Hypothalamic-Pituitary-Gonadal-Axis

STRESS

Hypothalamus
- GHRH
- (Endorphins)
- Neuropeptide
+ Dopamine

GnrH

Pituitary

GnrH

Inhibin

Fsh, Lh

Bh, Lh

Testosterone

Genads

Gonadal Primordium

TDF

Y

Ovary

Sertoli Cells

Leydig Cells

Anti-Müllerian Hormone

Müllerian Duct Regression

Wolffian Ducts

Dihydrotestosterone

Epididymis

Vas Deferens

Seminal Vesicles

Pens

Scrotum

(Modified from Grumbach MM. Genetic mechanisms of sex development.)
Germ Cells in the Ovary Throughout Life

Puberty and Pattern of LH Secretion
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: 1–668. © 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.)
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
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
Polycystic Ovarian Syndrome

BIOCHEMICAL FEATURES OF POLYCYSTIC OVARIAN DISEASE

• ↑ LH:FSH ratio
• ↑ Estrogen
• ↑ Androgens
• ↓ Sex hormone binding globulin
• Insulin resistance
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
- Hyperprolactinemia
Effect of Stress (Noise of Drilling) on LH Secretion in Ovariectomized Monkeys

Disruption of Gonadotropin Secretion by Prolactin
Turner Syndrome: 45X Gonadal Dysgenesis
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