Activity of the Adenophypophysis

- The tropic hormones (effect endocrine glands) that are released are:
  - Thyroid-stimulating hormone (TSH)
  - Adrenocorticotropic hormone (ACTH)
  - Follicle-stimulating hormone (FSH)
  - Luteinizing hormone (LH)

Growth Hormone (GH)

- Produced by somatotropic cells of the anterior lobe that:
  - Stimulate most cells
    - But target bone and skeletal muscle
  - Promote protein synthesis and encourage the use of fats for fuel
- Most effects are mediated indirectly by insulin-like growth factors (IGFs) (somatomedins)
  - Control uptake of amino acids (proteins) and sulfur (for chondroitin sulfate - cartilage)

Growth Hormone (GH)

- Antagonistic hypothalamic hormones regulate GH
  - Growth hormone–releasing hormone (GHRH)
    - Stimulates GH release
  - Growth hormone–inhibiting hormone (GHIH)
    - Inhibits GH release

Metabolic Action of Growth Hormone

- GH stimulates
  - Liver, skeletal muscle, bone, and cartilage
    - To produce insulin-like growth factors
- Direct action promotes lipolysis and inhibits glucose uptake

Metabolic Action of Growth Hormone

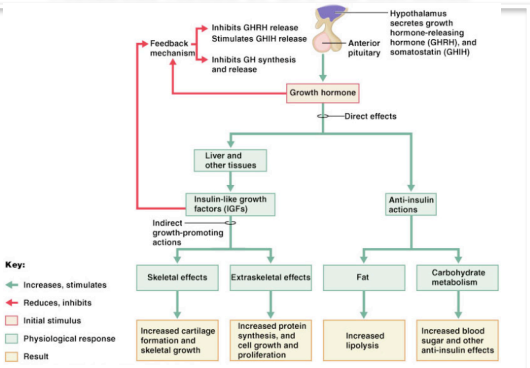


Figure 16.6

Growth Hormone Abnormalities

- Hypersecretion
  - Gigantism
    - In children before epiphyseal plates close
    - Results in elongation of long bones
    - Due to pituitary tumor
  - Acromegaly
    - In adults after epiphyseal plates close
    - Enlarges and thickens bones
    - Chronic hyperglycemia
      - Diabetes mellitus and atherosclerosis

Growth Hormone Abnormalities

- Hyposecretion
  - Pituitary dwarfism
    - In children
    - Delayed growth of long bones
    - Early closure of epiphyseal plates
    - Organs fail to grow
    - Slowed development of adult reproductive function
  - Progeria
    - In children
    - Genetic origin
    - Rapid premature ageing
    - Degenerative changes after first year

Thyroid Stimulating Hormone (Thyrotropin)

- Tropic hormone
  - Stimulates the normal development and secretory activity of the thyroid gland
    - Response to low triiodothyronine (T_3) and thyroxin (T_4)
- Triggered by thyrotropin-releasing hormone (TRH)
  - Hypothalamic peptide
- Rising blood levels of thyroid hormones (T_3, T_4)
  - Act on the pituitary and hypothalamus to block the release of TSH
    - Blocked by somatostatin (GHIH)

Adrenocorticotropic Hormone (Corticotropin)

- Stimulates the adrenal cortex to release corticosteroids
  - Most typically glucocorticoids such as cortisol
    - Help resist stress
  - Triggered by hypothalamic corticotropin-releasing hormone (CRH) in a daily rhythm
  - Internal and external factors such as fever, hypoglycemia, and stressors can trigger the release of CRH
- Negative feedback
  - High levels of ACTH triggers hypothalamic corticotropin-inhibiting hormone (CIH)

Gonadotropins

- Gonadotropins
  - Follicle-stimulating hormone (FSH) and luteinizing hormone (LH)
    - Regulate the function of the ovaries and testes
      - Stimulates gamete (egg or sperm) production
  - Absent from the blood in prepubertal boys and girls
  - Triggered by the hypothalamic gonadotropin-releasing hormone (GnRH) during and after puberty
    - Response to
      - Females: low estrogen, progesterone, inhibin
      - Males: low testosterone, inhibin

