

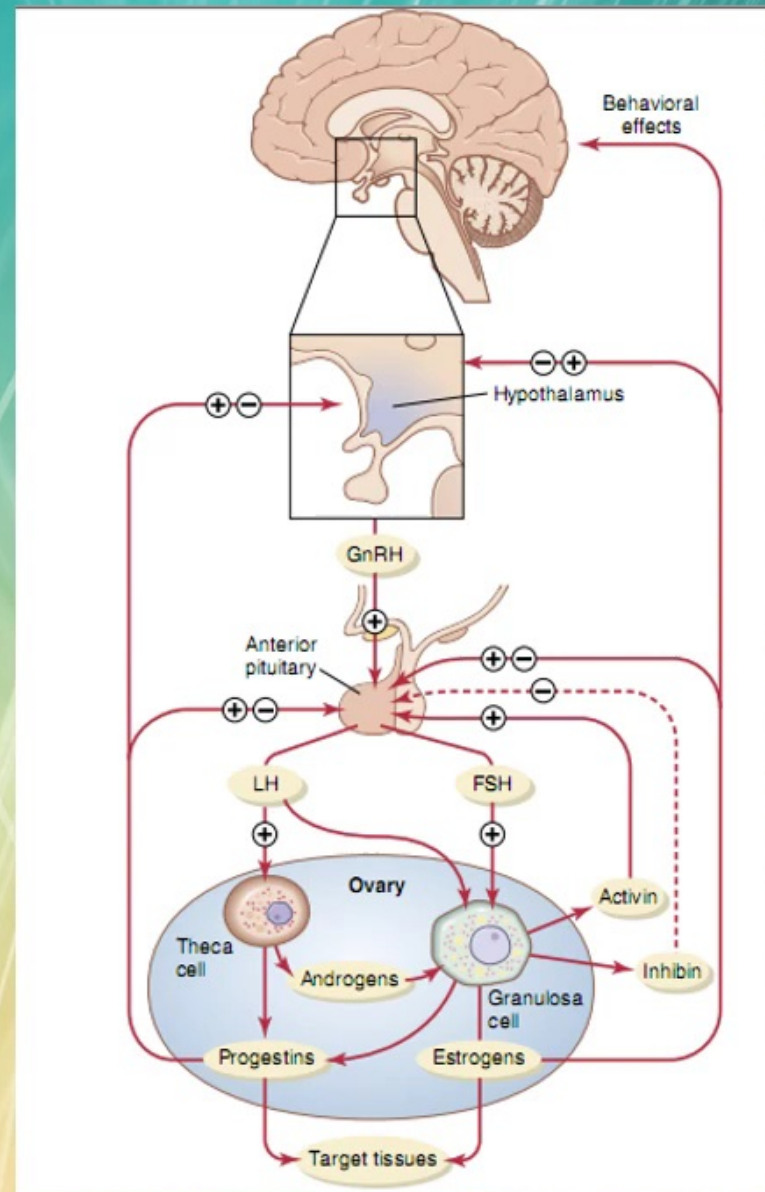


جامعة الأزهر - غزة
AL-AZHAR UNIVERSITY-GAZA



Female Physiology Reproductive System







Puberty

- Puberty means the onset of adult sexual life. It is marked by a gradual increase in the secretion of estrogen from developing follicles, which is driven by increasing concentrations of FSH and LH from the pituitary.





Menarche

- Menarche means the beginning of menstruation. It marks completion of the first cycle of the system, although the first several cycles usually do not include ovulation.





Abnormalities of ovarian cycle

Anovulatory cycles:

- Definition: Failure of ovulation
- Causes:
 - Physiological: 1st few cycles at puberty & last cycles at menopause
 - Pathological:
 - ✓ Lack of sufficient LH surge
 - ✓ Lack of ovarian response to LH
 - ✓ ++ Prolactin or stress → -- GnRH
- Characteristic: No C. Luteum → No progesterone, leading to:
 - ✓ Absence of secretory changes in endometrium
 - ✓ Short cycles: Mature Graafian follicle regresses with ovum inside
- Diagnosis of ovulation:
 - ✓ Endometrial biopsy: secretory pattern
 - ✓ Folliculometry by sonar
 - ✓ Midcycle LH surge by blood hormonal assay
 - ✓ Rise of body temp 0.5C in 2nd ½ of cycle
 - ✓ ++ Progesterone in plasma
 - ✓ Mittelschmerz pain i.e. lower abdominal pain at ovulation due to peritoneal irritation





