Adrenal Cortex

- Secretes glucocorticoids
  - Mobilize body for long-term stress
  - Influence carbohydrate, lipid, and protein metabolism in most cells
- Secretes mineralocorticoids
  - Aldosterone promotes sodium reabsorption and potassium secretion
- Secretes gonadocorticoids
  - Male sex hormones (androgens)

Addison's Disease

- Primary adrenocortical insufficiency
- Symptoms
  - Hypoglycemia, fatigue, hypotension
  - Increased skin pigmentation
  - GI disturbances: anorexia, vomiting, diarrhea
  - Low plasma cortisol, accompanied by high plasma ACTH levels

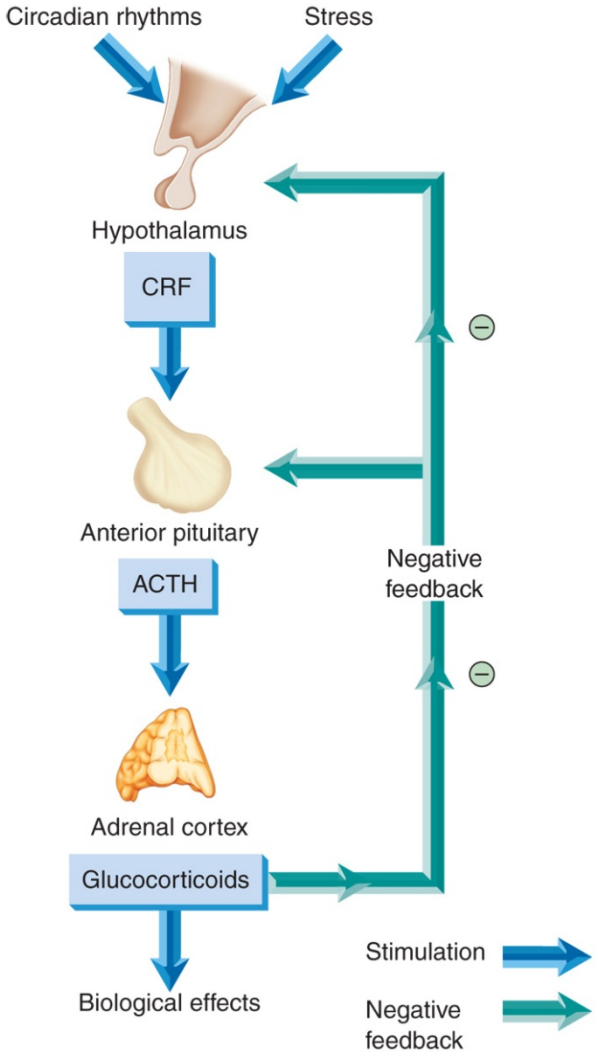
Cushing's Syndrome

- Caused by long-term administration of glucocorticoids
- Signs and symptoms
  - Moon face, buffalo hump, mood and personality disorders

control of the adrenal cortex

Corticotropin releasing factor

Adrenocorticotropic hormone



Pharmacotherapy of Adrenocorticotropic Hormone (ACTH)

- ACTH and related agents rarely used as medications
- Must be given parenterally and have many side effects
- Primary use is to diagnose adrenal disorders

Pharmacotherapy of Adrenocortical Insufficiency

- May be acute or chronic
- Glucocorticoids prescribed
  - Primary (Addison's disease), secondary adrenocortical insufficiency
  - Allergies, neoplasms, wide variety of other conditions

Corticosteroids

- Betamethasone
- Cortisone
- Hydrocortisone
- Dexamethasone (Decort®)
- MethylprednisolonePrednisolone
- Prednisone
- Triamcinolone

Inhaled corticosteroids used in asthma

- Budesonide
- Beclomethasone
- Fluticasone

Therapeutic uses of corticosteroids

1. Replacement therapy for primary adrenocortical insufficiency (Addison disease) or secondary or tertiary adrenocortical insufficiency

