Endocrinology

Abstract

Endocrinology (from Greek ἔνδον, *endon*, "within"; κρῖνω, *krīnō*, "to separate"; and -λογία, *-logia*) is a branch of medicine dealing with disorder of the endocrine system and its specific secretions called hormones, the integration of developmental events such as proliferation, growth, and differentiation (including histogenesis and organogenesis) and the coordination of metabolism, respiration, excretion, movement, reproduction, and sensory perception depend on chemical cues, substances synthesised and secreted by specialized cells.

Endocrinology is concerned with the study of the biosynthesis, storage, chemistry, and physiological function of hormones and with the cells of the endocrine glands and tissues that secrete them.

The endocrine system consists of several glands, in different parts of the body, that secrete hormones directly into the blood rather than into a duct system. Hormones have many different functions and modes of action; one hormone may have several effects on different target organs, and, conversely, one target organ may be affected by more than one hormone.

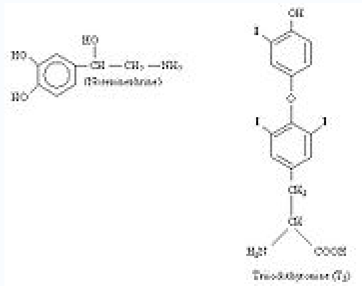
In the original 1902 definition by Bayliss and Starling (see below), they specified that, to be classified as a hormone, a chemical must be produced by an organ, be released (in small amounts) into the blood, and be transported by the blood to a distant organ to exert its specific function. This definition holds for most "classical" hormones, but there are also paracrine mechanisms (chemical communication between cells within a tissue or organ), autocrine signals (a chemical that acts on the same cell), and intracrine signals (a chemical that acts within the same cell).[1] A neuroendocrine signal is a "classical" hormone that is released into the blood by a neurosecretory neuron (see article on Neuroendocrinology).

Hormones act by binding to specific receptors in the target organ. As Baulieu notes, a receptor has at least two basic constituents:

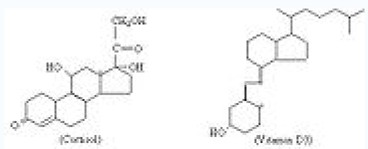
- a recognition site, to which the hormone binds
- an effector site, which precipitates the modification of cellular function.[2]

Between these is a "transduction mechanism" in which hormone binding induces allosteric modification that, in turn, produces the appropriate response.

Chemical classes of hormones



Amine hormones: norepinephrine and triiodothryonine



Steroid hormones: cortisol and vitamin D3

Griffin and Ojeda identify three different classes of hormone based on their chemical composition:[3]

Amines

Amines, such as norepinephrine, epinephrine, and dopamine, are derived from single amino acids, in this case tyrosine. Thyroid hormones such as 3,5,3’-triiodothyronine (T3) and 3,5,3’,5’-tetraiodothyronine (thyroxine, T4) make up a subset of this class because they derive from the combination of two iodinated tyrosine amino acid residues.

Peptide and protein

Peptide hormones and protein hormones consist of three (in the case of thyrotropin-releasing hormone) to more than 200 (in the case of follicle-stimulating hormone) amino acid residues and can have molecular weights as large as 30,000. All hormones secreted by the pituitary gland are peptide hormones, as are leptin from adipocytes, ghrelin from the stomach, and insulin from the pancreas.

Steroid

Steroid hormones are converted from their parent compound, cholesterol. Mammalian steroid hormones can be grouped into five groups by the receptors to which they bind: glucocorticoids, mineralocorticoids, androgens, estrogens, and progestagens.

History and key discoveries of endocrinology

The study of endocrinology began in China. The Chinese were isolating sex and pituitary hormones from human urine and using them for medicinal purposes by 200 BC[4]. They used many complex methods, such as sublimation.[5] Eventually, when Berthold noted that castrated cockerels did not develop combs and wattles or exhibit overtly male behaviour, European endocrinology began (however, it should be noted that the Chinese anticipated the science by over 1500 years.) [6] He found that replacement of testes back into the abdominal cavity of the same bird or another castrated bird resulted in normal behavioural and morphological development, and he concluded (erroneously) that the testes secreted a substance that "conditioned" the blood that, in turn, acted on the body of the cockerel. In fact, one of two other things could have been true: that the testes modified or activated a constituent of the blood or that the testes removed an inhibitory factor from the blood. It was not proven that the testes released a substance that engenders male characteristics until it was shown that the extract of testes could replace their function in castrated animals. Pure, crystalline testosterone was isolated in 1935.[7]

Although most of the relevant tissues and endocrine glands had been identified by early anatomists, a more humoral approach to understanding biological function and disease was favoured by classical thinkers such as Aristotle, Hippocrates, Lucretius, Celsus, and Galen, according to Freeman et al.,[8] and these theories held sway until the advent of germ theory, physiology, and organ basis of pathology in the 19th century.

