Endocrinal Function

There are two principle types of glands in the body: exocrine and endocrine. **Exocrine glands** produce substances that are secreted through ducts, into a body cavity, into the lumen of an organ or on a free surface, such as the skin. You should already be familiar with various exocrine glands, including the sudoriferous glands that produce sweat, mucous glands that produce mucus, and digestive glands that release digestive juices. **Endocrine** glands, on the other hand, are ductless, secreting the substances they produce directly into the blood stream. The endocrine glands include the pineal, pituitary, thyroid, parathyroid, thymus, pancreas, adrenals and gonads. It is interesting to note that the ancient Indian system of the *chakras,* a theory that states that there are energy vortices located in the body in a hierarchical fashion, in large part corresponds to the position of the various endocrine glands. It would be an error however to conclude that the *chakras* are in fact the endocrine glands, and vice versa, as some writers have suggested. Instead, the *chakras* should be seen as a grouping of energy vortices that can only be perceived in the realm subtle being, that act to direct the organization of increasingly grosser forms of existence. The capacity to measure or quantify the nature of reality in the subtle realm is substantially different from the rational observations of anatomy and physiology, and can only be understood through the power of spiritual Insight.

In the maintenance of homeostasis, the endocrine system shares the task, along with the nervous system, to coordinate the various functions of the body. Whereas the nervous system functions through the generation of action potentials and the release of chemical neurotransmitters, the endocrine system releases hormones. Unlike neurotransmitters, hormones are released into the blood to influence various tissues, even if the sites that they influence are a great distance away from the site of release. Together, the nervous and endocrine systems form the neuroendocrine system. Nervous impulses may influence the secretion of a hormone produced by a particular gland, and a hormone may promote or inhibit the generation of an action potential. In fact, some hormones appear to be neurotransmitters, and vice versa. Thus the division between them, and the other functions of the body is artificial.

Overview of Hormones

Hormones function to maintain homeostasis in several ways, including the ability to:

1. Regulate the chemical composition and volume of the internal environment
2. Help regulate metabolism and energy balance
3. Help regulate contraction of smooth and cardiac muscle fibers and secretion by glands
4. Help maintain homeostasis despite environmental stress
5. Regulate certain activities of immune system
6. Play a role in the sequential integration of growth and development
7. Contribute to the basic processes of reproduction

Hormone receptors

Hormones have intense effects upon the tissue or organ system it influences, even when in relatively small concentrations. Even still, a hormone maintains a high degree of specificity in activity, affecting specific cells called target cells. Recall from the prerequisite course Introductory Biology and Biochemistry, the presence of integral proteins called glycoproteins that reside in the plasma membrane of a cell. A hormone circulates through the blood to a target cell and chemically binds with such a protein, called a **receptor**. Receptors are constantly being broken down and replaced, and if a hormone or neurotransmitter is present in excess, the number of receptors may diminish, called **down-regulation**. This ability of decreasing the number of receptors allows for an even greater control over the degree to which the hormone will affect a cell. Similarly, when a hormone or neurotransmitter is deficient, more receptors may be synthesized to increase its overall activity. Some hormones however have the capacity to stimulate an increasing number of receptors even when present in excessive amounts, called **upregulation**. Excess levels of the female hormone estrogen for example, can promote cell growth and can increase the number of receptors on the plasma membrane of estrogen responsive cells. Thus, excessive estrogen has been linked to certain kinds of cancer, called estrogen-dependent cancer.

Local and Circulating hormones

Hormones that act on target cells close to their site of release are called **local hormones**. An example is the **paracrine** hormone histamine, which is released by local

tissues to enhance a localized inflammatory response in neighboring cells. **Autocrines** on the other hand, such as interlukin-2, act upon the same cell that secreted it. A feature of local hormones is that their effects are typically short-lived, and are quickly deactivated. Hormones that pass into the blood and act upon distant cells are called **circulating hormones**. Such hormones remain in the blood for longer period of time, a few minutes and even up to an hour after they have been released. Circulating hormones are deactivated by the liver and kidneys, and in diseases of these organs, excessive levels of hormones may build up, creating further problems. Herbalists regard liver function as especially important in regulating hormonal function, and even minor dysfunctions in liver metabolism can be a cause of endocrine abnormalities, in particular that of the female reproductive system.