Abnormalities of ovarian cycle

- Amenorrhea:
 - ✓ Primary: associated with immature sexual signs e.g. small breast
 - ✓ Secondary: stoppage of cycles after normal cycles, Causes:
 - Pregnancy (main cause)
 - Emotional stress & systemic diseases
 - Hypothalamic, pituitary & ovarian diseases
 - Menopause
- Hypomenorrhea: ↓ amount of menstrual blood
- Oligomenorrhea: ↓ Frequency of menstruation
- Metrorrhagia: bleeding between periods
- Menorrhagia: Abnormal profuse menstrual flow
- Dysmenorrhea: painful menstruation





Polycystic ovary syndrome (PCOS)

- A heterogeneous clinical syndrome characterized by hyperandrogenism, mainly of ovarian origin, menstrual irregularity, and hyperinsulinaemia
- PCOS is the most common endocrinopathy in ♀ of reproductive age; >95% of ♀ presenting to outpatients with hirsutism have PCOS.
- The estimated prevalence of PCOS ranges from 5 to 10% on clinical
- criteria. Polycystic ovaries on US alone are present in 20–25% of ♀ of reproductive age.
- First-degree ♂ relatives of women with PCOS have increased prevalence of metabolic syndrome and obesity than the general population.





Pathogenesis

- The fundamental pathophysiological defect is unknown, but both genetic and environmental factors are thought to play a role
- Familial aggregation of PCOS in 50% of ♀. A family history of type 2 diabetes mellitus is also more common in ♀ with PCOS.
- PCOS is probably a polygenic disorder.
- Implicated genes include those of the insulin pathway, testosterone biosynthesis enzymes, and obesity-related genes, including FTO gene.



Pathogenesis

- Hyperandrogenism

- ✓ The main source of hyperandrogenaemia is the ovaries, although there may also be adrenal androgen hypersecretion which is poorly defined.
- ✓ The biochemical basis of ovarian dysfunction is unclear. Studies suggest an abnormality of cytochrome P450c17 activity, but this is unlikely to be the primary event but rather an index of ↑ steroidogenesis by ovarian theca cells.
- ✓ There is also an increase in the frequency and amplitude of GnRH pulses, resulting in the increase in LH concentration which is characteristic of the syndrome. This is probably due to anovulation and low progesterone levels

- Hyperinsulinaemia

- ✓ Approximately 70% of ♀ with PCOS are insulin-resistant
- ✓ Insulin also inhibits SHBG synthesis by the liver, with a consequent androgen levels.





Features

- Onset of symptoms. Symptoms often begin around puberty, after weight gain, but can present at any time.
- Oligo-/amenorrhoea (70%). Due to anovulation. ♀ are usually well oestrogenized, so there is little risk of osteoporosis, unlike other causes of amenorrhoea.
- Hirsutism (66%): 25% of ♀ also suffer from acne or male pattern alopecia. Virilization is not a feature of PCOS.
- Obesity (50%). Symptoms worsen with obesity, as it is accompanied by ↑ testosterone concentrations as a result of hyperinsulinaemia. Acanthosis nigricans may be found in 1–3% of insulin-resistant ♀ with PCOS.
- Infertility (30%). PCOS accounts for 75% of cases of anovulatory infertility. The risk of spontaneous miscarriage is also thought to be higher than the general population, mainly because of obesity.





Menstrual function disorder

- Oligomenorrhoea is defined as the reduction in the frequency of menses to <9 periods a year.
- 1° amenorrhoea is the failure of menarche by the age of 16 years.
- 2° amenorrhoea refers to the cessation of menses for >6 months in ♀ who had previously menstruated.





Causes of amenorrhea

- Physiological
 - ✓ Pregnancy and lactation.
 - ✓ Post-menopause.
- Iatrogenic
 - ✓ Depot medroxyprogesterone acetate.
 - ✓ Levonorgestrel-releasing intrauterine device.
 - ✓ Progesterone-only pill.





Pathological amenorrhea—1°

- Chromosomal abnormalities—50%:
 - ✓ Turner's syndrome.
 - ✓ Other X chromosomal disorders.
- 2 hypogonadism—25%:
 - ✓ Kallmann's syndrome.
 - ✓ Pituitary disease.
 - ✓ Hypothalamic amenorrhoea.
- Genitourinary malformations—15%:
 - ✓ Imperforate hymen.
 - ✓ Absence of uterus, cervix, or vagina, e.g. Rokitansky syndrome, androgen insensitivity syndrome.
- Other—10%:
 - ✓ CAH.
 - ✓ PCOS.
- Most causes of 2 amenorrhoea can also cause 1 amenorrhoea





