Chapter 20: Other Hormones

Chapter 20 Outline

- Other hormones
  - Pituitary hormones
  - Thyroid hormones
  - Pancreatic hormones
  - Female sex hormones
  - Male sex hormones
  - Other agents that affect sex hormone systems

Other Hormones

- Haveles (p. 249)
  - Hormones are secreted by endocrine glands and transported by blood to target tissues, where they are biologically active
  - Endocrine glands include the pituitary, thyroid, parathyroids, pancreas, adrenals, gonads, and placenta
  - Help maintain homeostasis by regulating body functions and are controlled themselves by feedback systems

Pituitary Hormones

- Haveles (pp. 249-251)
  - Anterior pituitary
  - Posterior pituitary
  
  The pituitary gland (master gland) is located at the base of the brain; “master gland” due to its regulatory effect on other endocrine glands and organs of the body
  - Secrets peptide hormones that regulate the thyroid, adrenal, and sex glands; the kidney and the uterus; and growth
  - Also has a trophic effect; without gonadotropins, the entire reproductive system fails; without growth hormone and thyrotropin, normal growth and development are impossible

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Pituitary Hormones

- Haveles (pp. 249-250)
- Pituitary deficiency can produce loss of secondary sex characteristics, decreased metabolism, dwarfism, diabetes insipidus, hypothyroidism, Addison disease, loss of pigmentation, thinning and softening of the skin, decreased libido, and retarded dental development
- Hypersecretion of pituitary hormones can produce sexual precocity, goiter, Cushing disease, acromegaly, and gigantism
- The two parts to the pituitary gland are the anterior lobe (adenohypophysis) and the posterior lobe (neurohypophysis)

Anterior Pituitary

- Haveles (pp. 250-251) (Fig. 20-2)
- Secrets growth hormone (somatotropin), luteinizing hormone (LH), follicle-stimulating hormone (FSH), thyroid-stimulating hormone (TSH) or thyrotropin, adrenocorticotropic hormone (ACTH) or corticotropin, and prolactin
- β-Lipotropin is a precursor to β-endorphin

Anterior Pituitary

- Human growth hormone is used medically to treat children who lack it
- Pharmaceutical gonadotropin-releasing hormone (GnRH) is a synthetic analogue
- Leuprolide stimulates pituitary function and is used to treat infertility
- GnRH agonists are used to treat prostate cancer and endometriosis

Bromocriptine

- Haveles (p. 251)
- Inhibits pituitary function
- Not a hormone; it is a dopamine agonist that suppresses prolactin levels
- Used to treat prolactin-secreting adenomas, acromegaly, and Parkinson disease

Posterior Pituitary

- Haveles (p. 251)
- Secretes vasopressin (antidiuretic hormone [ADH]) and oxytocin
- Vasopressin (Pitressin) has vasopressor and antidiuretic hormone activity and is used to treat transient diabetes insipidus
  - Synthetic vasopressin analogues (desmopressin [DDAVP, Stimate] and lypressin [Diapid]) are used for chronic treatment of pituitary diabetes insipidus and for certain clotting disorders (hemophilia A and von Willebrand disease)
- Oxytocin (Pitocin, Suntocinon) is used to induce labor, control postpartum hemorrhage, and induce postpartum lactation

Thyroid Hormones

- Haveles (pp. 251-252)
- Iodine
- Hypothyroidism
- Hyperthyroidism
**Thyroid Hormones**

- Haveles (p. 251)
  - The thyroid gland secretes two iodine-containing thyroid hormones—triiodothyronine ($T_3$) and tetraiodothyronine (thyroxine [$T_4$]); in addition, calcitonin regulates calcium metabolism
  - Thyroid hormones are important for energy metabolism, growth, and development
  - Thyroid hormones are synthesized from iodine and tyrosine and stored as complex protein until TSH stimulates their release

**Iodine**

- Haveles (p. 251)
  - The thyroid gland requires intake of adequate iodine; if iodine intake is deficient, normal amounts of thyroid hormones cannot be made
  - TSH is secreted in excess, and the thyroid hypertrophies (simple or nontoxic goiter)
  - Marine life is the only common food that is naturally rich in iodine; iodized salt has decreased the incidence of simple goiter

**Hypothyroidism**

- Haveles (p. 251) (Box 20-1)
  - In the small child, hypothyroidism is called cretinism; in an adult, it is called myxedema or simple hypothyroidism
  - Patients are usually drowsy, weak, and listless and exhibit an expressionless, puffy face with edematous tongue and lips
  - Thyroid hypofunction is treated with exogenous thyroid hormones
    - The most common is levothyroxine

