperplasia caused by a deficiency in 21-hydroxylase, a 17αhydroxyprogesterone level should be drawn. Very high levels of total testosterone would indicate the presence of an androgen-secreting ovarian tumor. Elevated levels of dehydroepiandrostenedione would be consistent with PCOS. There is no role for ordering an isolated estrone level in the workup and evaluation of hirsutism.

4) Oral contraceptives have long been used in the management of PCOS because they suppress pituitary luteinizing hormone secretion, suppress ovarian androgen secretion, and increase circulating sex hormone-binding globulin (SHBG). Medications such as metformin that improve insulin sensitivity have been used to treat PCOS. Spironolactone, which is a diuretic and aldosterone agonist, has been used to treat PCOS because it binds to the androgen receptor as an antagonist. Weight loss is recommended as part of the treatment for women with PCOS because it reduces hyperinsulinemia. Metformin use is a simple step in the attempt to induce ovulation in patients with PCOS. Insulin is thought to act on the ovary to stimulate androgen secretion. In addition, hyperinsulinemia decreases SHBG. There is no role for the use of dexamethasone to treat

PCOS. Glucocorticoid therapy is indicated in cases of congenital adrenal hyperplasia

5) This patient has polycystic ovarian syndrome (PCOS), diagnosed by the clinical picture, abnormally high LH to-FSH ratio (which should normally be approximately 1:1), and elevated androgens but normal DHAS. DHAS is a marker of adrenal androgen production; when normal, it essentially excludes adrenal sources of hyperandrogenism. Several medications have been used to treat hirsutism associated with PCOS. For many years, contraceptives were the most frequently used agents; they can suppress hair growth in up to two-thirds of treated patients. They act by directly suppressing ovarian steroid production and increasing hepatic-binding globulin production, which binds circulating hormone and lowers the concentration of metabolically active (free unbound) androgen. However, clinical improvement can take as long as 6 months to manifest. Other medications that have shown promise include medroxyprogesterone acetate, spironolactone, cimetidine, and GnRH agonists, which suppress ovarian steroid production. However, GnRH analogues are expensive and have been associated with significant bone demineralization after only 6 months of therapy in some patients. Eflornithine hydrochloride is an antimetabolite topical cream indicated in the treatment of facial hirsutism. It is not indicated for the treatment of widespread hirsutism as in this patient's case