TRANSFORMATION

Dr. M's SCIENCE NOTES

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HORMONES, part 1
Basics of their Biochemistry

Basically, hormones are defined as biomolecule messengers regulating the body's metabolic functions. Hormones are molecules synthesized in very minute concentrations by a tissue or organ and are ultimately secreted into blood circulation to "travel" to a target group of cells (tissues) or organ to initiate a biological function. The synthesis and secretion of hormones is normally under the influence of a signaling mechanism. The tissues or organs responsible for synthesizing hormones are referred to as endocrine glands. The ensemble of the endocrine glands, their hormones, their biochemistry, and their clinical implications constitute the field of endocrinology.

Hormones must often be transported to their site of action before they take effect. Upon synthesis and secretion into the blood circulation, most hormones (except the water soluble hormones) are usually carried by transport molecules to their target organs. The transport mechanism constitutes an important regulation step in hormone function. Although hormones are often secreted into the blood to act at target organs located in other parts of the body, there are situations where a hormone will act directly on tissues adjacent to its site of synthesis or will act on cells directly involved in its synthesis. When a hormone acts on adjacent cells, the effect is called paracrine. When the hormone acts directly on the cells that synthesize it, the effect is said to be autocrine.

The normal signaling process involves a series of triggering mechanisms. The release of hormones follows a basic pathway that starts with neural stimulus acting on the hypothalamus. Following that neural stimulus, releasing or inhibitory factors are synthesized and sent to the pituitary gland. The pituitary gland in turn synthesizes and secretes into the circulation a hormone (depending on the nature of the stimulus) that will stimulate the synthesis of another hormone from a specific gland as dictated by the initial neural input. Based on that sequence of events, the hypothalamus constitutes the master gland that triggers the "conductor" (pituitary gland) to start the "symphony" and determine the "instrument(s)" that need to be "playing." Upon accomplishment of its function, every hormone should have a feedback mechanism that turns its synthesis and secretion off to maintain order and balance within the body.

This series of events is very important, as it is initiated based on the body's biological needs.

Any tempering or malfunction in the signaling process as described above can lead to either overproduction and/or underproduction of hormones resulting in imbalances in the overall biological functions and further creating a terrain for metabolic disorder(s). For instance, excess or imbalanced levels of gonadal hormone may trigger the onset of certain forms of cancer. Irregulated or excess secretion of insulin or insulin-like molecules may lead to insulin resistance or hypoglycemia. Also, excess cortisol production that does not respond to its shut down feedback mechanism can lead to undesired results such as immune suppression, tissue breakdown, insulin resistance, and other health challenges.

The basics of hormone biochemistry are related to the manner in which hormones interact with and influence the body. Biochemically, hormones are either made up of peptides or derived from cholesterol. For instance, insulin, glucagon, vasopressin, luteinizing hormone, and growth hormone are peptides. Histamine, serotonin, and catecholamines are derivatives of amino acids. The gonadal and glucocorticoid hormones, for instance, are steroids derived from cholesterol. The chemical nature of the hormone influences its action, including its transport and interaction with cellular receptors.

The biosynthetic process of hormones takes several steps to ensure that the secretion of hormones is well within the body's timely requirements and needs. For instance, most peptide hormones are synthesized as larger peptides or proteins that are subsequently cleaved at certain specific bonds to generate the final hormone peptide with full biological function. Cholesterol-derived hormones are synthesized from small precursors and undergo various biochemical modifications before resulting in the final hormone. These steps in the biosynthesis pathways are to ensure their further regulation and control within the body.

Recent studies have confirmed the tight connections among the various systems, namely the endocrine, nervous, and immune systems. Additionally, it can even be said that the endocrine system is itself distributed throughout the body and found in most other systems. For instance, the gastrointestinal (GI) tract synthesizes and secretes several hormones that affect the digestive system as well as other systems in the body. For instance, cholecystokinin, one of the main hormones synthesized in the duodenal cells to stimulate the exocrine function of the pancreas appears to also be synthesized in the nervous tissue. There are several kinds of hormones present in the system providing a variety of functions. However, most people are only familiar with the sexual and reproductive functions of hormones, such as development of the gametes, characterization of sexual dimorphism, and regulation of both sexual desire and reproductive function.

However, hormones also affect every other function in the body. Their biological functions involve a variety of systems important to the regulation of overall homeostasis.

- Regulation of body fluid volume and composition
- Regulation of fluid retention and excretion
- Control of the gastrointestinal function including food intake
- Control of acid-base balance
- Regulation of blood pressure and heart rate
- Regulation of body temperature
- Regulation of muscle, bone and fat mass
- Regulation of energy production, utilization and storage
- Regulation and modulation of growth and development
- Adaptation to environmental changes
- Adaptation to emotional changes

In some cases, one hormone can perform several different functions. In other conditions, one biological function may require the action of several different hormones. For instance, to insure that blood glucose does not drop to levels that could be fatal, the body allocates several hormones to help supply glucose and gluconeogenic substrates to the body. Examples of such glucose supply hormones include glucagon, cortisol, epinephrine, norepinephrine, growth hormone, and thyroid hormone. Under normal conditions, the hormonal secretion and effect will vary according to the biological needs of the body.

