

PEARSON Core Concepts in Pharmacology, Third Edition
Holand • Adams

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Core Concept 32.1

Testosterone, estrogen, and progesterone are the primary hormones contributing to the growth, health, and maintenance of the reproductive system.

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Estrogen

- Synthesized in ovaries
- estradiol, estrone, and estriol.
- Responsible for the maturation of the reproductive organs and for the appearance of the secondary sex characteristics in women.

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Estrogen

- Metabolic effects on nonreproductive tissues, including the brain, kidneys, blood vessels, and skin.

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Progestins/Progesterone

- Secreted by ovary
- Functions
 - In combination with estrogen, promotes breast development
 - Monthly changes in the ovaries and uterus known as the menstrual cycle.

Progestins/Progesterone

- Levels fall sharply at the end of the cycle, a portion of the inner lining of the uterus, the endometrium, is shed, menstrual bleeding occurs.
 - During pregnancy, progesterone secreted by the placenta maintains a healthy endometrium for the fetus and prevents premature labor contractions.

Androgens

- Male sex hormones.
- Secreted by testes
- Androgen responsible for maturation of the male sex organs and the secondary sex characteristics of men.
- Secretion of testosterone is relatively constant in adult men.

Androgens

- Metabolic effects in tissues outside the reproductive system.
 - Ability to build muscle mass, which contributes to the difference in muscle strength and body composition between men and women.

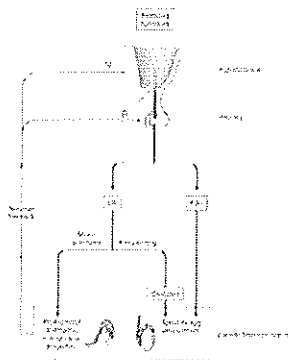
Regulation from Pituitary

- Follicle-stimulating hormone (FSH)
 - Regulates sperm or egg production.
- Leutinizing hormone (LH).
 - Females
- Triggers the release of the egg, a process known as ovulation

Regulation from Pituitary

- Promotes the secretion of estrogen and progesterone by the ovary.
 - In males
- Interstitial cell-binding hormone— regulates the production of testosterone.

Figure 32.1 Control of the reproductive hormones



Core Concept 32.2

Low doses of estrogens and progestins are used for contraception.

Oral Contraceptives – Mechanism of Action

- Prevent ovulation
 - Providing negative feedback to the pituitary that shuts down secretion of LH and FSH.
 - egg cannot mature, and ovulation is prevented.
- Make the lining of the uterus less favorable to receiving an embryo.

Contraceptive Formulations

- Oral
 - Monophasic
 - Biphasic
 - Triphasic
 - Progestin-only
- A deep IM of medroxyprogesterone acetate (Depo-Provera) provides 3 months of protection.

Contraceptive Formulations

- Subcutaneous implant - The Norplant system six small, plastic tubes filled with levonorgestrel implanted subcutaneously in the upper arm that provides contraception for up to 5 years.

Contraceptive Formulations

- Transdermal patch Ortho-Evra containing ethinyl estradiol and norelgestromin that is worn on the skin. The patch is changed every 7 days for the first 3 weeks, followed by no patch during week 4.

Table 32.1 (continued) Selected Oral Contraceptives

PROGESTIN ONLY		
Mevorin	None	levonorgestrel 0.02 mg
Mira QD	None	norgestrel 0.02 mg
Quorra	None	norgestrel 0.02 mg
EMERGENCY CONTRACEPTIVE		
Plan B One-Dose	None	levonorgestrel 0.1 mg

Hormone Replacement Therapy

- Menopause
 - Permanent cessation of menses
 - Lack of estrogen secretion by the ovaries.
- HRT Common over last 20 years

Hormone Replacement Therapy

- Concerns
 - Increased risk of coronary artery disease
 - Stroke
 - Venous thromboembolism.
- Women are now encouraged to discuss alternatives with their healthcare provider

TABLE 32.2 Potential Consequences of Estrogen Loss Related to Menopause

Early menopausal symptoms	Mood disturbances, depression, irritability Insomnia Hot flashes Irregular menstrual cycles Headaches
Mid-menopausal symptoms	Vaginal atrophy, increased infections, painful intercourse Skin atrophy Stress urinary incontinence Sexual disinterest
Postmenopausal conditions	Cardiovascular disease Osteoporosis Alzheimer's-like dementia Colon cancer

Core Concept 32.3

Estrogens have been used for replacement therapy and in the treatment of prostate cancer.

