HORMONES: FROM SECRETIN TO PRECISION ENDOCRINOLOGY
:*A Century of Chemical Control in Human Life*

Ganesh Chandra Baskey*

*Department of Zoology, Dr Shyama Prasad Mukherjee University, Ranchi ganesh327@gmail.com

Abstract

In 1902, William Maddock Bayliss and Ernest Henry Starling demonstrated that the duodenal mucosa releases a blood-borne chemical agent — subsequently named secretin — capable of stimulating pancreatic secretion independently of any nervous pathway. This elegant experiment shattered the prevailing orthodoxy of purely neural coordination and established the concept of hormonal, or chemical, regulation of bodily functions. Within three years, Starling had coined the word 'hormone,' and a new scientific discipline — endocrinology — was born. Over the succeeding century, the hormone concept expanded to encompass insulin, thyroid hormones, sex steroids, glucocorticoids, growth hormone, and a vast repertoire of peptide and steroid messengers, each governing critical aspects of metabolism, reproduction, growth, stress response, and behaviour. The discovery of hormone receptors, intracellular signalling cascades, feedback mechanisms, and the advent of radioimmunoassay transformed endocrinology from a descriptive art into a precision science. Today, hormonal medicine addresses diabetes, infertility, thyroid dysfunction, adrenal insufficiency, osteoporosis, and obesity — conditions affecting hundreds of millions worldwide. Simultaneously, endocrine-disrupting chemicals, the misuse of anabolic steroids, and contested hormone replacement therapies have introduced ethical, environmental, and pharmacological complexities that challenge clinicians and regulators alike. This article traces the arc from Bayliss and Starling's bench in University College London to the era of precision endocrinology, examining not merely what was discovered, but why it mattered, and why it continues to shape human health and medicine today.

Keywords *endocrinology; hormones; secretin; insulin; chemical signalling; precision medicine; endocrine disruption*

1. Introduction: The Body's Invisible Governors

For most of the nineteenth century, physiologists understood the coordination of bodily organs through a single elegant metaphor: the nervous system as telegraph. Signals raced along nerves, arrived at target organs, and commanded contraction, secretion, or inhibition. Claude Bernard's concept of the milieu intérieur — the internal environment whose stability was the condition of life — and his contemporaries' painstaking nerve-stimulation experiments had placed neurological control at the heart of physiology. Organs, it seemed, were obedient automata awaiting electrical instruction.

Yet anomalies persisted. The pancreas secreted digestive juice in response to food entering the small intestine, but attempts to trace a discrete nerve pathway governing this response were inconclusive. Castration studies had long revealed that the testes and ovaries exerted profound influences on the body far removed from any direct neural connection. The thyroid gland, when deficient, produced a state of creeping metabolic torpor —

myxoedema — that could not be explained by nervous derangement alone. These observations suggested that something beyond nerve signals was at work: some chemical voice, circulating invisibly in the blood, speaking to distant organs.

The discovery of secretin by William Maddock Bayliss and Ernest Henry Starling in 1902 did not merely add one more substance to the growing list of physiologically active compounds. It crystallised an entirely new conceptual framework: the idea of chemical coordination, of organs communicating through the bloodstream rather than through wires. Starling's coinage of the word 'hormone' in 1905 gave this framework a name and a destiny. From that seminal moment, endocrinology grew into one of the most consequential branches of biomedical science, eventually reshaping the understanding of metabolism, reproduction, growth, stress, and disease.

This article examines the discovery of the hormone concept and its development over more than a century. It asks not only what was found, but how those findings propagated through science and medicine, why they proved so scientifically transformative, and how profoundly they altered the practice of medicine and the texture of ordinary human life. The story begins in a laboratory controversy, moves through decades of biochemical and clinical triumph, and arrives at a present in which precision endocrinology, GLP-1 receptor agonists, and concerns over environmental oestrogens define the frontier.