Pathological amenorrhea—2°

- Ovarian—70%:
 - ✓ PCOS.
 - ✓ Premature ovarian failure.
- Hypothalamic—15%:
 - ✓ Hypogonadotrophic hypogonadism.
 - ✓ Hypothalamic amenorrhoea.
 - ✓ Weight loss.
 - ✓ Infiltrative lesions of the hypothalamus.
 - ✓ Drugs, e.g. opiates.
- Pituitary—5%:
 - ✓ Hyperprolactinaemia.
 - ✓ Hypopituitarism.
- Uterine—5%:
 - ✓ Intrauterine adhesions—Asherman's syndrome.
- Other endocrine disorders—5%:
 - ✓ Thyroid dysfunction.
 - ✓ Hyperandrogenism—Cushing's syndrome, CAH, tumour.





Menstrual function disorder

- PCOS is the only common endocrine cause of amenorrhoea with normal oestrogenization—all other causes are oestrogen-deficient. Women with PCOS, therefore, are at risk of endometrial hyperplasia, and all others are at risk of osteoporosis.





Premature ovarian insufficiency

- Definition POI is a disorder characterized by amenorrhoea, oestrogen deficiency, and elevated gonadotrophins, developing in ♀
- Epidemiology
 - ✓ Incidence—0.1% of ♀ <30 years and 1% of those <40 years. Accounts for 10% of all cases of 2 amenorrhoea. 20% familial. 80% idiopathic.
- Causes of POI
 - ✓ Chromosomal abnormalities (5–10%):
 - ✓ Turner's syndrome.
 - ✓ Fragile X premutations.
- Other X chromosomal abnormalities.
 - ✓ Gene mutations:
 - ✓ Galactosaemia.
- Autoimmune disease (20%).
 - ✓ Iatrogenic:
 - ✓ Chemotherapy.
 - ✓ Radiotherapy.
 - ✓ Pelvic surgery.
- Other:
 - ✓ Enzyme deficiencies, e.g. 17-hydroxylase deficiency.
 - ✓ Infections, e.g. mumps, CMV.
- Idiopathic:
 - ✓ ? environmental toxin.





Turner's syndrome

- Most common X chromosome abnormality in ♀, affecting 1:2,500 live ♀ births.
- Result of complete or partial absence of an X chromosome.
- Clinical features. Short stature and gonadal dysgenesis; 80% of affected ♀ have POI.
- Characteristic phenotype. Webbed neck, micrognathia, low-set ears, high arched palate, widely spaced nipples, and cubitus valgus.
- Other associated abnormalities. Aortic coarctation and other left-sided congenital heart defects, hypothyroidism, osteoporosis abnormalities, lymphoedema, coeliac disease, congenital renal abnormalities, and ENT abnormalities





Menopause

- The menopause is the permanent cessation of menstruation as a result of ovarian failure and is a retrospective diagnosis made after 12 months of amenorrhoea. The average age of ♀ at the time of the menopause is 50 years
- The perimenopause encompasses the menopause transition and the first year following the last menstrual period.





Physiology

- Ovaries have a finite number of germ cells, with maximal numbers at 20 weeks of intrauterine life. Thereafter, there is a gradual reduction in the number of follicles until the perimenopause when there is an exponential loss of oocytes until the store is depleted at the time of the menopause.
- Inhibin B and anti-Müllerian hormone (AMH) are ovarian glycoproteins produced by follicles, as they develop from preantral to antral stages. Both may participate in ovarian paracrine regulation and, with other molecules, regulate the rate of attrition of follicles.
- Falling inhibin B levels result in fluctuating rise in FSH. Contrary to previous belief, average serum oestradiol levels may be high at the onset of the menopause transition as a result of FSH rise, falling only towards the end as the follicles are depleted.
- AMH is a useful early marker of ovarian ageing, being stable throughout the cycle and unaffected by COCP and without the marked fluctuations of FSH. AMH measurements, however, add nothing in routine practice to established menopause.





Hormonal changes during the menopausal transition

	Premenopause (from age 36 years)	Early perimenopause	Advanced perimenopause	Menopause
Menstrual cycle	Regular, ovulatory	Irregular, often short cycles, increasingly anovulatory	Oligomenorrhoea	Amenorrhoea
FSH	Rising but within normal range	Intermittently raised, especially in follicular phase	Persistently ↑	↑↑
AMH	Declining	Low	low	Very low
E2	Normal	High normal	Normal/low	Low