DRUG	ROUTE AND ADJUT. DOSE	REMARKS
ESTROGENS		
ethinyl diol (Ethin, Estraderm, Estraderm)	PO, 1-2 mg/die Transdermal patch, 10-100 mcg spaced twice weekly	Available as vaginal cream and as a transdermal patch, also for breast and prostate cancer and to relieve postmen- opausal symptoms
hydroxyl acetate (Ethinogestrel, Estropipin)	IN, 1-5 mcg every 3-6 weeks	Menopausal and androgenous symptoms
estradiol valerate (Ethinogestrel, Duraspin II, Valgestin)	IN, 10-20 mcg every 4 weeks	Also for breast cancer and to relieve postmenopausal symptoms
estradiol, conjugated (Ethinogestrel)	PO, 0.3-1.25 mg/day for 21 days each month	Also for postmenopausal symptoms and breast cancer
estradiol (Ethinogestrel)	PO, 0.75-6 mg/day for 21 days each month	Also for female hypogonadism and palliative treatment of prostate cancer, available as a vaginal cream
PROGESTINS		
medroxyprogesterone (Provera)	PO, 5-10 mg/day on days 1-12 of menstrual cycle	Also for endometrial and oral contraceptives and breast cancer
norgestrel (Mirena or Levonelle)	PO, 0.15 mg/day beginning on day 1 of menstrual cycle	Also for endometritis
levonorgestrel acetate	PO, 5 mg/day for 2 weeks, increase by 2.5 mg/day every 2 weeks (PO, 15 mg/day)	Also for endometritis
progesterone micronized (Progestin)	PO, 400 mg at bedtime for 10 days	All oral and rectal forms available; intravaginal brand available for oral use only

Core Concept 32.4

Progestins are prescribed for dysfunctional uterine bleeding.

Dysfunctional Uterine Bleeding

- Hemorrhage occurs on a noncyclic basis or in abnormal amounts.

Dysfunctional Uterine Bleeding

- Types
 - Amenorrhea—absence of menstruation
 - Oligomenorrhea—infrequent menstruation
 - Menorrhagia—prolonged or excessive menstruation
 - Breakthrough bleeding—hemorrhage between menstrual periods
 - Postmenopausal bleeding—uterine hemorrhage after menopause

Dysfunctional Uterine Bleeding

- Caused by a hormonal imbalance between estrogen and progesterone.

Treatment

- Administration of a progestin
 - Pattern starting 5 days after the onset of menses and continuing for the next 20 days
 - Helps to establish a normal, monthly cyclic pattern.
- Oral contraceptives may also be prescribed for this disorder.

Core Concept 32.5

Oxytocin and tocolytics are drugs used to influence uterine contractions.

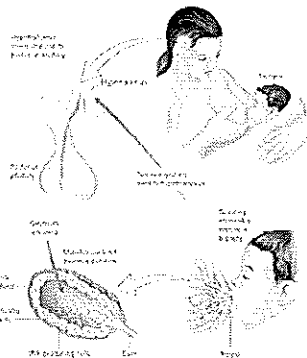
Oxytocin

- Natural hormone secreted by the posterior portion of the pituitary gland
- Primary functions:
 - To stimulate uterine contractions during childbirth

Oxytocin

- Tocolytics, are used to inhibit uterine contractions during premature labor.
 - To eject milk from the mammary glands following delivery.
- Oxytocin does not increase the volume of milk production.
- Prolactin increases the synthesis of milk.