Functions of Gonadotropins

- In females
  - LH works with FSH on follicular cells
    - To cause maturation of the ovarian follicle (oogenesis)
  - LH works alone on thecal cells
    - To trigger ovulation (expulsion of the egg from the follicle)
    - Promotes synthesis and release of estrogens and progesterone
    - Maintains corpus luteum
- Negative feedback
  - High estrogen, progesterone, inhibin
    - Hypothalamus releases gonadotropin inhibiting hormone (GnIH)

Functions of Gonadotropins

- In males
  - LH
    - Stimulates interstitial cells of the testes to produce testosterone
      - Also referred to as interstitial cell-stimulating hormone (ICSH)
  - FSH
    - Stimulates sustentacular cells of seminiferous tubules
      - Initiates spermiogenesis
- Negative feedback
  - High testosterone and inhibin
    - Hypothalamus releases GnIH

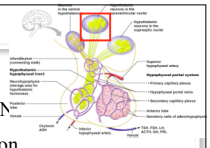
Prolactin (PRL)

- In females, prolactin release
  - Triggered by prolactin-releasing hormone (PRH) from hypothalamus
  - Stimulates milk production by alveolar cells of the breasts
  - Negative feedback control
    - Inhibited by prolactin-inhibiting hormone (PIH) from hypothalamus
      - Low blood estrogen triggers PIH
- Breastfeeding and high blood estrogen
  - Stimulates PRH release and encourages continued milk production
    - Positive feedback!

The Posterior Pituitary (neurohypophysis)

- Posterior pituitary
  - Made of axons of hypothalamic neurons
    - Stores antidiuretic hormone (ADH) and oxytocin
  - ADH and oxytocin are synthesized in the hypothalamus
    - ADH influences water balance
    - Oxytocin stimulates smooth muscle contraction in breasts and uterus
  - Both use PIP-calcium second-messenger mechanism

Oxytocin



- Oxytocin
  - Made in paraventricular nucleus (PvN)
  - Strong stimulant of uterine contraction
- Regulated by a positive feedback mechanism to oxytocin in the blood
  - Uterine stretching causes myometrial cells to send impulses to PvN
    - Leads to increased intensity of uterine contractions, ending in birth
  - Oxytocin triggers milk ejection ("letdown" reflex) in women producing milk
    - Myoepithelial cells contract

Oxytocin

- Synthetic and natural oxytocic drugs
  - Used to induce or hasten labor
- Plays a role in sexual arousal and satisfaction
  - In males and nonlactating females(?)

Antidiuretic Hormone (ADH)

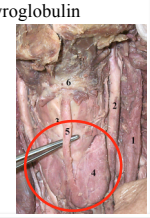
- ADH
  - Produced in supraoptic nucleus
  - Regulates water levels
    - Helps to avoid dehydration or water overload
    - Prevents urine formation
      - Conserves water
  - Osmoreceptors monitor the solute concentration of the blood
    - Or low blood volume, low blood pressure
    - With high solutes
      - ADH is synthesized and released, thus preserving water
    - With low solutes
      - ADH is not released, thus causing water loss from the body
  - Alcohol inhibits ADH release and causes copious urine output

Antidiuretic Hormone

- ADH
  - Targets kidney tubules and collecting ducts
    - Locations of water reabsorption
  - Negative feedback
    - High blood volume, high blood pressure, low solute concentration
      - Inhibit ADH release
  - Hyposecretion
    - Diabetes insipidus
      - High urine output
      - Increased thirst
  - Hypersecretion
    - Hyponatremia - low blood sodium

Thyroid Gland

- The largest endocrine gland
- Located inferior to larynx on anterior trachea
- Consists of two lateral lobes connected by a median tissue mass called the isthmus
- Composed of follicles
  - Follicular cells produce the glycoprotein thyroglobulin
- Colloid
  - Fills the lumen of the follicles
    - Thyroglobulin + iodine
      - Precursor of thyroid hormone
- Parafollicular cells
  - Produce the hormone (thyro)calcitonin



