Endocrine Glands

I. Pituitary (L. Pituita - phlegm)
   A. Location and Anatomy
      1. The pituitary gland or hypophysis hangs suspended from the hypothalamus and is protected by the sella turcica of the sphenoid bone.
      2. The pituitary is divided into the anterior lobe (adenohypophysis) and a posterior lobe (neurohypophysis).
         a. Development (see VDG pg. 568)
            (1) The anterior lobe forms at about week 3 of development from an epithelial lining of the pharyngeal roof (diverticulum called the hypophyseal (Rathke’s) pouch).
            (2) The posterior pituitary extends down from the neuroectoderm forming the neurohypophyseal bud.
            (3) At 8 weeks the hypophyseal pouch breaks away from the pharyngeal roof and joins the neurohypophysis
            (4) The neurohypophysis retains its connectivity to the nervous system via the infundibulum.
         b. adenohypophysis - three parts
            (1) Pars distalis (anterior pituitary)
            (2) Pars tuberalis (thin extension in contact with the infundibulum).
            (3) Pars intermedia (present in small children disappears in adulthood).
         c. neurohypophysis- two parts.
            (1) Pars nervosa - posterior pituitary
            (2) infundibulum (L. Funnel) Connects pars nervosa to the hypothalamus and contains nerve fibers.
   3. Relationship to brain
      a. Hypothalamohypophyseal portal system (see VDG fig. 19.15)
         (1) extends from hypothalamus to anterior pituitary.
         (2) delivers blood from hypothalamus to cells in the anterior pituitary
         (3) veins from the capillary system enter the general circulation.
         (4) Neurohormones: produced by the hypothalamus enter the primary capillary network and travel through the Hypothalamohypophyseal portal system to the anterior pituitary.
            (a) Act as either releasing or inhibiting hormones.
            (b) Act as chemical signals to regulate the secretory activity of the anterior pituitary.
            (c) Include: Thyroid releasing hormone (TRH), Corticotropin-releasing hormone (CRH), Gonadotropin-releasing hormone (GnRH), etc.
      b. The neurohypophysis does not have a portal system (VDG fig. 19.13)
         (1) Neurohormones are delivered to the posterior pituitary via axons in the hypothalamohypophyseal tract and are released from the axon terminals into the blood stream.

B. Posterior pituitary hormones
   1. Secreter two hormones: Antidiuretic hormone (ADH) and oxytocin.
   2. Antidiuretic hormone (ADH) (also called vasopressin)
      a. Prevents large output of urine.
      b. Constricts blood vessels and raises blood pressure.
      c. Synthesized in the supraoptic nucleus
         (1) Stored in axon terminals until released
      d. Primary target tissue is the kidney
         (1) promotes retention of water in blood
      e. Increase in blood osmolarity or a decrease in blood volume is detected by osmoreceptors that increase ADH release from neurons in hypothalamus.
      f. Effect: ADH causes a increase water retention in the kidney
         (1) - reduced urine output and decreases blood osmolarity, increases blood volume.
g. Inhibitors of ADH release
   (1) Alcohol consumption inhibits ADH release and causes copious amounts of urine production - result is dehydration of person.
   (2) Diuretic drugs have the same action as alcohol causing water to be flushed from the body. They are recommended when edema and congestive heart failure occur.

h. Hyposcretion:
   (1) A lack of ADH release is a cause of diabetes insipidus (Urine output may reach 20 L / day).
   (2) Not life threatening if thirst centers are functional.

3. Oxytocin
   a. Synthesized in paraventricular nuclei and stored in axon terminals within the neurohypophysis.
   b. Small peptide
   c. Function:
      (1) Stimulates smooth muscle cells of the uterus.
         (a) Important in delivery of fetus.
      (2) Responsible for milk ejection (let down response) in lactating females.
         (a) causes contraction of smooth muscle around alveoli of mammary glands.
      (3) Expulsion of epithelium and blood in nonpregnant women during menses.
      (4) Movement of sperm following sexual intercourse.
   d. Released in response to stretch of uterus, cervix or nipples through a reflex response involving the hypothalamus.
   e. Action potential generated in the oxytocin producing cells produce the release of oxytocin.

