ENDOCRINOLOGY

Juhani Leppäluoto
Department of Physiology, University of Oulu, Finland

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Summary

Hormones are powerful chemicals secreted from glands to blood circulation and to target tissues. Thyroid hormones ensue proper metabolism of carbohydrates, fats and proteins and normal heart and brain functions. Cortisol is secreted in response to stress and increases glucose and amino acids to be used by cells. It also diminishes allergic and immune reactions. Estrogens and testosterone induce female and male sexual

characteristics, respectively. In women estrogen and progesterone maintain reproductive cycles and pregnancy. GH together with thyroid hormones and sex steroids are necessary for linear growth. PTH and D-vitamin regulate tightly blood calcium levels. Glucose is one of the major energy sources of the body. After a meal elevated glucose stimulates insulin secretion and insulin activates the glucose uptake of the cells. During dehydration blood sodium increases and stimulates the secretion of vasopressin. Vasopressin has antidiuretic effects in the kidney tubules and body water is saved to counter dehydration. Ingestion of food requires a synergic function between gastrointestinal hormones. In the stomach food stimulates gastrin and becomes partly digested in acidic milieu. Digested food in the intestine stimulates secretion of secretin and CCK leading to the secretion of enzymes degrading carbohydrates, proteins and fats for intestinal absorption.

Most cells secrete tissue hormones from a cell to a neighboring cell. They bind to cell membrane receptors as hormones. Prostaglandins render effects on blood vessels, blood cell aggregation and smooth muscle. Injuries liberate prostaglandins producing pain and inflammation. Salicylates inhibit formation of prostaglandins and prevent blood cell aggregation, pain and inflammation. A gaseous compound nitric oxide is formed from arginine and it relaxes blood vessels.

The endocrine system sends and receives messages to and from the body, including the brain, to ensure optimal conditions in all stages of development and environmental challenges.

1. Introduction

Sending messages from a cell to other cells in the human body is a demanding task. If we think that the size of a cell equals the size of an adult man, sending a message from the brain to the big toe corresponds to a distance around 300 kilometers. In the human body there are two systems specialized for sending messages—the neural and endocrine systems. The neural system is fast and often it hits a small target. The endocrine system is slow and usually has widespread effects.

Glands that secrete chemical compounds—hormones—are the basis of the endocrine system. Hormones travel to their target tissues by means of blood circulation.

Target tissues have specific receptors that recognize and bind the hormone. Binding of the hormone to its receptor leads to the activation of the target cells to produce perhaps other hormones, enzymes or other important factors for the whole body. In addition to the blood-borne hormones there are also local hormones that usually travel only a short distance from a cell to another close-by cell through the extracellular space.

Hormones are derivatives of amino acids, polypeptides (chains of amino acids), steroids or modified unsaturated fatty acids. Local hormones are mostly derivatives of fatty acids or polypeptides. The origins of hormones are presented in Table 1.

Localization	**Hormone**	**Structural components**

Hypothalamus	Corticotropin releasing hormone (CRH)	Polypeptide
	Growth hormone releasing hormone (GRH)	
	Gonadotropin-releasing hormone (GnRH)	
	TSH-releasing hormone (TRH)	
	Oxytocin	
	Somatostatin	
	Vasopressin (antidiuretic hormone (ADH))	
Pineal gland	Melatonin	Amino acid
Pituitary gland	ACTH (corticotrophin)	Polypeptide
	Beta-endorphin	Polypeptide
	Growth hormone (GH)	Polypeptide
	Follicle stimulating hormone (FSH)	Polypeptide, sugar
	Luteinizing hormone (LH)	Polypeptide, sugar
	Thyroid stimulating hormone (TSH)	Polypeptide, sugar
	Prolactin	Polypeptide
Thyroid gland	Thyroxine, triiodothyronine	Amino acid
Parathyroid gland	Parathyroid hormone	Polypeptide
Adrenal gland, cortex	Cortisol, aldosterone	Steroids
Adrenal gland, medulla	Noradrenaline, adrenaline	Amino acid
Pancreas	Insulin	Polypeptide
	Glucagon	
Gastrointestinal tissues	Gastrin	Polypeptide
	Secretin	
	Cholecystokinin	
Liver	Insulin-like growth factors	Polypeptide
Gonadal glands	Estrogen	Steroid
	Progesterone	
	Testosterone	
	Inhibins	Polypeptide
Heart	Natriuretic peptides	Polypeptide
Kidneys	Erythropoietin	Polypeptide
	Renin	
	D-Vitamin	Steroid
Blood cells	Interleukins, growth factors	Polypeptides
Local hormones	Prostaglandins	Unsaturated fatty acid derivative
	Nitrous oxide	Oxide
	Endothelin	Polypeptide

Table 1. Origin of various example hormones.