The action of hormones is often mediated by a variety of receptors. These may be on the cell surface (peptide hormones), within the cytoplasm (steroid hormones), and/or in the nucleus (thyroid hormones). Thus, peptide hormones will interact with their receptors on the cell surface. Steroid hormones, on the other hand, enter the cell freely and then bind to their cytoplasmic receptors before entering the nucleus, where the complex receptor-hormone binds to specific DNA sequence that will result in increased transcription. Thyroid hormones, in contrast, do not bind to either cell surface or cytoplasmic receptors, but rather enter the cell, enter the nucleus, and then bind to specific areas of the chromatin to initiate their biological effect.

The action of some hormones also varies according to the developmental stage of the body. As a result of growth, tissue differentiation, and maturation, cells will respond to hormones differently. Of course, the presence of receptors will determine to a great extent the rate and nature of hormonal effect on the cells. Additionally, hormonal response may vary from person to person as a function of health, physiological state, nutritional status, and many other conditions.

The body has physiological control of hormone production. Some hormones are produced daily as a function of a circadian rhythm, whereas others are produced monthly, as in the menstrual cycle of an adult woman. For example, consider the high levels of specific hormones found in females during pregnancy but not at other times of their life cycle. Otherwise, conditions such as fear, anxiety, and chronic stress can create a stimulus for the secretion of several hormones, including epinephrine, norepinephrine, and cortisol. Although their secretion is necessary to prepare the body for potential reaction to a stimulus, the perpetual mental disposition to secrete them continuously could lead to severe health consequences. Thus, the use of various mental relaxation exercises to bring the body back into balance becomes necessary.

Ordinarily, as a result of the molecular structure of their receptors, hormones are very specific in their binding and biological function. However, there are instances of hormonal cross-binding. This happens because of similarities where hormones such as testosterone will cross-bind to an estrogen receptor. This binding of testosterone to an estrogen receptor will reduce the estrogen effect, as fewer of its receptors will be available, thereby ultimately creating an anti-estrogenic effect in the body. Also, testosterone has been shown to cross-bind to a cortisol receptor, thus helping to minimize the catabolic effects of cortisol. Toxins, proteins, or other molecules can bind to receptors, thereby blocking or altering normal hormone-receptor interaction.

These types of cross-reactions further explain the fact that some hormone-like substances in the environment such as pesticides and other xenobiotics could bind to a receptor in the body and elicit a specific hormonal response when that biological function is not needed. As a general rule, however, hormones have response elements within the DNA structure. An uncontrolled stimulation of those response elements may create unhealthy imbalances and untimely transcriptions of certain genes.

The secretion and biological function of hormones in the body needs to be carefully monitored and ensured for optimal wellness, since these specific biomolecule messengers control all body functions. Based on the various regulatory and biochemical characteristics of hormones mentioned previously, adequate hormone function requires the following:

- Good nutrition to ensure the presence of all building blocks for adequate biosynthesis of the hormone
- Adequate control of catabolic functions that otherwise could impair synthesis of needed hormones
- Good neural function to deliver the initial signaling input at the level of the hypothalamus
- Adequate synthesis of functional hormone molecules
- Good blood circulation to ensure timely delivery of needed hormones to their target organ(s)
- Good antioxidant environments to prevent oxidation of the hormones, their carriers, and/or their receptors
- Normal endocrine gland function to avoid underproduction or overproduction of hormones
- Proper signaling mechanisms for synthesis and shutdown, depending on the case

There is a wide range of variability in the distribution of hormones within different tissues and also as a result of physiological and biochemical reactions within the body. In older people, as a result of various forms of free radical damage in the body, there may be risks of improper hormonal response, as the receptors can no longer bind to their respective hormones. In addition to the presence or lack of a receptor, hormones are also regulated by their half life in the body, which basically refers to the relative length of time they remain active in the body.

Although hormones are important in modulating and controlling the body functions, their long-term persistence in the system when they are not needed could compromise wellness. That is why any efforts to control the perpetuation of free radicals in the system could ultimately optimize the timely secretion and response of various hormones and thereby ensure wellness, longevity, and resistance to disease.

Adequate hormone function requires the above factors of an optimal internal environment to help prevent disease. Even premature exposure of a fetus or newborn to hormones or xenobiotics with hormone-like activities may be an important health concern. Recent developmental studies have already shown that some hormones are expressed in the fetus and that several receptors are also present even though their respective hormones are not fully developed or expressed as a result of growth and tissue differentiation. This fact implies that even infants while still in the womb could be exposed to the untimely effect of some hormones from the environment and/or from the hormonal secretions of their mothers. This topic needs to be further investigated to determine its impact on growth and the risks of developing various diseases.