Thyroid Gland

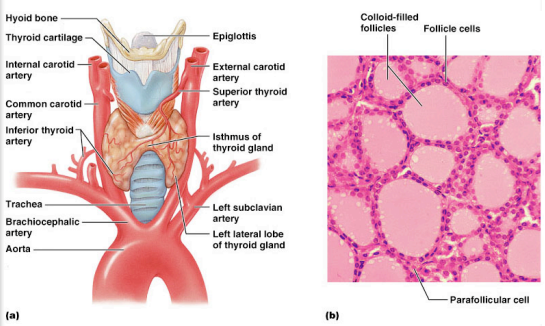
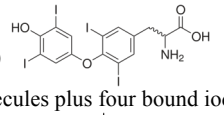


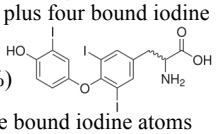
Figure 16.7

Thyroid Hormone

- Thyroid hormone
  - The body's major metabolic hormone
- Consists of two closely related iodine-containing compounds
  - T_4 – thyroxine (90%)



    - Two tyrosine molecules plus four bound iodine atoms
  - T_3 – triiodothyronine (10%)



    - Two tyrosines with three bound iodine atoms

Effects of Thyroid Hormone

- Three effects of Thyroid hormone
  1. Regulation of metabolism
     - 60-100% increase
       - Anabolism
         - Protein synthesis
       - Catabolism
         - Carbohydrate and lipid breakdown
     - ⇑ glucose catabolism + ⇑oxygen consumption = ⇑ATP production = ⇑basal metabolic rate = ⇑heat production

Effects of Thyroid Hormone

- Three effects of Thyroid hormone (cont.)
  2. Regulation of growth and development
     - With HGH and insulin = ⇑growth and development
  3. Maintenance of normal nervous system function
     - Large role in fetal and newborn nervous system development
       - Fetal hypothyroidism - fewer neurons, defective myelination
         - Mental retardation
       - Child hypothyroidism - small stature, decreased organ development

Synthesis of Thyroid Hormone

- Thyroglobulin
  - Synthesized and discharged into the lumen of follicle
    - Iodides (I^-)
      - Actively taken into the cell
      - Oxidized to iodine (I_2), and released into the lumen
        - Iodine attaches to tyrosine, mediated by peroxidase enzymes, forming T_1 (monoiodotyrosine, or MIT), and T_2 (diiodotyrosine, or DIT)
        - Iodinated tyrosines link together to form T_3 and T_4
  - Colloid is then endocytosed from colloid back to cells
    - Combined with a lysosome, where T_3 and T_4 are cleaved and diffuse into the bloodstream

Synthesis of Thyroid Hormone

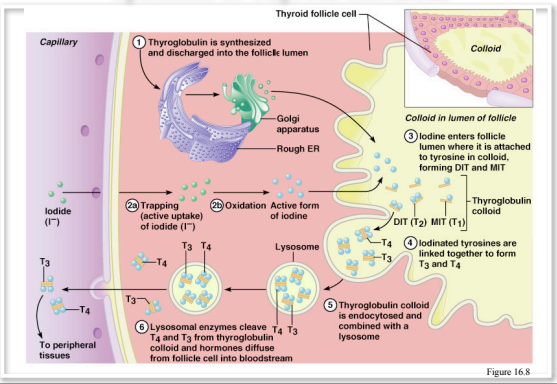


Figure 16.8

Transport and Regulation of TH

- T_4 and T_3
  - Bind to thyroxine-binding globulins (TBGs) produced by the liver
    - Transported as protein-bound iodine (PBI)
  - Both bind to target receptors
    - But is ten times more active than T_4
      - T_3 may
        1. Bind membrane receptor
        2. Enter cell and bind nuclear receptor
        3. Enter cell and bind mitochondria, ⇑ O2 uptake

Transport and Regulation of TH

- Peripheral tissues convert T_4 to T_3
  - By removal of one iodine
- Mechanisms of activity are similar to steroids
  - May up-regulate specific protein synthesis
- Negative feedback
  - Falling TH levels trigger TSH from adenohypophysis
  - Rising TH feeds back to inhibit hypothalamic-adenohypophyseal axis
    - Shutting off TSH release
  - Hypothalamic thyrotropin-releasing hormone (TRH) can overcome the negative feedback
    - For pregnancy and infant cold exposure