Fat soluble hormones

Among the most prominent fat-soluble, non-polar hormones are the **steroids**, synthesized from dietary cholesterol. All steroid hormones are derived from a basic four ring chemical structure, and slight variations in the attached side groups are responsible for a surprising diversity of function. Steroids are manufactured in the smooth endoplasmic reticulum of the cell. Examples of steroidal hormones include cortisol (adrenal cortex), calcitrol (kidneys), testosterone (testes) and estrogen (ovaries). Many plants also have steroid-like constituents that are known to affect human physiology, such as those found in *Glycyrrhiza glabra* (Licorice root) and *Dioscorea villosa* (Wild Yam root).

Thyroid hormones (T3 and T4) are not steroids but are manufactured from an amino acid tyrosine molecule and two attached iodides that make it fat-soluble. **Nitric oxide** is also considered to be a fat soluble hormone, as well as a neurotransmitter, and is found widely throughout the body as regulatory agent.

Water soluble hormones

Water soluble hormones include biogenic amines, peptides and proteins and eicosanoids.

Biogenic amines are the simplest of the hormones, synthesized from dietary sources of amino acids. Examples are the two catecholamines (epinepherine and nor-epinepherine) secreted by the adrenal medulla (inner layer of the adrenal) derived from the amino acid tyrosine. The thyroid hormones (T3 and T4) are also amines derived from tyrosine, but the attached iodides make this amine fat soluble. Histamine is derived from the amino acid histidine and is secreted by mast cells and platelets. The indolamines (serotonin and melatonin) are derived from the amino acid tryptophan.

Peptide and **proteins** are chains of amino acids, anywhere from 3 to about 200 hundred, and are synthesized in the rough endoplasmic reticulum. Peptide and protein hormones include all of the releasing and inhibiting hormones of the hypothalamus, oxytocin (hypothalamus), all the anterior pituitary hormones, parathormone (parathyroid), calcitonin (thyroid), digestive hormones secreted by the stomach and small intestine, and insulin and glucagon (pancreas).

Eicosanoids are a class of locally acting hormone-like compounds derived from dietary fatty acids such linoleic (omega-6) and linolenic (omega-3) acid. They include four major groups including prostaglandins (PG), prostacyclins (PGI), leukotrienes (LT) and thromboxanes (TX). Unlike neurotransmitters they are not stored in tissues but are synthesized on demand, acting for short periods of time in very low concentrations.

Mechanisms of Hormone Activity

The same hormone may have a different effect when it binds to its receptor on different target cells. The hormone insulin for example, stimulates the synthesis of glycogen in hepatocytes, but in adipose tissue, insulin initiates the synthesis of triglycerides with the target cell. Thus, hormones influence the activities of cell, such as changing plasma membrane permeability, stimulating the uptake or secretion of certain chemicals, altering metabolic activity or initiating contraction in muscle cells. The reason for this variability of activity is due, in part, to the mechanisms of hormone action.

Activation of Intracellular Receptors

Being non-polar and lipid soluble, steroids, thyroid hormones and nitric oxide pass easily through the plasma membrane. Upon entering the target cell, the non-polar hormone binds to and activates an intracellular receptor, located within nucleus of the cell. This activated receptor alters gene expression, and as new DNA is transcribed, mRNA forms and leaves the nucleus to direct the synthesis of new proteins, such as enzymes.

Activation of Plasma Membrane Receptors

Unlike fat-soluble hormones, water-soluble hormones such as the catecholamines and

peptide and protein hormones cannot diffuse through the plasma membrane. In order to affect the function of the cell, such hormones must bind with receptors on the external surface of plasma membrane, and are called **first messengers**. The **second messenger** then relays message inside cell.

The most common secondary messenger is a chemical called **cyclic AMP (cAMP)** that is synthesized from ATP by **adenylate cyclase**. The activities of cAMP are regulated by the activities of an enzyme called **phosphodiesterase**. Hormones that up-regulate the function of a cell's activity always involve the increased synthesis of cAMP. The few hormones that down-regulate the activities of a cell slow the synthesis of cAMP when it binds to its receptor.