C. Anterior Pituitary Hormones.
Hormones released from the anterior pituitary are influenced by releasing and inhibitory factors from the hypothalamus via the hypophyseal portal system.

Some hormones released from the anterior pituitary are called tropic hormones because they effect other endocrine glands throughout the body (ie. TSH, LH, FSH, ACTH).

1. Growth hormone (somatotropin).
   a. GH is produced by cells known as somatotrophs
   b. GH increases mitotic activity within the cell.
   c. Indirect effect on growth
      (1) stimulates the liver and other organs to produce somatomedins:
         (a) somatomedins stimulate the uptake of amino acids from blood and incorporation into proteins
         (b) stimulates the uptake of sulfur for the incorporation into cartilage matrix esp. at epiphyseal plates.
   d. Direct effect in liver
      (1) Causes fatty stores to be mobilized
      (2) decreases glucose uptake
      (3) increases glycogen breakdown both of which increase the amount of blood sugar available for energy.
   e. Regulation of GH release by 2 hormone releasing hormones:
(1) Growth hormone releasing hormone (GHRH)
(2) Growth hormone inhibiting hormone GHIH (Somatostatin)

f. Other factors may influence the release of GH
   (1) Stress, nutrition, sleep patterns.
   (2) Follows a diurnal pattern highest during sleep
   (3) Peaks in adolescence and decreases with age.

g. Secretion abnormalities
   (1) Hypersecretion:
      (a) Gigantism during growing years - result is exaggerated growth of long bones and thus excessively tall individuals
      (b) Acromegaly - after the epiphyseal plate closure. Hypersecretion results in heavier facial features, course, enlargement of soft tissue.
   (2) Hyposecretion:
      (a) Dwarfism in childhood - small features; no affect in adults occasional atrophy of muscle and bone.

2. Thyroid stimulating hormone (TSH) or thyrotropin
   a. Releases by thyrotropes (regulatory pathway discussed later: see thyroid gland below).
   b. Effect: regulates the development and secretory activity of the thyroid gland
   c. Regulated by thyrotropin releasing hormone (TRH) from the hypothalamus

3. Adrenocorticotropic hormone (ACTH) or corticotropin
   a. Secreted by corticotrophs of the anterior pituitary
      (1) Produced as part of a larger molecule Proopiomelanocortin (POMC)
      (a) Other products of POMC include:
         i) Lipotropins, - fat breakdown
         ii) beta endorphin, - analgesia, regulation of body temp, water/food intake, sex.
         iii) melanocyte stimulating hormone (MSH) - increases melanin in skin
      b. Effect: Stimulates the adrenal cortex to release corticosteroid hormones,
         (1) most importantly glucocorticoids (See Adrenal gland below)
         (a) help the body to resist stress.
      c. Regulated by corticotropin releasing hormone (CRH) form the hypothalamus
   d. Other:
      (1) Diurnal rhythm with peak levels in the morning shortly after you arise.
      (2) Increased levels of glucocorticoids feedback block secretion of CRH and consequently ACTH release
      (3) Can also be stimulated by fever, hypoglycemia and other stressors.

4. Gonadotropins: two types (A complete discussion of gonadal hormones will be presented with reproduction)
   a. Follicle stimulating hormone (FSH)
      (1) produced by gonadotrophes
      (2) Effect: stimulates gamete production; sperm and egg.
      (3) Regulation:
         (a) release is regulated by the hypothalamic hormone gonadotropin releasing hormone (GnRH) / luteinizing hormone releasing hormone (LHRH).

\[\text{Hypothalamus} \rightarrow \text{GnRH(LHRH)} \rightarrow \text{Anterior Pituitary} \rightarrow \text{Gonadotrophins (FSH & LH)} \rightarrow \text{Gonads} \rightarrow \text{Sex steroid Hormones (estrogen & androgens)} \]
(b) Suppressed by gonadal hormones, testosterone and estrogen.