2. Relief of inflammatory symptoms including asthma, arithritis, etc.

3. Treatment of allergies

4. Acceleration of lung maturation

Adrenal Drugs—Glucocorticoids (continued)

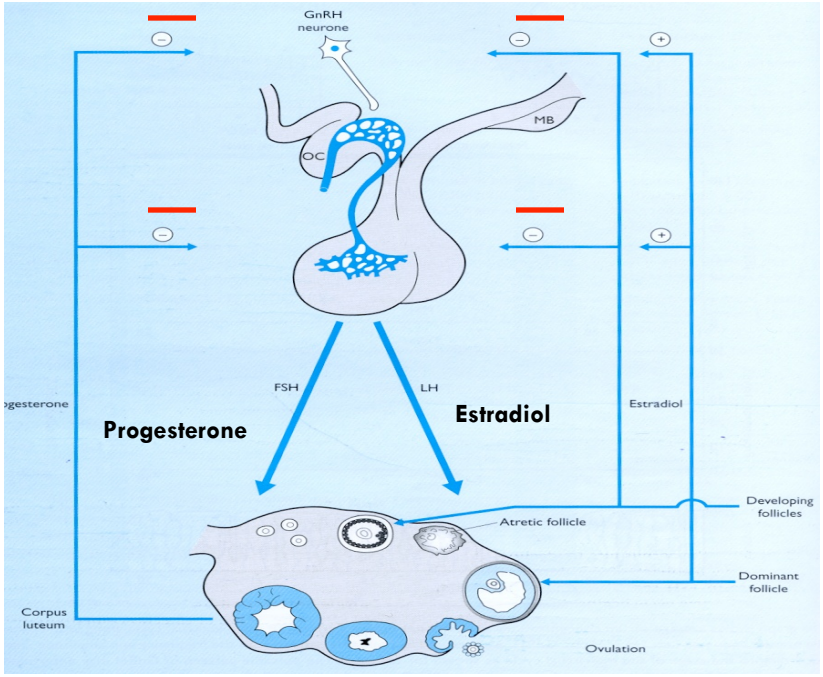
- **Adverse effects:** sodium and fluid retention
  - CNS effects: insomnia, anxiety, headache, vertigo, confusion, depression
  - Cardiovascular effects: Hypertension, tachycardia
  - Peptic ulcer disease
  - Hyperglycemia
  - Osteoporosis
  - Immunosuppression
  - Cushing's syndrome
    - Can occur with long-term therapy

Corticosteroids Adverse effects

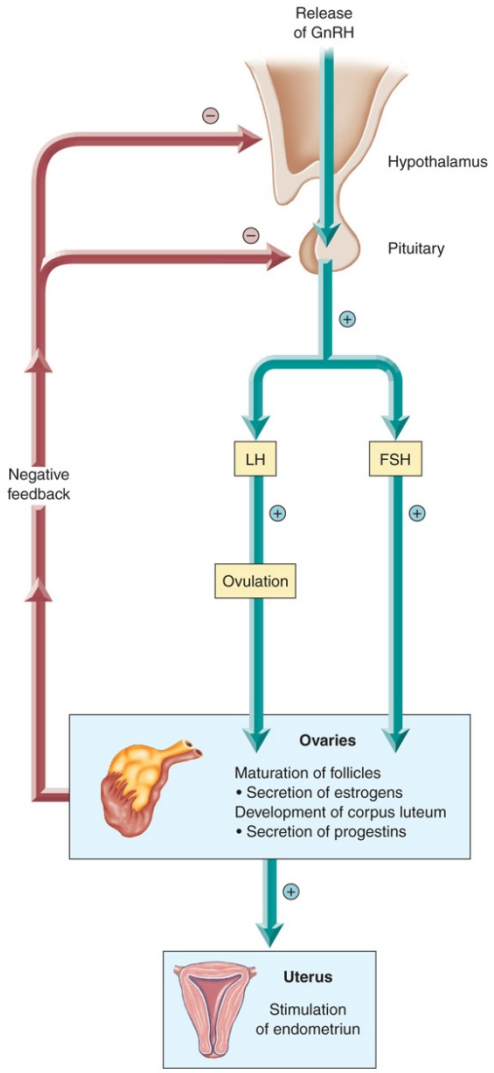
Antiadrenal Drugs

- Used to treat severe Cushing's syndrome
  - Occurs with prolonged glucocorticoid therapy
    - Inhibits corticosteroid synthesis
- Antiadrenal drugs not curative
  - Use usually limited to three months of therapy