Hormone receptors do not directly attach to adenylate cyclase to activate the synthesis of cAMP, but rather, are attached to molecules called **G-proteins** that are directly attached to the receptor. When a hormone binds to a receptor the G-protein is activated, which in turn activates adenylate cyclase to synthesize cAMP. Unless further stimulated the activity of a G-protein gradually slows down. In certain disease such as cholera, the toxin produced by the bacteria modifies the activities of G-proteins, so they remain in an activated state. As a result, the level of cAMP increases greatly in the cells that line the intestines, which stimulates the activity of the Na+ active transport pump to release Na+ into the lumen. As a result of this change in the osmotic gradient, water is pulled from the tissues into the lumen of the bowel, resulting in the watery stools of diarrhea.

When the first messenger binds to its receptor on the outer surface of membrane, it activates adenylate cyclase through the G-protein. Adenylate cyclase then converts ATP into cAMP, which then acts as a second messenger to alter the function of the cell. Special enzymes called protein kinases are activated by cAMP, which may be free or bound to the plasma membrane. **Protein kinases** are called *phosphorylating* enzymes, because they remove a phosphate group from ATP and add it to a protein, usually another enzyme. **Phosphorylation** affects the function of other enzymes that act upon substrate molecules, and can activate or deactivate them, working much like an on/off switch. The process of phosphorylation regulates the activities of the cell, such as the initiation of protein or glycogen synthesis, or changing the permeability of the plasma membrane.

An amplification of the effect of the hormone occurs as the first messenger activates 100 or so G-proteins, each of which then activates an adenylate cyclase molecule. If each adenylate cyclase then activates about a thousand cAMP molecules, this would result in the activation of over 100,000 secondary messengers in cell through the act of phosphorylation. It is the millions of phosphorylated enzymes that catalyze these chemical reactions that produce the physiological changes induced by the hormone.

The Hypothalamic-Pituitary Axis

The hypothalamus is a small region of the brain located below the two lobes of the thalamus and is the main integrative link between the nervous and endocrine systems. It receives input from various parts of the brain including the cerebral cortex, limbic system, reticular activating system and thalamus. Sensory input into the hypothalamus comes from afferent pathways in the somatic and visceral sense organs, and it is the task of the hypothalamus to coordinate responses to these stimuli. The major functions of the hypothalamus include:

1. the control and integration of the activities of the ANS (e.g. smooth and cardiac muscle contraction, glandular secretion, heart rate, movement of food through the GIT, contraction of the urinary bladder)
2. rage and aggression responses
3. the regulation of body temperature
4. the regulation of food intake through the inhibitory activity of the satiety centre
5. the regulation of thirst, stimulated by the rising osmotic pressure in the extracellular fluid
6. assisting in the coordination of arousal and sleep patterns.

On the ventral portion in the middle of the hypothalamus is the **tuber cinereum**, a mass of gray matter that connects to the **infundibulum**, a stalk-like structure that connects the hypothalamus to the pituitary gland. The tuber cinereum contains neurons that synthesize the **hypothalamic regulating hormones** that regulate the hormonal secretions of the anterior pituitary gland. In addition, nerves fibers extend from the hypothalamus to form the supraopticohypophyseal tract, extending into the infundibulum to the posterior

pituitary, transporting antidiuretic hormone (ADH) and oxytocin.

The Pituitary Gland

The pituitary gland is a pea-sized structure that is attached to the hypothalamus via the infundibulum. The pituitary has two distinctive anatomical regions that have separate functions. The **anterior pituitary gland** (or **anterior lobe**) is the largest part of the pituitary, making up over 75% of its weight, and contains many glandular epithelial cells. The release of hormones manufactured in the anterior lobe is stimulated by the releasing hormones and suppressed by inhibiting hormones secreted from the hypothalamus. The **posterior pituitary gland** (or **posterior lobe**) contains the axons and axon terminals of the **supraopticohypophyseal** tract, and thus secretes ADH and oxytocin.

The hypothalamic hormones travel to the anterior pituitary through a network of blood vessels that connects the two regions. There are five principal types of cells that are affected by the release and inhibiting hormones of the hypothalamus, that in turn secrete seven major hormones.