In medieval Persia, Avicenna (980-1037) provided a detailed account on diabetes mellitus in *The Canon of Medicine* (c. 1025), "describing the abnormal appetite and the collapse of sexual functions and he documented the sweet taste of diabetic urine." Like Aretaeus of Cappadocia before him, Avicenna recognized a primary and secondary diabetes. He also described diabetic gangrene, and treated diabetes using a mixture of lupine, trigonella (fenugreek), and zedoary seed, which produces a considerable reduction in the excretion of sugar, a treatment which is still prescribed in modern times. Avicenna also "described diabetes insipidus very precisely for the first time", though it was later Johann Peter Frank (1745-1821) who first differentiated between diabetes mellitus and diabetes insipidus.[9]

In the 12th century, Zayn al-Din al-Jurjani, another Muslim physician, provided the first description of Graves' disease after noting the association of goitre and exophthalmos in his *Thesaurus of the Shah of Khwarazm*, the major medical dictionary of its time.[10][11] Al-Jurjani also established an association between goitre and palpitation.[9] The disease was later named after Irish doctor Robert James Graves,[12] who described a case of goiter with exophthalmos in 1835. The German Karl Adolph von Basedow also independently reported the same constellation of symptoms in 1840, while earlier reports of the disease were also published by the Italians Giuseppe Flajani and Antonio Giuseppe Testa, in 1802 and 1810 respectively,[13] and by the English physician Caleb Hillier Parry (a friend of Edward Jenner) in the late 18th century.[14]

In 1902 Bayliss and Starling performed an experiment in which they observed that acid instilled into the duodenum caused the pancreas to begin secretion, even after they had removed all nervous connections between the two.[15] The same response could be produced by injecting extract of jejunum mucosa into the jugular vein, showing that some factor in the mucosa was responsible. They named this substance "secretin" and coined the term *hormone* for chemicals that act in this way.

Von Mering and Minkowski made the observation in 1889 that removing the pancreas surgically led to an increase in blood sugar, followed by a coma and eventual death—symptoms of diabetes mellitus. In 1922, Banting and Best realized that homogenizing the pancreas and injecting the derived extract reversed this condition.[16] The hormone responsible, insulin, was not discovered until Frederick Sanger sequenced it in 1953.

Neurohormones were first identified by Otto Loewi in 1921.[17] He incubated a frog's heart (innervated with its vagus nerve attached) in a saline bath, and left in the solution for some time. The solution was then used to bathe a non-innervated second heart. If the vagus nerve on the first heart was stimulated, negative inotropic (beat amplitude) and chronotropic (beat rate) activity were seen in both hearts. This did not occur in either heart if the vagus nerve was stimulated. The vagus nerve was adding something to the saline solution. The effect could be blocked using atropine, a known inhibitor to heart vagal nerve stimulation. Clearly, something was being secreted by the vagus nerve and affecting the heart. The "vagusstuff" (as Loewi called it) causing the myotropic effects was later identified to be acetylcholine and norepinephrine. Loewi won the Nobel Prize for his discovery.

Recent work in endocrinology focuses on the molecular mechanisms responsible for triggering the effects of hormones. The first example of such work being done was in 1962 by Earl Sutherland. Sutherland investigated whether hormones enter cells to evoke action, or stayed outside of cells. He studied norepinephrine, which acts on the liver to convert glycogen into glucose via the activation of the phosphorylase enzyme. He homogenized the liver into a membrane fraction and soluble fraction (phosphorylase is soluble), added norepinephrine to the membrane fraction, extracted its soluble products, and added them to the first soluble fraction. Phosphorylase activated, indicating that norepinephrine's target receptor was on the cell membrane, not located intracellularly. He later identified the compound as cyclic AMP (cAMP) and with his discovery created the concept of second-messenger-mediated pathways. He, like Loewi, won the Nobel Prize for his groundbreaking work in endocrinology.[18]

Endocrinology as a profession

Although every organ system secretes and responds to hormones (including the brain, lungs, heart, intestine, skin, and the kidney), the clinical specialty of endocrinology focuses primarily on the *endocrine organs*, meaning the organs whose primary function is hormone secretion. These organs include the pituitary, thyroid, adrenals, ovaries, testes, and pancreas.