b. **Luteinizing hormone (LH)**
   (1) produced by gonadotrophs
   (2) Effect: stimulates the development of the gonads in both sexes
      (a) Female:
         i) LH works with FSH to mature the egg containing follicle in the ovary.
         ii) LH by itself causes the release (ovulation) and promotes the release of estrogen
      (b) Male: LH causes the production of testosterone

5. **Prolactin (PRL)**
   a. Similar in structure to GH
   b. Produced by the lactotrophs of the pituitary.
   c. Effect: stimulates the production of milk
   d. Regulation:
      (1) released in response to prolactin-releasing hormone (PRH),
      (2) suppressed by prolactin inhibiting hormone (PIH) same as dopamine.
      (3) **Male**: PIH predominates
      (4) **Female**:
         (a) low estrogen levels stimulate PIH release and high estrogen levels stimulate PRH release.
         (b) Brief rise in estrogen at the end of the menstrual period accounts for the slight swelling in the breasts but usually no milk is present.
         (c) **Pregnancy**: toward the end estrogen levels increase and milk production begins
         (d) Direct stimulation of the breast by the infant causes PRH release and therefore prolactin and milk production.
   e. Hypersecretion:
      (1) hyperprolactinemia - sign of adenohypophyseal tumor,
         (a) females: inappropriate lactation (glactorrhea), lack of menses, infertility
         (b) **Male**: Impotence

II. **Thyroid Gland**
   A. Location and Anatomy
      1. Located in throat below prominence of the thyroid cartilage
      2. Bilobed structure connected by isthmus
   B. Hormones of the thyroid
      1. 2 different hormones
         a. **Thyroxine (T4)** and **Triiodothyronine (T3)**
         b. Overall effects: Effects virtually every cell in the body except adult brain, spleen, testes, uterus, and thyroid gland.
            (1) Tends to increase basal metabolic rates (proteins, fats and carbohydrates) in cells.
            (2) Can cause an increase in adrenergic receptors in blood vessels therefore important in blood pressure regulation.
            (3) Important regulator of tissue growth and development especially skeletal and nervous system, and reproductive
c. Regulated by TSH from anterior pituitary
   (1) Falling levels of thyroxine in blood causes TSH release and thyroxine release.
   (2) TSH causes hypertrophy and hyperplasia (increased cell number) of the thyroid gland.
   (3) TRH-TSH-T3 & T4
      (a) cold and stress increase TRH release
      (b) prolonged fasting decreases TRH release

d. Biosynthesis:
   (1) Synthesized as large proteins called thyroglobulins made up of tyrosine.
   (2) Requires Iodine

e. Hypersecretion:
   (1) Graves disease (autoimmune disorder) in which persons body makes antibodies which mimic TSH.

   (2) Symptoms include increased metabolic rate, sweating, rapid irregular heart beat, weight loss, nervousness, exophthalmous (protruding of the eyes due to mucoprotein deposits behind the eyes).

f. Hyposecretion: in adults:
   (1) Myxedema (mucous swelling) low metabolism, constipation, feeling chilled, puffy eyes, thick dry skin.
   (2) Iodine deficiency: hypothyroidism caused by lack of iodine in diet results in endemic goiter (enlargement of the thyroid gland). (Inadequate thyroid hormone synthesis leads to elevated TSH secretion - thyroid enlarges to compensate.
   (3) Hashimoto’s disease -autoimmune disease in which thyroid function is normal or depressed.

g. Hyposecretion in children:
   (1) Cretinism results in a short disproportionate body; thickened tongue, neck and facial features; mental retardation; decreased basal metabolic rate; and general lethargy.
      (a) Genetic deficiency of thyroid hormone that is preventable by thyroid hormone replacement therapy.