1. Somatotrophs produce human growth hormone (hGH) that stimulates body growth and helps to regulate metabolism
2. Lactotrophs synthesize prolactin which initiates milk production and the mammary glands of the breast.
3. Corticotrophs synthesize adrenocorticotropic hormone (ACTH), which stimulates the adrenal cortex to secrete glucocorticoids. Some corticotrophs also secrete melanocyte stimulating hormone (MSH) to affect skin pigmentation.
4. Thyrotrophs synthesize thyroid stimulating hormone (TSH) that induces hormone production in the thyroid gland.
5. Gonadotrophs synthesize follicle stimulating hormone (FSH) and luteinizing hormone (LH) which manage reproductive activities in the body.

The secretion of anterior pituitary hormones is regulated by the hypothalamic releasing and release inhibiting hormones and by negative feedback from target gland hormones.

Anterior Pituitary Hormones

Human Growth Hormone

Human growth hormone (hGH) has three basic activities in the body: (1) the stimulation of protein synthesis and inhibition of protein catabolism; (2) the stimulation of lipolysis, breaking down triglycerides into fatty acids and glycerol; and (3) inhibiting the use of glucose for ATP production. The activities of hGH are manifest through the synthesis and secretion of protein hormones called **insulin growth factor (IGF)**, released by tissues in the liver, skeletal muscle, cartilage, and bone in response to hGH. IGFs are then released locally or into the blood stream, causing cells to grow and multiply, increasing the uptake of amino acids and ATP and protein synthesis. Thus hGH is secreted in the greatest volumes during childhood and puberty to stimulate growth and development, and in maturity to stimulate repair and regeneration. IGFs also enhance lipolysis in adipose tissue, increasing the availability of fatty acids for ATP synthesis, and tend to decrease glucose uptake and the use of glucose for ATP synthesis.

The secretion of hGH from the pituitary gland is controlled by two hypothalamic hormones: **growth hormone releasing hormone (GHRH,** or **somatotropin),** and **growth hormone inhibiting hormone (GHIH,** or **somatostatin**). Factors which promote the release of hGH include low blood glucose, low levels of fatty acids and amino acids in the blood, deep sleep, sympathetic nervous activity, vigorous physical exercise and the activities of other hormones (e.g. cortisol, glucagon, estrogens and insulin). Factors which inhibit the release of hGH are high blood glucose levels, increased fatty acids and decreased amino acids in the blood, REM sleep, emotional deprivation, obesity, low thyroid activity and hGH (through negative feedback).

Thyroid Stimulating Hormone

Thyroid stimulating hormone (TSH) stimulates the synthesis and secretion of two hormones, triiodothyronine (T3) and thyroxine (T4), in the thyroid. The release of TSH is regulated by the **hypothalamic thyrotropin releasing hormone (TRH).** The release of TRH depends upon the levels of TSH, T3, blood glucose levels, metabolic rate according to a negative feedback system. TSH levels are often assessed to determine thyroid function, but because TSH levels to tend fluctuate according to diurnal variations, this test is not all that accurate to determine thryroid activity.

Follicle Stimulating Hormone

Follicle stimulating hormone (FSH) is released into the blood by the pituitary and

travels to the ovaries in women and testes in men. In women, FSH initiates the development of the ovarian follicles that release the ovum and stimulates the secretion of estrogen. In males, FSH stimulates sperm production in the testes. The release of FSH is stimulated by the secretion of the **hypothalamic gonadotropin releasing hormone (GnRH).** The release of GnRH and FSH is suppressed by estrogen in women and testosterone in men through negative feedback systems.

Luteinizing Hormone

Luteinizing hormone (LH) in association with FSH stimulates estrogen secretion in the ovaries and initiates ovulation (the release of the ovum into the fallopian tubes). Additionally, LH stimulates the formation of the corpus luteum in women after ovulation, and the secretion of progesterone by the corpus luteum. In men, LH stimulates the interstitial cells in the testes to secrete testosterone. The secretion of LH is initiated by GnRH, as it is for FSH, and is inhibited by a similar feedback mechanism.