Hormones are powerful chemicals. Therefore the human body must have systems to ensure that the right amount of hormone is secreted. The hypothalamus, the pituitary gland and a peripheral gland, e.g. the thyroid, form a system that guarantees that an optimal amount of hormone is secreted. The hypothalamus secretes hormones that stimulate the pituitary gland. The pituitary gland secretes other hormones that stimulate the peripheral glands and the secretion of the final hormone is increased. After the proper amount of the final hormone in the blood circulation is achieved, the extra amounts of the final hormone secreted inhibit the hypothalamus and pituitary gland. When the amount of the final hormone in blood circulation decrease to a low level, the hypothalamus and pituitary gland sense it and become stimulated. This is a negative feedback system that guarantees a proper amount of the final hormone is available to meet the prevailing situation.

The concentrations of hormones in blood circulation are extremely low. The blood concentration of usual nutrients is high e.g. blood glucose is at millimolar levels. Many hormones circulate at picomolar levels, i.e. 1 000 000 000 times less than blood glucose levels. It is impossible to measure hormone levels by the same method as is used, for example, for blood glucose analysis.

Fortunately, the immunoglobulins are capable of recognizing and binding chemical compounds, even in very tiny amounts. They can be produced in humans and other animals by vaccination and nowadays also by *in vitro* methods. Usually animals are vaccinated by the selected human hormone and the serum of the vaccinated animal is collected after some months. The immunoglobulins produced are capable of binding the antigen hormone in extremely low concentrations, even diluted 1 000 000 times. These immunoglobulins are used in many types of immunoassays. In the radioimmunoassay (RIA) specific immunoglobulins, known amounts of a hormone labeled by a radioactive atom are incubated in a test tube. Nowadays several methods using non-radioactive labels are generally used. In the ELISA method (enzyme linked immunosorbent assay) an enzyme is attached to a hormone or to immunoglobulins and the assay can be performed in multi-well plates. Although immunoassays were first developed for the measurement of hormones, they are widely used in measurement of other substances such as drugs, antibodies, bacteria and viruses.

Hormone receptors bind the specific hormone and initiate cellular responses typical for that hormone. Usually water-soluble hormones such as polypeptides cannot penetrate the cell membrane. On the other hand, steroid and fatty acid derived hormones, as well as some amino acid derivatives, are lipid-soluble and readily penetrate the cell membrane. Therefore, the receptors of hormones reside either in the cell or on the cell membrane.

The receptors for steroids and thyroid hormones are in the cytosol or in the nucleus. Steroids and thyroid hormones bind to the intracellular receptors and the hormone-receptor complex thus formed binds to the specific gene and increase its transcription. In case of estrogens there apparently are receptors both in the cell membrane and within the cell nucleus.

The receptors for polypeptide hormones are localized on the cell membrane. These receptors are long amino acid chains with extracellular and intracellular endings. The hormone binds to the extracellular ending and activates the intracellular ending, which usually has a guanosine diphosphate (GDP) (see *G Protein-Coupled Receptors*). The hormone is called the first messenger. The activation leads to phosphorylation of GDP to GTP that initiates the second messenger chain. The second messenger chain may include cyclic AMP, inositol phosphates or calcium ions and result in the potentiation of the first messenger system.

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Biographical Sketch

Prof. Juhani Leppäluoto was born in Helsinki, Finland, in 1939. He has an MD 1966 from the University of Helsinki, and in 1972 he also defended his Dr. Med. Sci. dissertation at the Department of Physiology of this University. He has served as researcher at the Universities of Helsinki and Oulu. He worked for three years in Prof. Roger Guillemin's Laboratory at Salk Institute, USA. He became associate professor in 1974 and Professor of Physiology in the University of Oulu and Chairman of the Department in 1991. He has served also as Director of the International Arctic Research Center. He retired in 2004, but he continues his research. His research interests have been in the area of endocrinology, at first thyroid hormones and then mostly on the seasonal and diurnal variations of melatonin secretion. Cardiac hormones have been other research topics. He has contributed to the development of methods of hormone analysis. He is currently serving as the President of the Finnish Physiological Society. He has been active in the Board of the Nordic Physiological Society and in the Editorial Board of Acta Physiologica Scandinavica, and Editor in Chief of the International Journal of Circumpolar Health