2. Calcitonin
   a. Produced by the parafollicular cells of the thyroid gland in response to an increase in blood calcium levels.
   b. Effect:
      (1) Inhibits osteoclast activity and increases osteoblast activity
         (a) therefore leads to more bone formation and less bone destruction.
         (b) Overall effect is to remove excess calcium from the blood and incorporate into bones.
      (2) Levels decrease with age causing osteoporosis.
III. Parathyroid Glands
A. Anatomy and Location:
1. Located on the posterior side of each lobe of the thyroid gland (usually four glands).
2. Essential for life
3. Not discovered until physicians began to notice the differences in survival of partial vs complete thyroidectomy patients.
B. Parathyroid hormone
1. Produced by chief cells
2. Functions:
   a. Stimulates osteoclast to digest bone matrix and reabsorption of calcium in kidneys.
   b. Enhances reabsorption of calcium from intestine. This is an indirect effect. PTH enhances the transformation of vitamin D from its inactive state to an active one. Vitamin D then enhances calcium absorption from intestine.
3. Regulation:
   a. Stimulated by low blood calcium
   b. Inhibited by rising blood calcium levels.
4. Hypersecretion:
   a. Hyperparathyroidism -
      (1) Rare - leads to leaching of minerals from bones, abnormally high calcium levels in blood, depressed nervous system, slow and abnormal reflexes, weakness of skeletal muscles, formation of kidney stones.
      (2) Bone deposits may form in other soft tissue.
5. Hyposecretion:
   a. Hypothyroidism -
      (1) May result from gland trauma or removal. Symptoms are hyperexcitability, tetany, loss of sensation, muscle twitches, laryngeal paralysis, and eventually death from respiratory paralysis.

IV. Adrenal Glands (Suprarenal)
A. Location and Anatomy
1. Pyramidal shaped glands positioned in the fatty pads above each kidney.
2. Consists of an outer adrenal cortex and inner adrenal medulla which function as separate glands.
   a. Cortex is divided into three layers zona glomerulosa, zona fasciculata, zona reticularis.
B. Hormones of the Adrenal cortex: Three types collectively called corticosteroid hormones (formed from cholesterol).
1. Mineralocorticoids (most common is aldosterone)
   a. Produced by the zona glomerulosa cells.
   b. Functions:
      (1) Decreases sodium excretion from the body. Primary target is the distal tubules of the kidneys where it stimulates reabsorption of sodium from the urine.
      (2) Enhances sodium reabsorption from perspiration,
saliva and gastric juices.

(3) Regulates water volume: Where sodium goes, water will follow. Preventing sodium excretion causes water retention.

c. Regulated by:
(1) Decreased sodium or potassium ions in the blood will stimulate ADH release.
(2) Decreased blood volume and decreased sodium or potassium will stimulate kidneys to secrete renin which is converted to angiotensin II in the lungs. Angiotensin II stimulates aldosterone release.
(3) Stress will cause CRH release from the hypothalamus which will cause ACTH to be released from the pituitary which will stimulate aldosterone.
(4) Aldosterone release is inhibited by atrial natriuretic factor (ANF) which is released in response to increased sodium levels or increased blood pressure.

d. Hypersecretion: Excess aldosterone release results in hypertension, edema and water retention. Symptoms: muscle weakness and slow nervous responses.
e. Hyposcretion: Addison’s disease - Generally involves both a deficiency in mineralocorticoids and glucocorticoids. Symptoms: weakness, fatigue, weight loss, increased pigmentation of the skin and decreased blood pressure.

2. **Glucocorticoids**, main one is cortisol
a. Produced by the zona fasciculata.
b. Effects:
(1) Metabolic
   (a) Gluconeogenesis - synthesis of glucose by cell
   (b) Mobilizes fatty stores.
   (c) Decreases glucose and amino acid uptake in skeletal muscle.
   (d) Results is increased blood glucose levels and a ready store of glucose for the body to use.
(2) Anti-inflammatory
   (a) inhibit the normal inflammatory responses
   (b) depresses the immune system.
(3) Developmental
   (a) maturation of fetal lungs
   (b) production of epinephrine and norepinephrine receptors.
c. Regulation: ACTH causes the release of glucocorticoids.
(1) ACTH release from the pituitary is secreted under influence of CRH from the hypothalamus in response to stress. Rising levels of CRH shut off the pituitary and hypothalamus.
d. Hypersecretion:
(1) Cushing’s disease may result from a pituitary tumor or from clinical overdose of glucocorticoids.
   (a) Result: persistent hyperglycemia (steroid diabetes); dramatic loss of muscle and bone; protein,
Control of Glucocorticoid Release