Prolactin

Prolactin initiates and maintains milk secretion by the mammary glands. The actual ejection of milk however is initiated by oxytocin. Together, the activities of prolactin and oxytocin that result in milk secretion and ejection are referred to as **lactation**. The monoamine dopamine (also called **prolactin inhibiting hormone**, or **PIH**) inhibits the release of prolactin from the pituitary gland. A slight decrease in dopamine levels in the luteal phase of the menstrual cycle, resulting in increased prolactin, can cause premenstrual breast tenderness. In men the activity of prolactin is not well understood, but has been associated with erectile dysfunction.

Melanocyte Stimulating Hormone

Although its exact role in humans is unclear, **melanocyte stimulating hormone (MSH)** increases skin pigmentation by dispersing melanin granules in melanocytes in amphibians. Some research in humans suggests that it may play a role in brain function. Excessive corticotropin-releasing hormone can produce a darkening of the skin, whereas dopamine has been shown to inhibit MSH release.

Adrenocorticotropic Hormone

Corticotrophs synthesize a large protein called **pro-opiomelanocortin (POMC)**, which when cleaved into fragments, gives rise to **adrenocorticotropin hormone (ACTH**), MSH and other neuropeptides. ACTH is by far the most abundant product of this process in the anterior pituitary gland. The hypothalamic hormone corticotropin releasing hormone (CRH) stimulates the secretion of ACTH by the corticotrophs. Sympathetic nervous activity such as low blood glucose or physical injury and a substance called interleukin-2 released by macrophages also stimulate ACTH release. Glucocorticoids cause the negative feedback inhibition of CRH and ACTH release.

Posterior Pituitary Hormones

Unlike the anterior pituitary, the posterior lobe of the pituitary does not synthesize any hormones, but stores and releases hypothalamic hormones released by neurons in the supraopticohypophyseal tract.

Antidiuretic Hormone

The principal activity of antidiuretic hormone (ADH, or vasopressin) is to decrease urine output by causing the kidneys to make a more concentrated urine. Without ADH, urine output would be almost 10 times that of normal. When the body is dehydrated specialized receptors in the hypothalamus called osmoreceptors detect the high osmotic pressure (low water concentration) in the blood. This results in the secretion of ADH which in turn causes the kidneys to produce a more concentrated urine to conserve water, and inhibit perspiration. Additionally, ADH causes the vasoconstriction of the arterioles.

Oxytocin

Recall the example of a positive feedback loop, as described in Lesson I. During labour, oxytocin is secreted to initiate the expulsion of the fetus, and after delivery, acts upon the breast tissue to stimulate the ejection of milk. The subsequent suckling of the infant stimulates the secretion of oxytocin, and the inhibition of dopamine (PIH). Besides suckling, other stimuli such as the infants crying or genital stimulation encourages the secretion of oxytocin. A midwifery technique of old is to massage the nipples and clitoris of the pregnant woman when labor is stalled, resulting in the increased contractile force of uterus.

The Thyroid

The **thyroid** is located just below the larynx in the neck. It has two lateral lobes that sit on either side of the trachea and are connected by a mass of tissue called the **isthmus**. Contained in the thyroid are microscopic spherical sacs called **thyroid follicles** that

manufacture the thyroid hormones: **thyroxine (T4)** made with four atoms of iodine; and **triiodothyronine (T3)** made with three atoms of iodine. A few other follicles in the thyroid produce **calcitonin**.

Iodine is an important rate-limiting factor in the synthesis of the thyroid hormones. Iodine is ingested in food and water, and is actively taken up by the follicular cells of the thyroid gland, which under the influence of **thyroid stimulating hormone (TSH),** uses it and the amino acid **tyrosine** to form T3 and T4. These hormones are then released by the thyroid where they are bound to thyroid hormone-binding serum proteins for transport. **Thyroxine-binding globulin (TBG**) accounts for 75% of thyroid hormone-binding proteins, and has high affinity but low capacity for T4 and T3. Other thyroid hormonebinding proteins include **transthyretin (prealbumin),** which has high affinity but low capacity for T4, and **albumin**, which has low affinity but high capacity for T4 and T3. Approximately 0.03% of the total serum T4 and 0.3% of the total serum T3 are free from carrier proteins.