Reproductive Hormones



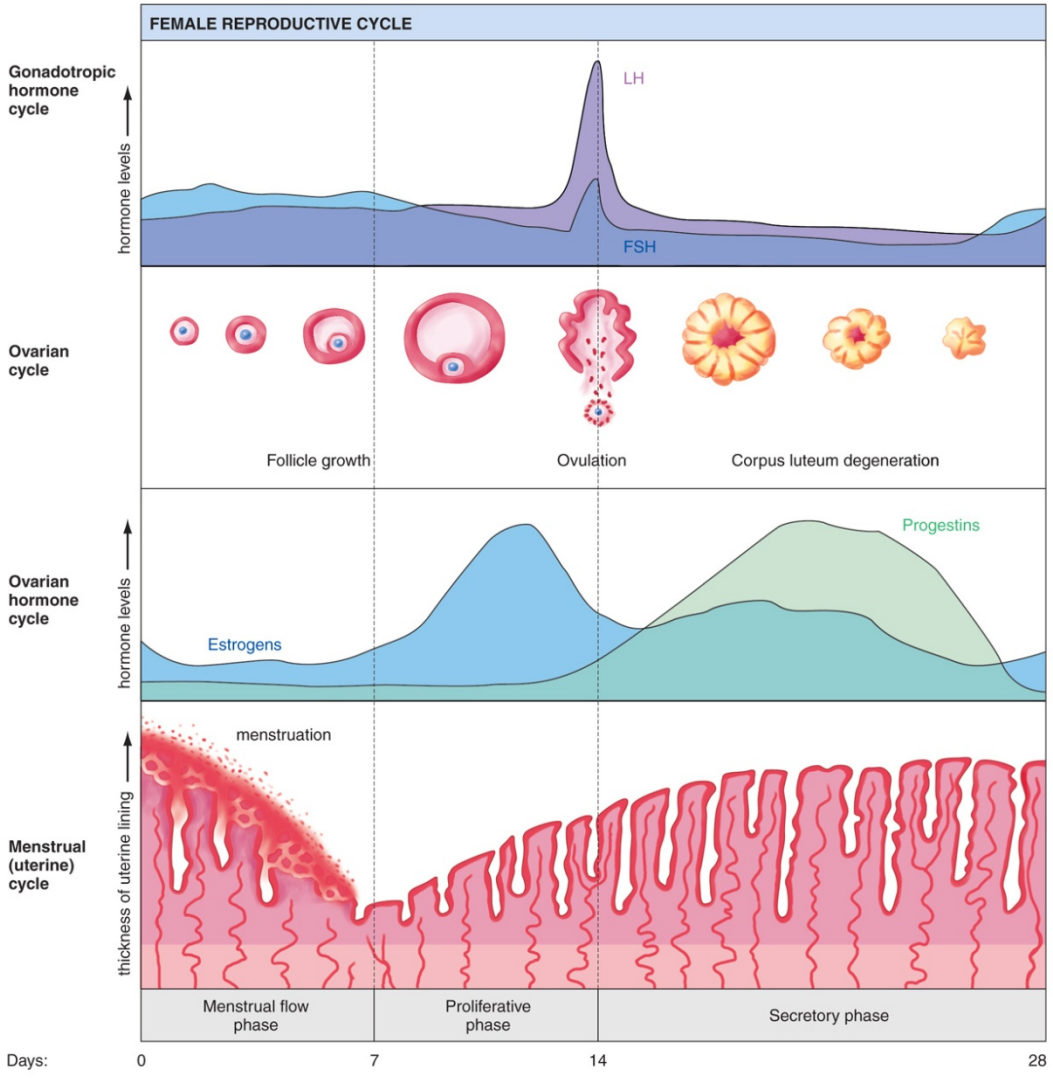
Control of Female Reproductive Hormones



Hypothalamus and Pituitary Regulation of Female Reproductive System

- Hypothalamus secretes gonadotropin-releasing hormone (GnRH)
  - Stimulates pituitary to secrete follicle-stimulating hormone (FSH) and luteinizing hormone (LH)
    - Act on ovary and cause immature ovarian follicles to begin developing to dominant follicles
  - Pituitary hormones
    - Rising and falling levels create two interrelated cycles: ovarian and uterine

Hormonal Changes During the Ovarian and Uterine Cycles



Estrogens: Actions and Therapeutic Uses

Actions:

1- Feminization at puberty

2- Fat deposition

3- Promotion of uterine development

4- Calcium retention

5- Promotion of salt and fluid retention

Therapeutic uses of estrogens:

1- Oral contraceptives in combination with progestins

2- Hormone replacement therapy in menopausal women

Minimize bone loss, prevent hot flashes, and decrease incidence and severity of vaginitis

No longer recommended

Estrogen-Progestin Contraceptives

- Act by providing negative feedback to pituitary
  - Shuts down secretion of LH and FSH; prevent ovulation and implantation of fertilized ovum
- Three types: monophasic, biphasic, triphasic
- Progestin-only oral contraceptives (minipills)
  - Preferred for women who are breastfeeding, in risk of DVT or women who have heart disease.
  - Produce thick, viscous mucus at entrance to uterus
    - Discourages penetration by sperm
- Progestins also thin the endometrium preventing the implantation of a fertilized ovum.

Emergency Contraception

- May be administered within 72 hours after unprotected sex
- Prevents implantation of fertilized egg
  - Plan B: levonorgestrel in two doses, 12 hours apart
  - Preven: combination of ethinyl estradiol and levonorgestrel

Emergency Contraception

- Other agents may be given to abort implanted embryo