**Hyperthyroidism**

- Haveles (pp. 251-252)
  - Two forms of thyroid hyperfunction
    - Diffuse toxic goiter (Graves disease) is characterized by a diffusely enlarged, highly vascular thyroid gland
      - Common in young adults and considered a disorder of the immune response
    - Toxic nodular goiter (Plummer disease) is characterized by nodules that secrete excessive hormone while the rest of the glandular tissue is atrophied
      - Occurs primarily in older patients

**Excess levels of circulating thyroid hormone produce thyrotoxicosis**

- Adverse effects include excess production of heat, increased sympathetic activity, increased neuromuscular activity, increased sensitivity to pain, ophthalmopathy, exophthalmos, and anxiety
- Oral manifestations include accelerated tooth eruption, marked loss of alveolar process, diffuse demineralization of jawbone, and rapidly progressive periodontitis
- Direct inotropic effect in cardiovascular system

**Treatment:**

- The two most common treatments are radioactive iodine ($^{131}$I) and thyroidectomy
- Either treatment usually results in hypothyroidism
Antithyroid Agents

- Antithyroid agents such as propylthiouracil (PTU) and methimazole (Tapazole) are used in patients who cannot tolerate surgery or treatment with $^{131}$I.
- These drugs interfere directly with the synthesis of thyroid hormones by inhibiting the iodination of tyrosine moieties and the coupling of iodotyrosines.

Pancreatic Hormones

- Two primary hormones secreted by islets of Langerhans of the pancreas are insulin and glucagon.
- Insulin promotes fuel storage (glucose out of blood).
- Glucagon promotes fuel mobilization (glucose into the blood).

Types of Diabetes

- Type I: usually develops in persons younger than age 30 years and results from autoimmune destruction of pancreatic beta cells.
- Associated with a complete lack of insulin secretion, increased glucagon secretion, rapid onset of disease, ketosis, and severe symptoms.
- Without insulin, type I DM is fatal.
- Must be treated with injections of insulin.

Diabetes Mellitus

- A group of metabolic disorders characterized by persistent hyperglycemia.
- Type I (insulin-dependent DM [IDDM]): associated with a complete lack of insulin secretion.
- Type II (non-insulin-dependent DM [NIDDM]): symptoms and complications result, usually from inadequate or poorly timed secretion of insulin from the pancreas and/or insulin resistance of the cells.
- Insulin resistance develops and the pancreas gives out.
Complications of Diabetes

- Xerostomia: pronounced susceptibility to caries; the xerostomia is secondary to an increase in urination
- Periodontal disease: patients with uncontrolled or undiagnosed diabetes are more prone to periodontal disease
- Advanced glycation end-products (AGEs): collagen becomes cross-linked; thickening of blood vessels is associated with elevated AGEs

Dental Issues

- Dental appointments should not interfere with meals and should involve minimal stress
- Patients with diabetes have fragile blood vessels, delayed wound healing, and a tendency to develop infections
- Surgical therapy should be approached with caution

Cautions and Contraindications

- Drugs that may decrease insulin release or increase insulin requirements, such as epinephrine, glucocorticoids, or opioid analgesics, should be used with caution in patients with diabetes

Systemic Complications of Diabetes

- Cardiovascular system: incidence of problems is higher in patients with diabetes
- Retinopathy: microvascular disease affects the blood supply to the retina
- Neuropathy: leads to reduced and sometimes absent feelings, especially in the lower extremities
- Infections: gangrene can occur in the peripheral extremities due to depressed immunity, less effective white blood cells, microvascular changes, and neuropathy
- Healing: slower healing

Effect of Drugs on Complications of Diabetes

- Intensive treatment of patients with IDDM can substantially reduce the onset and progression of diabetic retinopathy, nephropathy, and neuropathy
  - The risk of hypoglycemia is increased three times, and the increase in weight gain tends to be greater

Evaluation of the Dental Patient With Diabetes

- Two laboratory tests useful in evaluating a patient’s glucose control are serum glucose and glycosylated hemoglobin
  - Serum glucose is a measure of the patient’s glucose control at the time that the blood is sampled
  - Glycosylated hemoglobin (HbA1C) reflects glucose control over a 2- to 3-month period
### Treatment of Hypoglycemia

- **Haveles (p. 256)**
  - When the patient is conscious, treatment consists of any source of sugar: fruit juice, cake icing, glucose gel, or soluble carbohydrate.
  - If the patient is unconscious and lacks a swallowing reflex, treatment consists of intravenous dextrose (50%).

