Hypothalamic-Pituitary-Gonadal Axis

- Stress
- CRH
- Kisspeptin
- Norepinephrine
- Dopamine
- GSH (Gonadotropin-Releasing Hormone)
- Inhibin
- Estradiol
- Testosterone
- FSH (Follicle-Stimulating Hormone)
- LH (Luteinizing Hormone)
- Gonads
(Modified from Grumbach MM. Genetic mechanisms of sex development.)
Germ Cells in the Ovary Throughout Life

![Graph showing the number of germ cells at different life stages: 2 months, 5 months, birth, menarche, and menopause. The graph indicates a peak in the number of germ cells during the 5th month of pregnancy, with a significant reduction at birth and further decline until menopause.](image)
Puberty and Pattern of LH Secretion

[Graphs showing LH secretion levels during different stages of development: Prepuberty, Midpuberty, and Adulthood.]
Figure 12-11. Median age and range of the signs of female sexual development during puberty. (Adapted from Speroff L, Glass RH, Kase NG. Clinical Gynecologic Endocrinology and Infertility. 4th ed. Baltimore: Williams & Wilkins, 1989: 1-688. © 1989, the Williams & Wilkins Co., Baltimore.)
Figure 12-12. Diagrammatic representation of Tanner stages I to V of human breast maturation. (Adapted from Marshall WA, Tanner JM. Variations in patterns of pubertal changes in girls. Arch Dis Child 1969; 44:291-303.)
The Menstrual Cycle: Fluctuations in Basal Body Temperature and Hormone Levels

- Basal body temperature
- Progesterone
- 17β-Estradiol
- FSH
- LH

Day of cycle

Follicular Development
EVALUATION OF AMENORRHEA

• Is the patient pregnant?
• Is she making estrogen?
• If low estrogen, are gonadotropins high indicating ovarian failure or low indicating a hypothalamic or pituitary problem?
• If high estrogen, does she make progesterone? Are there disorders of the uterus or outflow tract? Are androgens elevated?
INDICES OF ESTROGEN SECRETION

- Breast development
- Body fat distribution
- Bone maturation
- Vaginal cell cornification
- Cervical mucus
- Proliferative endometrium
- Withdrawal bleeding after progesterone
INDICES OF PROGESTERONE SECRETION

• Increase in basal body temperature
• Cervical mucus becomes more viscous
• Secretory endometrium
INDICES OF ANDROGEN SECRETION

- Hirsutism
- Acne
- Temporal balding
- Voice deepening
- Changes in body habitus
- Clitoromegaly
- Menstrual dysfunction
Sources Of Circulating Androgens In Normal Women

- Plasma Androstenedione
  - Adrenal (50%)
  - Conversion from Prehormones
    - OVARY (25%)
    - Plasma Testosterone (75%)
- Plasma DHEA + DHEAS (90-95%)
CAUSES OF INCREASED ANDROGEN SECRETION

- Polycystic ovarian disease
- Androgen producing tumors of the ovary
- Cushing's syndrome
- Adrenal hyperplasia
CLINICAL SYMPTOMS OF POLYCYSTIC OVARIAN DISEASE

- Amenorrhea
- Dysfunctional bleeding
- Hirsutism
- Infertility
- Obesity
FIGURE 98-10. Twenty-three-year-old woman with the syndrome characterized by massive obesity, severe hirsutism, acanthosis nigricans (arrow), glucose intolerance with insulin resistance, hyperandrogenism, and hyperuricemia.
BIOCHEMICAL FEATURES OF POLYCYSTIC OVARIAN DISEASE

- ↑ LH:FSH ratio
- ↑ Estrogen
- ↑ Androgens
- ↓ Sex hormone binding globulin
- Insulin resistance
Pathophysiological Characteristics of the Polycystic Ovary Syndrome
Pathophysiological Characteristics of the Polycystic Ovary Syndrome

OBJECTIVES IN TREATMENT OF POLYCYSTIC OVARIAN DISEASE

• Restoration of fertility
• Treatment of hirsutism
• Treatment of endometrial hyperplasia
• Treatment of metabolic syndrome
CAUSES OF HYPOTHALAMIC AMENORRHEA

• Diet/Weight Loss
• Exercise
• Stress
• Hyperprolactininemia
Effect of Stress (Noise of Drilling) on LH Secretion in Ovariectomized Monkeys
Disruption of Gonadotropin Secretion by Prolactin

BRAIN

Hypothalamus

GnRH

Hypothalamic-Hypophyseal Portal System

Anterior Pituitary

FSH/LH

Excess Prolactin

Gonads

Prolactin
Turner Syndrome: 45X Gonadal Dysgenesis
Hypothalamus

Uninhibited

LH, FSH

Scared, atrophic ovarian stroma

Decreased production of oestrogen secondary to depletion of developing follicles

By peripheral conversion to oestrone

Paucity of primordial follicles refractory to the effects of high gonadotrophins

Secretion of androstenedione by ovarian stroma

Skin
CLINICAL PROBLEMS ASSOCIATED WITH ESTROGEN DEFICIENCY

• Vasomotor symptoms
• Genitourinary changes
• Osteoporosis
• Lipid and cardiovascular effects
• ? CNS effects
CONSIDERATIONS FOR ESTROGEN REPLACEMENT

• Clinical symptoms
• Risk of osteoporosis
• Risk of breast cancer
• Risk of endometrial cancer
• Risk of cardiovascular disease