  - Mifepristone (antiprogesterone)
  - Misoprostol (Prostaglandin analogue used for GI ulcer) FDA off-label.

Hormone Replacement Therapy (HRT)

- Estrogen-progestin combinations used during and after menopause
- Long-term use may have serious adverse effects
- Commonly used to treat unpleasant symptoms of menopause
- Prevents long-term consequences of estrogen loss

Hormone Replacement Therapy (continued)

- Women's Health Initiative (WHI) suggested increased risks
  - Cardiac problems, stroke, cancer
  - HRT appears to prevent osteoporotic bone fractures
- Women now encouraged to discuss alternatives with health-care provider
  - http://www.rcog.org.uk/files/rcog-corp/uploaded-files/SIP_No_6.pdf

Progestins: Actions and Therapy

Actions:

1- Promote development of endometrium

2- Maintenance of pregnancy

3- With estrogen, mammary gland stimulation

Therapeutic uses:

1- Oral contraceptives with estrogens

Estrogen component: ethinyl estradiol

Progestin component: norethindrone, norgestrel, levonorgestrel

2- Dysfunctional uterine bleeding

3- Dysmenorrhea

Dysfunctional Uterine Bleeding

- Hemorrhaging that occurs on noncyclic basis or in abnormal amounts
- Health problem most frequently reported by women
  - Common reason for hysterectomy
- Often an imbalance between estrogen and progesterone
- Progestins are drugs of choice for treating uterine abnormalities

Role of Hormones in Treatment of Cancer

- Estrogens are used in combination with other agents for chemotherapy of cancer
- Used alone, estrogen increases risk of uterine cancer
  - Only considered appropriate for clients who have had hysterectomy
- High doses of estrogens sometimes used to treat prostate and breast cancer
  - Prostate cancer usually dependent on androgens for growth
  - Administration of estrogens will suppress androgen secretion (no longer recommended for its side effects)