Increased levels of free thyroid hormones T3 inhibit TSH secretion from the pituitary, whereas decreased levels of T4 and T3 result in an increased TSH release from the pituitary. TSH secretion however is also influenced by **thyrotropin-releasing hormone (TRH),** an amino acid peptide synthesized in the hypothalamus, which binds to a specific TRH receptor on the thyrotropic cells of the anterior pituitary and causes the subsequent release of TSH.

The thyroid hormones act to **increase protein synthesis** and **O2 consumption** in virtually every body tissue, increasing or enhancing the **basal metabolic rate**. Although T4 is much more abundant among the thyroid hormones, only T3 is thought to be metabolically active. Once taken up by a cell however, T4 can be deiodinated into T3. About 20% of the circulating T3 is produced by the thyroid and the remaining 80% is produced by the monodeiodination (removal of one iodine atom) in the *outer* ring of T4. The monodeiodination of the *inner* ring of T4 results in **reverse T3** or **rT3**, mostly occurring in peripheral tissues. Unlike normal T3, rT3 has minimal metabolic activity and increases in certain diseases, e.g. chronic liver and renal disease, acute and chronic illness, starvation, and carbohydrate-deficient diets. Reverse T3 may also act to inhibit T4 conversion into the metabolically active T3, and is used as marker to rule out hypothyroidism (in which T3 levels are decreased). Some researchers speculate that rT3 may block T3 receptor sites, competitively inhibiting the activity of T3.

To review, the thyroid hormones have three basic functions:

1. To increase the basal metabolic rate and temperature of the body by stimulating the use of cellular oxygen to produce ATP.
2. To regulate metabolism by stimulating protein synthesis, lipolysis, cholesterol secretion in the bile and the use of glucose for ATP manufacture.
3. To accelerate body growth and in particular that of nervous tissue, in association with hGH and insulin.

The thyroid hormones also enhance the activity of the catecholamines epinepherine and nor-epinepherine due to the upregulation □-receptors. This is why excess levels of thyroid hormones in hyperthyroidism cause increased myocardial contraction, an increase blood pressure and nervous irritability.

The control of thyroid activity is dependent upon the level of iodine and by negative feedback system that involves the hypothalamus and the anterior pituitary. Low blood levels of T3 cause the hypothalamus to secrete TRH, which in turn causes the pituitary to secrete TSH. Increased ATP demand, such as cold temperature, hypoglycemia, high altitude, all trigger negative feedback mechanisms to increases the secretion of thyroid hormones.

Calcitonin, along with parathormone secreted by the parathyroid, regulates calcium metabolism in the body. Essentially, calcitonin lowers blood calcium and phosphates by accelerating uptake by the bones and inhibiting the activity of osteoclasts. The secretion of calcitonin is stimulated by high blood calcium levels (hypercalcemia)

Parathyroid gland

The **parathyroid gland** is attached to the posterior surface of the thyroid gland, and in most cases, are two small round masses on each lobe of the thyroid. The parathyroid secretes a hormone called **parathormone (PTH)** which functions to increase blood calcium and magnesium levels and phosphate by increasing the activity of the osteoclasts. PTH also activates vitamin D (calcitrol) in the kidneys, increasing the absorption of calcium and magnesium from the small intestine, and promoting the

excretion of phosphate by the kidneys.

The Adrenals

The paired adrenal glands are superior to the kidney, and contain two functional regions: an inner adrenal medulla and a surrounding outer adrenal cortex, the latter of which makes up the bulk of the gland.

^ back to top

Adrenal cortex

The adrenal cortex secretes three distinct classes of hormones: mineralcorticoids, glucocorticoids and gonadocorticoids. The **mineralcorticoids** help to maintain water and electrolyte balance (primarily Na+ and K+). About 95% of the mineralcorticoids secreted by the adrenal cortex is aldosterone. **Aldosterone** acts upon the kidney tubules to increase the reabsorption of Na+, and thus prevents sodium depletion. The reabsorption of Na+ also leads to the reabsorption of Cl- and HCO3- and the retention of water. At the same time, aldosterone also promotes K+ excretion and the excretion of H+ which prevents acidosis. The control of aldosterone secretion involves at least two mechanisms. The **renin-angiotensin pathway** promotes the secretion of aldosterone in response to a decrease in blood volume from dehydration, and, promotes vasoconstriction. Another mechanisms of aldosterone secretion is the increased volume of K+ in the extracellular fluid, which causes the kidneys to eliminate excess K+..