- (b) Symptoms: moon face, redistribution of body fat to the abdomen and posterior neck, a buffalo hump,
- (c) Infections are generally masked until they become overwhelmingly severe.

- e. Hyposcretion:
  1. Addison’s disease, hyposcretion of both glucocorticoids and mineralocorticoids,
  2. Symptoms: weight loss, severe dehydration and hypotension are common.

3. Gonadocorticoids
   a. most common gonadocorticoids are the androgens or male sex hormones.
   b. These include androstenedion which is ineffective as a male hormone but is converted to testosterone or dihydrotestosterone in the tissues.
   c. Effect:
      1. Male: insignificant compared to the amounts of hormones produced by the testes, but may be an important part of causing puberty to occur.
      2. Female: stimulate pubic and axillary hair growth and sexual drive;
      3. In post-menopausal women, androgens may are to estrogen in the peripheral tissues to replace the loss of estrogen from inactive ovaries.
   d. Hypersecretion:
      1. masculinization.
         a. In adult males, no differences, in pre-pubescent males, causes precocious puberty.
         b. In females it will cause masculine body patterns, beards and male body hair distribution. The clitoris will also elongate to resemble a penis

C. Hormones of the Adrenal medulla
1. Epinephrine and Norepinephrine (Adrenaline)
   a. Produced by chromaffin cells in the adrenal medulla
   b. Released in response to stimulation of sympathetic nerves due to emotional excitement, stress, exercise or low blood glucose.
   c. Effects
      1. Epinephrine prolongs the fight or flight response
         a. Increased cardiac output, increase blood flow to skeletal muscles and heart, increased release of glucose and fatty acids into blood (prep for physical activity).
   d. Hypersecretion: Due to pheo-chromocytoma

V. Pancreas
A. Location and Anatomy
1. Located just below and behind the stomach. The body of the pancreas extends toward the left side of the body toward the spleen.
2. Histology: It is comprised of different types of cells and has both endocrine and exocrine functions.
   a. Islets of Langerhans or pancreatic islets:
      (1) Alpha cells produce glucagon
      (2) Beta cells produce insulin.

B. Hormones of the Pancreas

1. Glucagon
   a. Produced by alpha cells with the islets of Langerhans.
   b. Effect: to raise the blood glucose levels
      (1) Potent stimulator of the liver to release stores of glucose from glycogen.
         (a) One molecule of glucagon can cause the release of 100 million molecules of glucose from glycogen (glycogenolysis).
         (b) Glucose is released from the liver into the blood
      (2) Stimulates gluconeogenesis
         (a) building of glucose from secondary stores such as lactic acid, fat and certain amino acids.
   c. Regulation:
      (1) Declining blood levels of sugar stimulates the production of glucagon.
      (2) High protein meals will also stimulate glucagon production.
      (3) High blood sugar suppresses glucagon release.

2. Insulin
   a. Produced by the beta cells in the pancreas.
   b. Effect: lowers blood sugar levels.
      (1) Enhances the entry of blood-born sugars into cells and tissues that need them, such as muscles.
      (2) Inhibits the breakdown of glycogen to glucose
      (3) Catalyzes the joining of glucose together to form glycogen.
      (4) Converts glucose to fat.
   c. Regulation:
      (1) Increased blood sugar stimulates insulin release.
   d. Hyposcretion of Insulin
      (1) diabetes melitus (type I) insulin dependent
      (2) Symptoms: Rapid weight loss, high urine output, thirst, weakness, lethargy, acetone (sweet) breath.