Thyroid Disorders

- Hypothyroid disorders
  - Myxedema
    - Adult hypothyroidism
      - Swollen, puffy face, and dry skin
      - ⇓ heart rate = ⇓ metabolic rate = ⇓body temp
      - Constipation
      - ⇓ mental alertness

Hypothyroid Disorders

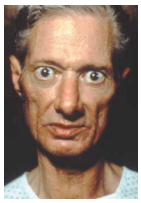
- Goiter (endemic or colloidal)
  - ⇓ iodine
    - Follicles increase in size due to filling with unusable colloid
      - Leads to continued high TSH in the blood
        - Stimulates more unusable colloid
        - Glandular collapse

Hypothyroid Disorders

- Cretinism
  - Child myxedema
    - Looks like adult hypothyroidism patient
      - Round face, thick nose/tongue/neck
      - Mental retardation
      - Dwarfism
      - Inhibited sexual development
      - All nonreversible
    - Treat with thyroid hormone replacement

Hyperthyroid Disorders

- Graves Disease
  - Autoimmune due to presence of thyroid gland stimulating antibodies (TSAb's)
    - Antibodies stimulate thyroid hormone overproduction
      - ⇑ metabolic rate, excessive perspiration, ⇓ weight
      - ⇑ heart rate/pulse/body temp, moist flushed skin
  - Treatment
    - Surgery or radioactive iodine to destroy most active thyroid cells



Hyperthyroid Disorders

- Exophthalmic goiter
  - Overactive thyroid due to tumor
    - Enlarged thyroid gland from being overworked
    - Protruding eyes due to post-ocular edema
      - As in Graves

(Thyro)Calcitonin

- Thyrocalcitonin
  - A peptide hormone produced by the parafollicular, or C, cells
  - Lowers blood calcium levels in children
  - Antagonist to parathyroid hormone (PTH)

(Thyro)Calcitonin

- Calcitonin targets the skeleton, where it:
  - Inhibits osteoclast activity
    - and thus bone resorption
    - and release of calcium from the bone matrix
  - Stimulates calcium uptake and incorporation into the bone matrix
  - Regulated by a humoral negative feedback mechanism
    - Calcium ion concentration in the blood
      - Directly acts on thyroid gland
        - No input from pituitary on feedback
    - ⇓ calcium resorption in the kidney tubules
    - ⇓ calcium absorption in small intestine

Parathyroid Glands

- Tiny glands embedded in the posterior aspect of the thyroid
  - ~ Four
- Cells are arranged in cords containing oxyphil and chief cells
- Chief (principal) cells secrete PTH
  - Oxyphil cell function unknown
- PTH (parathormone) regulates calcium balance in the blood
  - Antagonist of calcitonin

Parathyroid Glands

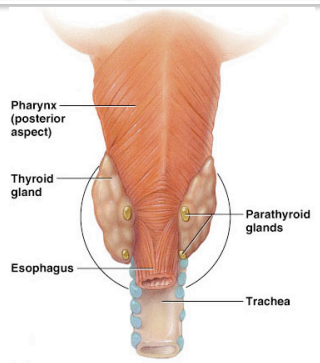


Figure 16.10a

Effects of Parathyroid Hormone

- PTH release
  - Increases Ca^{2+} in the blood as it:
    - Stimulates osteoclasts to digest bone matrix
    - Enhances the reabsorption of Ca^{2+} and the secretion of phosphate by the kidneys
      - Decreases or stops Ca^{2+} secretion in kidneys
    - Increases absorption of Ca^{2+} by intestinal mucosal cells
- Rising Ca^{2+} in the blood inhibits PTH release
  - Humoral control acts directly on parathyroid

Effects of Parathyroid Hormone

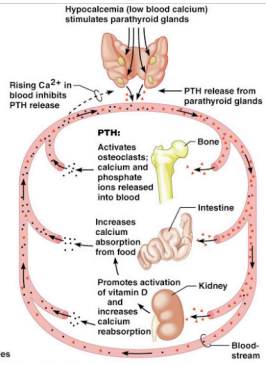


Figure 16.11