An *endocrinologist* is a doctor who specializes in treating disorders of the endocrine system, such as diabetes, hyperthyroidism, and many others (see list of diseases below).

[edit] Work

The medical specialty of endocrinology involves the diagnostic evaluation of a wide variety of symptoms and variations and the long-term management of disorders of deficiency or excess of one or more hormones.

The diagnosis and treatment of endocrine diseases are guided by laboratory tests to a greater extent than for most specialties. Many diseases are investigated through *excitation/stimulation* or *inhibition/suppression* testing. This might involve injection with a stimulating agent to test the function of an endocrine organ. Blood is then sampled to assess the changes of the relevant hormones or metabolites. An endocrinologist needs extensive knowledge of clinical chemistry and biochemistry to understand the uses and limitations of the investigations.

A second important aspect of the practice of endocrinology is distinguishing human variation from disease. Atypical patterns of physical development and abnormal test results must be assessed as indicative of disease or not. Diagnostic imaging of endocrine organs may reveal incidental findings called incidentalomas, which may or may not represent disease.

Endocrinology involves caring for the person as well as the disease. Most endocrine disorders are chronic diseases that need life-long care. Some of the most common endocrine diseases include diabetes mellitus, hypothyroidism and the metabolic syndrome. Care of diabetes, obesity and other chronic diseases necessitates understanding the patient at the personal and social level as well as the molecular, and the physician–patient relationship can be an important therapeutic process.

Apart from treating patients, many endocrinologists are involved in clinical science and medical research, teaching, and hospital management.

[edit] Training

There are roughly 4,000 endocrinologists in the United States.[*citation needed*] Endocrinologists are specialists of internal medicine or pediatrics. Reproductive endocrinologists deal primarily with problems of fertility and menstrual function—often training first in obstetrics. Most qualify as an internist, pediatrician, or gynecologist for a few years before specializing, depending on the local training system. In the U.S. and Canada, training for board certification in internal medicine, pediatrics, or gynecology after medical school is called residency. Further formal training to subspecialize in adult, pediatric, or reproductive endocrinology is called a fellowship. Typical training for a North American endocrinologist involves 4 years of college, 4 years of medical school, 3 years of residency, and 3 years of fellowship. Adult endocrinologists are board certified by the American Board of Internal Medicine (ABIM) in Endocrinology, Diabetes and Metabolism.

[edit] Professional organizations

In North America the principal professional organizations of endocrinologists include The Endocrine Society,[19] the American Association of Clinical Endocrinologists,[20] the American Diabetes Association,[21] the Lawson Wilkins Pediatric Endocrine Society,[22] and the American Thyroid Association.[23]

In the United Kingdom, the Society for Endocrinology[24] and the British Society for Paediatric Endocrinology and Diabetes[25] are the main professional organisations. The European Society for Paediatric Endocrinology[26] is the largest international professional association dedicated solely to paediatric endocrinology. There are numerous similar associations around the world.

[edit] Patient education

Because endocrinology encompasses so many conditions and diseases, there are many organizations that provide education to patients and the public. The Hormone Foundation is the public education affiliate of The Endocrine Society and provides information on all endocrine-related conditions. Other educational organizations that focus on one or more endocrine-related conditions include the American Diabetes Association, National Osteoporosis Foundation, Human Growth Foundation, American Menopause Foundation, Inc., and Thyroid Foundation of America.

[edit] Diseases

See main article at *Endocrine diseases*

A disease due to a disorder of the endocrine system is often called a "hormone imbalance", but is technically known as an *endocrinopathy* or *endocrinosis*.

[edit] Endocrinology in popular culture

- Dr. Lisa Cuddy, a character on the television show *House M.D.*
- Elliot Reid, a character becomes an expert in the field in the *Scrubs* episode "My Way Home"
- Naomi Bennett, a character on the television show *Private Practice* who is also a fertility specialist

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