Oxytocics

- Natural hormones secreted by posterior pituitary
- Stimulate uterine contractions to induce labor
- Suckling stimulates release of oxytocin
  - Causes more milk ejection

Tocolytics

- Slow uterine contractions to delay labor
- Used in clients with premature labor
- Example: beta agonists such as terbutaline

Treatment of Female Infertility

- Causes of female infertility are varied
  - Lack of ovulation, pelvic infection, physical obstruction of uterine tubes
- For infertility with an endocrine etiology, pharmacotherapy may be of value
  - Can occur at level of hypothalamus, pituitary, or ovary
  - Pharmacotherapy targeted to specific cause of dysfunction

Treatment of Female Infertility

- **Clomiphene** is drug of choice for female infertility
  - Compete with estrogen for receptor binding, inhibit negative feedback effect of estrogen on gonadotropin production, promote ovulation and sustained function of corpus luteum
  - Rise in LH level sufficient to induce ovulation in 90% of treated women

Anti-Progestins

Antiprogestins

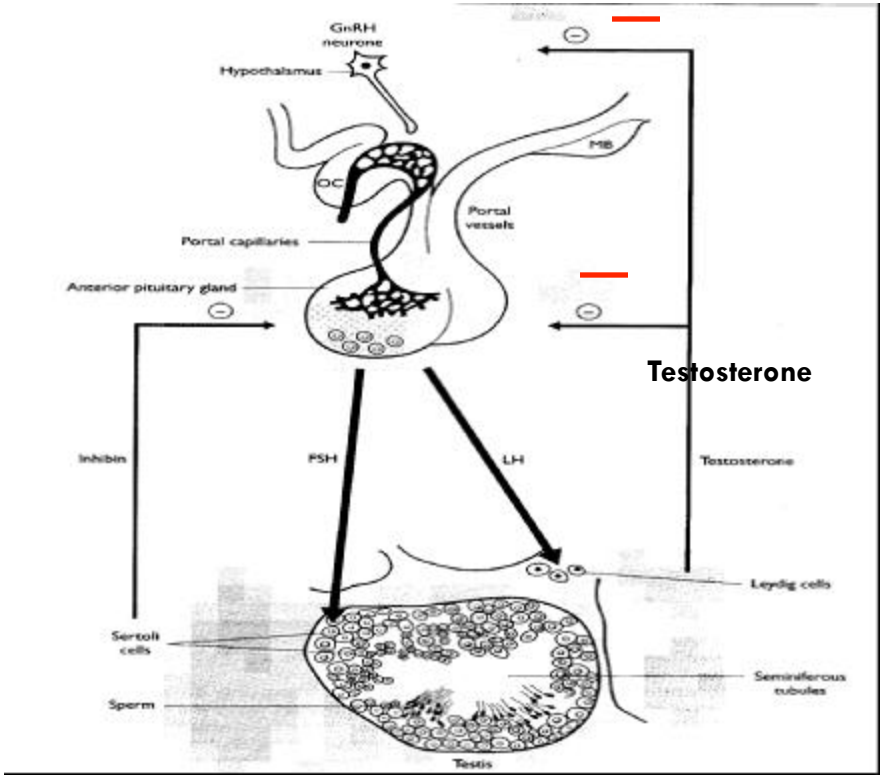
Mifepristone

Indication: Early termination of pregnancy defined as 49 days or less.

Mechanism of action: Competitive binding to intra-cellular progestin receptors

Side Effects: Recent reports of serious bacterial infections, bleeding, and sometimes death prompted FDA to place a black label warning.