Figure 32.3 Oxytocin and breastfeeding



Uterine Stimulants and Relaxants		
DRUG	ROUTE AND ADULT DOSE	REMARKS
STIMULANTS (OXYTOXICS)		
Prostaglandin synthase (NSAID), Preval, Fentanyl	Intravenous 10 mg	For inducing pregnancy through second trimester following fetal death or for induction of labor
ergometrine dihydrogen sulfate (Ergometrol)	PO: 1 tablet (0.2 mg) q 4hr (as needed)	Erythrocyte
oxytocin (Pitocin, Syntocinon)	PO: 0.2-0.4 mg tid-qid	PO: 0.2-0.4 mg tid-qid
misoprostol (Cytotec)	PO: 0.2 mg in a single dose	PO: 0.2 mg tid-qid
misoprostol (Cytotec)	PO: 100 mcg in a single dose	PO: 0.2 mg tid-qid
oxytocin (Pitocin)	IV (subcutaneous), IM, intranasal (nasal) dose to stimulation of uterine activity	PO: 0.2 mg tid-qid
RELAXANTS (TOCOLYTICS)		
magfloxacin (Mg)	PO: 1-4 g in 12 hours by slow infusion	Approved as an anticonvulsant in severe cases of eclampsia
calcium (Mg), Fentanyl (see page 337 for the Drug Handbook)	PO: 0.2 mg in a single dose (oral) 10 mg in 15 min	Calcium channel blockers approved for cardiovascular disorders
nitroglycerin (Nitrostat)	PO: 10-120 mg in 15 min (oral) (sublingual) PO: 20 mg in 15 min (oral) (sublingual)	See also for beta-adrenergic receptors, not to be used
nitroglycerin (Nitrostat)	PO: 10 mg in 15 min (oral) (sublingual)	Selective beta-2-adrenergic receptor agonists available in oral and sublingual forms for bronchodilation

Core Concept 32.6

Androgens are used to treat hypogonadism or delayed puberty in men and breast cancer in women.

Selected Androgens		
DRUG	ACUTE AND ADULT DOSE	REMARKS
Testosterone (Depo-Testosterone)	IM, 100-200 mg every 4-6 weeks	For hypogonadism, hypogonadotropic hypogonadism, and delayed puberty in men
Testosterone (Sustanon)	IM, 25-50 mg daily for hypogonadism	For hypogonadism, breast cancer, and postoperative hypogonadism
Methylglutaminamide (Mesterolone, Provir)	PO, 50-80 mg daily	For hypogonadism, breast cancer, and postoperative hypogonadism
Stanozolol (Winstrol, Winstrol-Valeryl)	IM, 40-100 mg every week	For breast cancer only
Testosterone (Testolone)	PO, 25-50 mg/d	For breast cancer only
Testosterone (Andro 100, Androval, Androval-Valeryl)	PO, 10-25 mg every 2-3 days	IM, topical, and oral preparations for hypogonadism and delayed puberty in men; breast cancer in women
Mestranolone (Provera, Provera-10, Provera-20, Provera-30)	PO, 50-80 mg every 2-4 weeks	For hypogonadism, breast cancer, and hypogonadotropic hypogonadism
Testosterone enanthate (Androval, Androval-Valeryl, Sustanon)	IM, 50-400 mg every 2-4 weeks	For hypogonadism and breast cancer

Erectile Dysfunction

- Increases with advancing age, may occur in adult men of any age.

Core Concept 32.7

Erectile dysfunction is a common disorder successfully treated with drug therapy.

Erectile Dysfunction

- Causes
 - Diseases: atherosclerosis, diabetes, stroke, hypertension
 - Psychogenic causes: depression, fatigue, guilt, fear of sexual failure.
 - Adverse effect of drugs: thiazide diuretics, phenothiazines, serotonin-reuptake inhibitors, tricyclic antidepressants, propranolol (Inderal), diazepam (Valium).

Erectile Dysfunction

- Treatment: sildenafil (Viagra), vardenafil (Levitra) tadalafil (Cialis).

Core Concept 32.8

In its early stages, benign prostatic hypertrophy may be treated successfully with drug therapy.

Drugs for BPH

- Alpha1-blockers
 - Doxazosin (Cardura), terazosin (Hytrin), tamsulosin (Flomax)

Drugs for BPH

- Finasteride (Proscar)
 - Inhibits an enzyme responsible for converting testosterone to one of its metabolites, 5-alpha-dihydrotestosterone.
 - Category X drug, and women who are pregnant or who may become pregnant should avoid the semen of men taking the drug.