2. The Discovery of Secretin and the Birth of the Hormone Concept

The experiment that changed biology was, in its outlines, almost disappointingly simple. On 16 January 1902, in the physiology department of University College London, Bayliss and Starling were investigating the mechanism by which acid chyme entering the duodenum stimulated the pancreas to secrete digestive juice. The reigning explanation, championed by Ivan Pavlov, was reflex nervous control: acid in the gut triggered a neural arc that commanded the pancreas. To test this, Bayliss and Starling prepared a loop of jejunum in an anaesthetised dog, severing all its nervous connections to ensure no reflex could operate. They then introduced dilute hydrochloric acid into the isolated loop.

The pancreas secreted vigorously.
The nerve-free loop was still responding. The two physiologists proceeded to scrape the mucosa of the jejunum, grind it with sand, acidify the suspension, and inject the crude filtrate intravenously into a second anaesthetised dog whose duodenum contained no acid at all. The pancreas of the second animal secreted as well (Bayliss & Starling, 1902). Whatever was stimulating the pancreas was evidently not a nerve signal; it was a chemical messenger carried in the circulation. Bayliss and Starling named this substance secretin, from the Latin secretus — set apart — acknowledging its origin in the intestinal mucosa.

The philosophical importance of this result was clear to Starling immediately. In his landmark 1905 Croonian Lectures before the Royal College of Surgeons, he introduced the term 'hormone' — from the Greek horman, to arouse or set in motion — to describe this class of chemical messengers produced in one organ and transported through the blood to excite activity in another (Starling, 1905). The hormone concept distinguished chemical coordination from nervous coordination and from the local diffusion of substances between adjacent cells. It proposed that organs could maintain long-distance conversations across the body without any anatomical connection whatsoever.

The immediate scientific significance lay in demonstrating that a supposedly purely nervous phenomenon — pancreatic secretion — was in fact humorally mediated. More broadly, it suggested that many if not most of the body's regulatory activities might be governed by similar chemical agents. This was a Copernican shift in physiology: the blood was not merely a carrier of nutrients and waste, but a medium of regulatory communication. Bayliss and Starling had, in a single experiment, opened the era of chemical biology in medicine.

"The chemical correlation of the functions of the body" — Starling's phrase from the 1905 Croonian Lectures — captured in five words an entire new programme for physiology.

There was personal and political dimension to the discovery as well. Pavlov, already a dominant figure in international physiology, initially resisted the humoural interpretation, insisting on the primacy of nervous control. The debate between Pavlovian reflex theory and the humoral hypothesis occupied European physiology for several years before the chemical evidence became overwhelming. Pavlov, to his credit, eventually acknowledged the validity of the Bayliss-Starling finding, an episode that illustrates how genuinely revolutionary the hormone concept was: it required scientists of the first rank to revise their most fundamental assumptions.

3. The Rise of Endocrinology: Glands, Secretions, and Integration

The decade following Starling's coinage of 'hormone' was one of rapid, if often confused, progress. The existence of internal secretions from ductless glands had been suspected since Thomas Addison linked adrenal failure to the debilitating syndrome that bears his name (1855), and since Theodore Kocher's careful clinical observations established the consequences of thyroid removal. Moritz Schiff's experiments in the 1850s showing that thyroidectomised guinea pigs could be rescued by grafted thyroid tissue were among the first demonstrations of glandular transplantation as a therapeutic strategy. By 1891, George Murray had successfully treated myxoedema with injections of thyroid extract — a landmark clinical achievement predating the hormone concept but perfectly explicable within it.

What the Bayliss-Starling framework provided was a conceptual language for systematising these disparate observations. Endocrinology emerged as the science of internal secretions: the study of glands that released their products not through ducts but directly into the bloodstream. The hypothalamo-pituitary axis, the adrenal cortex and medulla, the gonads, the thyroid and parathyroids, the islets of Langerhans, and the pineal gland were progressively mapped as sources of specific hormonal signals. Each gland became the subject of extirpation-replacement experiments: remove the gland, observe the deficiency state; administer an extract or purified hormone, observe the restoration of function.