Androgens


GnRH neurone
Hypothalamus
MB
OC
Portal vessels
Portal capillaries
Anterior pituitary gland
Testosterone
Inhibin
FSH
LH
Testosterone
Leydig cells
Sertoli cells
Seminiferous tubules
Sperm
Testis

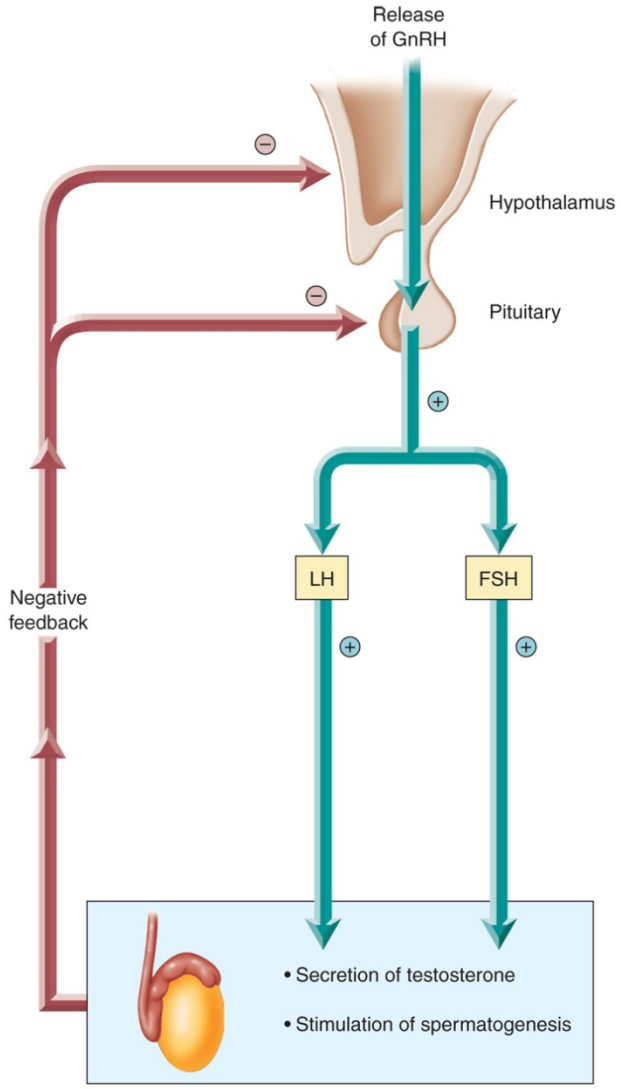
Pituitary Hormones

- Gonadatropin releasing hormone (GRH) from hypothalamus
- Follicle stimulating hormone (FSH)
  - Regulates sperm production
- Luteinizing hormone (LH)
  - Regulates production of testosterone

Testes Secrete Testosterone

- Androgen and primary hormone of male reproductive system
  - Contributes to growth, health, maintenance
  - Responsible for maturation of male sex organs
  - Responsible for secondary sex characteristics of men

Hormonal Control of the Male Reproductive Hormones



Androgens

- Include testosterone and related hormones
  - Control many aspects of male reproductive function
- Used to treat hypogonadism in males
  - Primary hypogonadism due to testicular failure
  - Secondary due to lack of follicle stimulating hormone (FSH) or luteinizing hormone (LH)

Androgens: Actions and Therapy

Actions:

1- Promote growth, sexual maturation and masculinization of male.

2- Maintenance of sexual function.

Therapeutic uses:

1- Replacement therapy for hypogonadism.

2- Breast cancer. (Rarely used)

Adverse Effects:

1- Inappropriate virilization.

2- Cardiovascular disease, liver damage and masculinizing effect in females.

Androgens

- **Prototype drug:** Testosterone
- **Mechanism of action:** Stimulates RNA synthesis and protein metabolism
- **Primary use:** For treatment of hypogonadism in males
- **Adverse effects:** Virilization
  - Salt and water often retained
    - Causes edema, liver damage, acne and skin irritation

Anabolic Steroids

- Testosterone-like compounds
- Frequently abused by athletes, even though illegal
- Can result in serious adverse effects with long-term use
  - Increased cholesterol levels, low sperm count, impotence
  - Menstrual irregularities and the appearance of male characteristics in women
  - Aggression, psychological dependence

Anti-Androgens: Therapy

Indication: Prostate cancer

Mechanism of Action:

Androgen receptor blockade e.g. cyproterone

GnRH agonist; Leuprolide

5-α-reductase inhibition; Finastride (Proscar ®)