There are three glucocorticoids: **cortisol, corticosterone** and **cortisone**. Of the three, cortisol is the most abundant, responsible for 95% of the activity of the glucocorticoids. The glucocorticoids have three basic effects:

1. To promote normal metabolism and ensure that sufficient ATP is available, by promoting gluconeogenesis. Glucocorticoids also promote lipolysis and the release of fatty acids from adipose tissue.
2. To provide resistance to stress, by increasing glucose availability in the manufacture of ATP. Glucocorticoids also make the blood vessels more sensitive to vasoconstrictive chemicals, raising blood pressure, especially when there is a decrease in blood volume due to blood loss.
3. To inhibit inflammation, by reducing the number and size of the mast cells that secrete histamine; by reducing the release of lysosomal enzymes; by decreasing blood capillary permeability and by depressing phagocytosis. In this way, glucocorticoids also retard wound healing and depress the immune response.

The control of glucocorticoid secretion is a negative feedback mechanism in which low levels of glucocorticoids result in the release of the hypothalamic hormone CRH and as a result, the secretion of ACTH. In response to stress, the hypothalamus will also increase the secretion of CRH.

The adrenal cortex also secretes both male and female **gonadocorticoids**, called androgens and estrogens, respectively. In men, the level of **androgens** such as testosterone secreted by the adrenal cortex is minimal in comparison to that which is secreted by the testes. In women however, adrenal androgens contribute significantly to libido and sexual behaviour. Additionally, androgens can be converted into estrogens, which is an important source of estrogens when the estrogen producing ovaries atrophy after menopause.

Adrenal medulla

The adrenal medulla secretes norepinepherine (NE) and epinepherine (E) which belong to a class of compounds called the catecholamines. **Epinepherine**, and to a lesser extent, **norepinepherine**, are concentrated in the tissues of the adrenal medullae and are secreted in response sympathetic stimulation. The adrenal medullae are actually modified sympathetic ganglionic fibers, as opposed to an actual endocrine gland, and secrete E and NE directly into the blood stream. As previously mentioned, all of the catecholamines require tyrosine as the base nutrient for their creation.

The Pancreas

The pancreas is flattened organ located slightly posterior and slightly inferior to the stomach, and is comprised of a head, body and tail. Scattered throughout the pancreas are tiny clusters of endocrine tissue called islets of Langerhans. There are four types of hormone secreting cells in the pancreas:

1. Alpha cells: which secrete glucagon, which raises blood glucose levels.
2. Beta cells: which secrete insulin, which lowers blood glucose levels.
3. Delta cells: which secrete somatostatin that acts as a paracrine gland to

inhibit the secretion of both insulin and glucagon.
4. F cells: which secrete pancreatic polypeptide that regulates the exocrine pancreas.

Insulin

Insulin has six basic functions in the body:
1. Facilitates the transport of glucose from the blood into the cells, especially muscle fibers.
2. Promotes the conversion of glucose into glycogen (glycogenolysis)
3. Facilitates the entry of amino acids into cells and protein synthesis
4. Promotes the conversion of glucose and other nutrients into fatty acids (lipogenesis)
5. Slows glycogenolysis (break down of glycogen)
6. Slows gluconeogenesis (the conversion of substances other than carbohydrates into glucose).

The level of blood glucose regulates the secretion of insulin as does glucagon, in a negative feedback cycle. Certain hormones also promote insulin secretion, such as hGH and ACTH, as do the activities of the parasympathetic nervous system after the consumption of a meal. Somatostatin, on the other hand, inhibits insulin secretion, as does a meal rich in proteins and fats.

Glucagon

Glucagon has two basic functions in the body, acting primarily on the liver:
1. Accelerating glycogenolysis.
2. Promoting the formation of glucose from lactic acid and amino acids (gluconeogenesis).

The primary effect of glucagon therefore, is to increase the blood levels of glucose. The control of glucagon is the level of blood glucose through a negative feedback mechanism. High protein meals stimulate glucagon secretion, whereas somatostatin inhibits it. With the increased activity of the sympathetic nervous system the level of glucagon increases.

Todd Caldecott, medical herbalist