### Drugs Used to Manage Diabetes

- **Haveles (pp. 256-282)**
  - Insulins
  - Oral antidiabetic agents
  - Other new drugs
  - Glucagon

### Selected Insulin Preparations

- **Haveles (p. 256) (Table 20-4)**
  - Rapid acting
    - insulin aspart (Novolog)
    - insulin lispro (Humalog)
    - insulin glulisine (Apidra)
  - Short acting
    - insulin regular (Novolin R, Humulin R)

- **Haveles (p. 256) (Table 20-4)**
  - Intermediate acting
    - insulin NPH (Humulin N, Novolin N)
    - Humulin L Lente
  - Long acting
    - insulin detemir (Levimir)
    - insulin glargine (Lantus)
Drugs Used to Manage Diabetes

- Haveles (pp. 257) (Box 20-4)
  - Hypoglycemia is the most common adverse reaction to insulin
    - May be caused by unintentional overdose (insulin shock), failure to eat, or increased exercise or stress
    - Symptoms are explained by increased release of epinephrine from the adrenals, include sweating, weakness, nausea, and tachycardia
    - Symptoms from glucose deprivation of the brain include headache, blurred vision, mental confusion, incoherent speech, and eventually coma, convulsions, and death

Oral Antidiabetic Agents

- Haveles (pp. 257-259, 260-261) (Table 20-6)
  - Currently four groups of oral agents
    - The oldest is sulfonylureas; oral hypoglycemic agents
    - Antihyperglycemic agents: lower elevated blood sugar but do not produce hypoglycemia
      - Biguanides
      - Nonsulfonurea secretagogues
      - α-Glucosidase inhibitors
      - Thiazolidinediones
      - cont’d...

Oral Antidiabetic Agents

- Haveles (p. 257)
  - Biguanides: metformin (Glucophage) increases hepatic and peripheral insulin sensitivity
  - cont’d...

Oral Antidiabetic Agents

- Haveles (pp. 257-258) (Fig. 20-6)
  - Sulfonylureas: the only orally active agents used to manage diabetes for many years
    - Mechanism of action includes stimulation of release of insulin from the beta cells of the pancreas, reduction of glucose from the liver, reduction in serum glucagon levels, and increase in sensitivity of target tissues to insulin
    - Indicated for patients with NIDDM who cannot be treated with diet and exercise alone

Oral Antidiabetic Agents

- Haveles (pp. 257-258) (Fig. 20-6)
  - Sulfonlureas: the only orally active agents used to manage diabetes for many years
    - Mechanism of action includes stimulation of release of insulin from the beta cells of the pancreas, reduction of glucose from the liver, reduction in serum glucagon levels, and increase in sensitivity of target tissues to insulin
    - Indicated for patients with NIDDM who cannot be treated with diet and exercise alone

Other New Drugs

- Haveles (p. 259)
  - exenatide (Byetta): an incretin mimetic that has an amino acid sequence similar to human glucagon-like peptide-1 (GLP-1) and in the presence of glucose acts to stimulate insulin secretion
  - pramlintide (Symlin): an amylinomimetic agent responsible for modulation of gastric emptying, prevention of postprandial rise in plasma glucagon, and satiety, which leads to decreased caloric intake and potential weight loss
  - cont’d...
Other New Drugs

- Colesevelam: a bile-acid sequestrant used to lower low-density lipoprotein (LDL) cholesterol
- Dipeptidyl-peptidase-4 inhibitors: sitagliptin (Januvia) is an oral medication approved for use in the treatment of type II diabetes as monotherapy or in combination with metformin, a sulfonlurea, or a thiazolidinedione

Glucagon

- A polypeptide hormone produced by a cells of the pancreas
  - Increases liver glycogenolysis by stimulating cyclic adenosine monophosphate (cAMP) synthesis and increasing phosphorylase kinase activity
  - An antagonist to insulin
  - May be used parenterally for emergency treatment of hypoglycemia, glucose is usually preferred

Female Sex Hormones

- Estrogens
- Progestins
- Hormonal contraceptives

- Estrogen and progesterone levels vary daily
  - Changes are dependent on the pituitary gonadotropic hormones FSH and LH
  - On day 1 of an average 28-day cycle, secretions of FSH and LH begin to increase
  - This release is caused by a reduction in the blood levels of estrogen and progesterone, which normally inhibit their release

- An ovarian egg matures in response to increased FSH
  - The follicle in which it is contained grows in size and begins to secrete estrogen
  - On approximately day 12, the rate of secretion of FSH and LH increases markedly to cause a rapid swelling of the follicle
  - This culminates in ovulation on day 14
Female Sex Hormones

