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

Activity of the Adenohypophysis

- 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

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)

- 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
      - Hyponatremia - low blood sodium
  - Hypersecretion
    - Increased thirst
      - 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 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
Chapter 16: Endocrine System

**Effects of Thyroid Hormone**

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

- Regulation of growth and development
  - With HGH and insulin = \( \uparrow \) growth and development

- 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

- $T_4$ 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, $\uparrow$ O2 uptake

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, $\uparrow$ O2 uptake

- 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
  - Shut off TSH release
  - Hypothalamic thyrotropin-releasing hormone (TRH) can overcome the negative feedback
    - For pregnancy and infant cold exposure

Chapter 16: Endocrine System
Thyroid Disorders

- Hypothyroid disorders
  - Myxedema
    - Adult hypothyroidism
      - Swollen, puffy face, and dry skin
      - \( \text{\( \downarrow \) heart rate = \( \downarrow \) metabolic rate = \( \downarrow \text{body temp} \) } \)
      - Constipation
      - \( \downarrow \text{mental alertness} \)

- Hypothyroid Disorders
  - Goiter (endemic or colloidal)
    - \( \downarrow \text{iodine} \)
      - 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 non reversible
        - 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)
**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
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