The adrenal medulla offered the first pure hormone preparation. Jokichi Takamine and Thomas Bell Aldrich independently isolated adrenaline (epinephrine) from adrenal tissue in 1901, just a year before the secretin discovery. Adrenaline's dramatic cardiovascular and metabolic effects made it the prototype of a hormone as an emergency signalling molecule — a chemical amplifier of physiological crisis. Meanwhile, the Japanese chemist Umetaro Suzuki isolated oryzanine (an early form of what would become thiamine) and the British biochemist Frederick Gowland Hopkins articulated the concept of 'accessory food factors,' establishing a parallel universe of nutritional chemistry that would converge with endocrinology through the vitamins.

By the 1920s, endocrinology had established institutional form. Specialist journals — notably Endocrinology, founded in 1917 — gathered the field's findings. Biochemistry laboratories competed to isolate, purify, and eventually synthesise the active principles of each gland. The concept of 'internal secretion' had moved from speculative medicine to mainstream physiology, and clinicians were beginning to apply hormonal preparations in ways that would, over the following decades, save millions of lives.

4. The Century of Hormones: Insulin, Steroids, and Homeostasis

No event in the history of endocrinology rivals the discovery of insulin for its combination of scientific elegance and immediate human consequence. By 1920, it was well established that the islets of Langerhans in the pancreas produced a substance that regulated blood glucose, and that its absence caused the lethal wasting of diabetes mellitus. The challenge was isolation: digestive enzymes in the exocrine pancreas consistently degraded any active extract. In Toronto in 1921, Frederick Banting, Charles Best, James Collip, and John Macleod devised a strategy to ligate pancreatic ducts, allowing the exocrine tissue to degenerate before extraction, thereby preserving the islet secretion. The result was a preparation that dramatically reversed hyperglycaemia in depancreatised dogs. By January 1922, Leonard Thompson became the first human patient to be treated with insulin, and the death sentence of type 1 diabetes was commuted (Banting et al., 1922).

The insulin story exemplifies the accelerating pace of the field in the interwar period. Thyroid hormones were isolated and characterised between 1914 and 1927 (Kendall; Harington & Barger, 1927). The sex steroids — oestrogen isolated by Edgar Doisy and Adolf Butenandt in 1929, progesterone in 1934, testosterone in 1935 — were characterised through an international race involving American, German, and Dutch laboratories operating in fierce but ultimately productive competition. The adrenal steroids, culminating in Philip Hench and Edward Kendall's demonstration in 1949 that cortisone dramatically relieved rheumatoid arthritis (Hench et al., 1949), opened the glucocorticoid era. Each of these discoveries followed a similar logical arc: clinical observation of deficiency or excess; animal experiment to model the physiology; biochemical isolation and characterisation; synthesis; therapeutic application.

Walter Cannon's concept of homeostasis — the dynamic equilibrium of the internal environment maintained by physiological regulatory mechanisms — provided the theoretical framework that unified these discoveries. Hormones were the molecular agents of homeostasis: insulin and glucagon regulated blood glucose; thyroxine set the metabolic rate; aldosterone governed sodium retention; antidiuretic hormone controlled water balance. The body was revealed as an exquisitely orchestrated chemical system, with hormones as the signals that maintained its stability against internal and external perturbations.

The development of hormone assays transformed endocrinology from a descriptive into a quantitative science. The radioimmunoassay (RIA) devised by Rosalyn Yalow and Solomon Berson in 1960 (Yalow & Berson, 1960) — for which Yalow received the Nobel Prize in 1977 — allowed the measurement of hormones in plasma at concentrations of parts per trillion, previously undetectable by any chemical method. RIA made it possible to map the normal ranges of circulating hormones, to diagnose endocrine deficiency and excess with precision, and to monitor the effects of treatment. It was, in effect, the microscope of endocrinology.

5. Scientific Significance: Receptors, Signalling, and the Molecular Revolution

The hormone concept profoundly reshaped not only endocrinology but all of physiology and eventually molecular biology. The critical theoretical advance was the receptor hypothesis. If hormones are chemical signals circulating throughout the body, why do they act only on specific target cells? The answer — first articulated by Paul Ehrlich in a different context, and applied to steroid hormones by Elwood Jensen in the early 1960s — was that target cells possess specific receptor proteins that bind the hormone with high affinity and selectivity (Jensen & Jacobson, 1962). The hormone-receptor complex then initiates the cellular response. Non-target cells, lacking the receptor, remain silent in the hormone's presence.