- Haveles (p. 263) (Fig. 20-7)
  - After ovulation, LH causes secretory cells of the follicle to develop into a corpus luteum that secretes large quantities of estrogen and progesterone
  - This causes a feedback decrease in the secretion of both FSH and LH

- The corpus luteum completely degenerates on approximately day 26
  - The decrease in estrogen and progesterone leads to menstruation and increased release of FSH and LH
  - The FSH initiates growth of new follicles to begin a new cycle

Estrogens

- Haveles (pp. 263-264) (Table 20-8)
  - Overview
  - Estrogens are largely responsible for the changes that take place during puberty
  - Synthetic estrogens can be used for therapy and conception
  - The most common side effects of estrogen therapy are nausea and vomiting
    - Other side effects include uterine bleeding, vaginal discharge, edema, thrombophlebitis, weight gain, and hypertension

- Estrogen therapy may also promote endometrial carcinoma in postmenopausal women
  - This risk may be cancelled out by administration of a progestin

- Effect on oral tissues
  - Changes in sex hormone levels are related to gingivitis at puberty, during pregnancy, and after menopause
  - The increase in gingival inflammation may occur even with a decrease in the amount of plaque

Progestins

- Haveles (p. 264)
  - The corpus luteum is the primary source of progesterone during the normal female sexual cycle
    - Progesterone promotes secretory changes in the endometrium and prepares the uterus for implantation of the fertilized ovum
      - If implantation does not occur, progesterone secretion declines and menstruation occurs
      - If implantation takes place, the trophoblast secretes chorionic gonadotropin, which sustains the corpus luteum, maintaining progesterone and estrogen levels and preventing menstruation
Progestins

- Haveles (p. 264)
  - Progestins are used in a variety of dose forms
    - Parenteral medroxyprogesterone (Depo-Provera) is administered every 3 months as a contraceptive
    - Progestin-only “minipills” are used orally
    - A progestational agent can be administered as an intrauterine device (IUD) or implant under the skin of the arm

Hormonal Contraceptives

- Haveles (pp. 264-265) (Box 20-5)
  - Oral contraceptives are the most common dose forms of hormonal contraceptives and consist of estrogens and progestins in various combinations
    - These are the most common birth control pills and are more than 99% effective
  - The combination type of oral contraceptive is taken for 21 days of each month
    - The seven pills in the fourth week contain no active ingredient

Hormonal Contraceptives

- Haveles (p. 265)
  - Seasonale is the newest in combination oral contraceptives
    - An extended cycle contraceptive
  - The contraceptive vaginal ring is a new dose form that introduces hormonal contraception into the body
  - An injectable contraceptive is also available

Male Sex Hormones

- Haveles (p. 266) (Box 20-6; Table 20-10)
  - Androgens
    - Testosterone, the main androgen, has both androgenic and anabolic effects
    - Androgens are responsible for the development of secondary male sex characteristics

Hormonal Contraceptives

- Haveles (p. 265) (Table 20-9)
  - Certain antibiotics have been said to reduce the effectiveness of hormonal contraceptives
    - They are thought to do so by indirectly suppressing the intestinal flora and thus diminishing the availability of hydrolytic enzymes to regenerate the parent steroid molecule
    - Consequently, plasma concentrations of steroids are said to be abnormally low, and the steroid is cleared more rapidly from the body than under normal circumstances

Hormonal Contraceptives

- Haveles (p. 265)
  - Hormonal contraceptives are associated with a significant increase in the frequency of dry sockets after extractions
  - Contraindications for use of oral contraceptives include thromboembolic disorders, significant dysfunction of the liver, known or suspected carcinoma of the breast or other estrogen-dependent neoplasm, and undiagnosed genital bleeding
Male Sex Hormones

- Androgens are used illicitly for muscle mass gain
- Androgenic steroids are schedule III controlled substances because of their abuse
- Side effects of androgenic steroids include nausea, cholestatic jaundice, hepatocellular neoplasms, increased serum cholesterol, habituation, and depression and excitation

Other Agents that Affect Sex Hormone Systems

- Clomiphene has the ability to induce ovulation in some anovulatory women
- Leuprolide is used in the management of endometriosis and to treat infertility
- Tamoxifen is indicated in the palliative treatment of breast cancer in postmenopausal women
- Danazol is used to treat endometriosis and fibrocystic disease in women
- Aromatase inhibitors reduce almost the entire amount of estrogen made in the bodies of postmenopausal women