Hirsutism

- Hirsutism (not a diagnosis in itself) is the presence of excess hair growth in ♀ as a result of ↑ androgen production and ↑ skin sensitivity to androgens.
- Causes of hirsutism
 - ✓ Ovarian PCOS 95%
 - ✓ Androgen-secreting tumours <1%
 - ✓ Adrenal Congenital adrenal hyperplasia 1%
 - ✓ Cushing's syndrome <1%
 - ✓ Acromegaly <1%
 - ✓ Severe insulin resistance <1%
 - ✓ Idiopathic Normal US and endocrine profile 3%



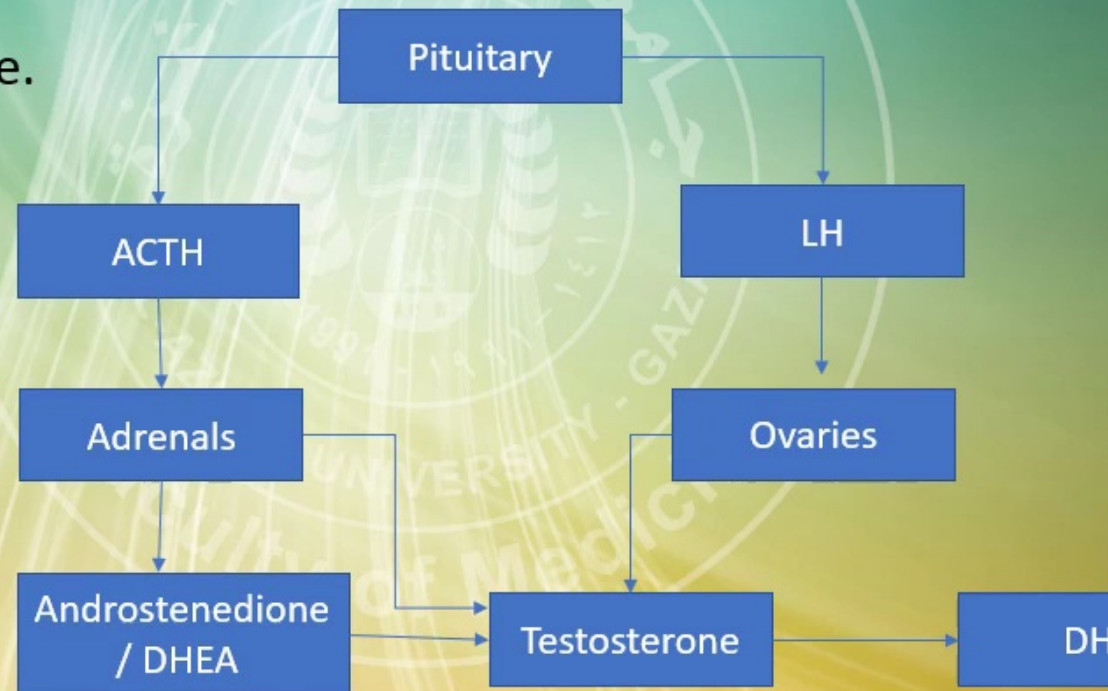


Adrenals Ovaries Androstenedione/ DHEA DHT

Regulation of androgen production in ♀.

- Signs of virilization

- ✓ Frontal balding.
- ✓ Deepening of voice.
- ✓ ↑ muscle size.
- ✓ Clitoromegaly





FEMALE FERTILITY

- Female fertility depends on properly timed ovulation, ability of sperm to reach the ovum in the fallopian tube within 24 hours of ovulation, and the ability of the zygote to implant and survive in the endometrium.
- Several problems can make a woman infertile.

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FEMALE FERTILITY

- Failure to ovulate can result from the following:
 - ✓ Mechanical obstruction on the surface of the ovary resulting from the presence of a thickened capsule.
 - ✓ scarring from infection
 - ✓ Overgrowth of the surface by cells of endometrial origin, a condition referred to as endometriosis
 - ✓ Absence of an LH surge or other hormonal abnormalities.
 - ✓ Obstruction of the fallopian tubes is often a result of infection or endometriosis.





FEMALE SEXUAL ACT

- Psychic and local sensory stimulation are important for satisfactory performance of the female sexual act.
- Sexual desire is affected to some extent by estrogen and testosterone levels in the female; consequently, desire may be greatest a few days before ovulation, when estrogen secretion from the follicle is greatest.
- Erectile tissue analogous to that in the penis is located around the introitus and extending into the clitoris.





FEMALE SEXUAL ACT

- Dilation of the arteries leading into the tissue is mediated by parasympathetic nerves that release nitric oxide from their nerve endings on the vascular smooth muscle of the arteries.
- Parasympathetic stimulation also causes secretion of mucus from Bartholin's gland, which is located underneath the labia minora.
- With appropriate local sensory and psychic stimulation, reflexes are initiated that cause the female orgasm.