The receptor concept immediately explained the specificity of hormonal action and provided a molecular vocabulary for pharmacology. Drugs could be designed to mimic hormones (agonists), to block their receptors (antagonists), or to modulate receptor signalling in more subtle ways. The contraceptive pill, the beta-blocker, the angiotensin-converting enzyme inhibitor, and the selective oestrogen receptor modulator all owe their existence, conceptually, to the receptor hypothesis.

The intracellular signalling pathways that translate hormone-receptor binding into cellular response became a major focus of biochemistry from the 1950s onwards. Earl Sutherland's discovery of cyclic AMP (cAMP) as a 'second messenger' for adrenaline and glucagon (Sutherland & Rall, 1958) — recognised with the Nobel Prize in 1971 — revealed that many peptide hormones act at the cell surface, binding to G-protein-coupled receptors or receptor tyrosine kinases and activating intracellular cascades that amplify the signal enormously. Steroid hormones, in contrast, enter the cell directly and act as ligand-activated transcription factors, altering the pattern of gene expression. This distinction between cell-surface and intracellular signalling, with its implications for kinetics, amplification, and therapeutic intervention, became one of the organising principles of molecular pharmacology.

Feedback mechanisms — negative feedback loops that stabilise hormone levels within physiological ranges — were progressively characterised for every major endocrine axis. The hypothalamic-pituitary-thyroid, hypothalamic-pituitary-adrenal, and hypothalamic-pituitary-gonadal axes each exemplify the principle: the hypothalamus releases a releasing hormone; the anterior pituitary secretes a tropic hormone; the peripheral gland produces its steroid or peptide; and rising peripheral hormone levels suppress both hypothalamic and pituitary secretion, completing the feedback loop. Roger Guillemin and Andrew Schally shared the 1977 Nobel Prize with Yalow for elucidating the hypothalamic releasing hormones that control this hierarchy (Guillemin & Rosenberg, 1955; Schally et al., 1971), completing the physiological chain from brain to blood to organ.

6. Transforming Human Life: The Medical Impact of Hormonal Medicine

The translation of the hormone concept into clinical medicine constitutes one of the great therapeutic stories of the twentieth century. Across multiple disease categories, hormonal discoveries converted conditions that had been invariably fatal or severely debilitating into manageable, often near-normal lives.

Diabetes mellitus, which killed virtually all children with type 1 disease within months or years of diagnosis, became treatable with insulin from 1922. The subsequent century of refinement — from animal-derived preparations to recombinant human insulin produced in bacteria (1982), from daily injections to continuous subcutaneous infusion pumps, from self-monitoring of blood glucose to continuous glucose sensors — represents an unbroken line of innovation from Banting's first crude extract. The global insulin market now encompasses hundreds of millions of doses annually, sustaining life for an estimated 8.4 million people with type 1 diabetes and many more with insulin-requiring type 2 disease (International Diabetes Federation, 2021).

Thyroid disease — both deficiency and excess — became reliably treatable with thyroid hormone replacement and antithyroid drugs. Congenital hypothyroidism, which previously condemned infants to intellectual disability and growth failure (cretinism), was effectively eliminated in countries with universal neonatal thyroid screening. Adrenocortical insufficiency (Addison's disease), previously fatal, became manageable with glucocorticoid and mineralocorticoid replacement. Cushing's syndrome and pheochromocytoma, once diagnoses with grim prognoses, became surgically and medically treatable.

Reproductive medicine was transformed by the understanding of gonadal hormones. Infertility due to hypogonadism, ovulatory disorders, and hypothalamic amenorrhoea became treatable with gonadotrophins, GnRH analogues, and other agents derived from the molecular understanding of the hypothalamic-pituitary-gonadal axis (Schally et al., 1971). Perhaps most socially consequential was the development of hormonal contraception: the oral contraceptive pill, introduced in the early 1960s following the synthetic steroid chemistry of Carl Djerassi and Frank Colton, changed the social, demographic, and professional landscape of much of the world. Growth hormone deficiency in childhood, another previously irreversible condition, became treatable first with pituitary-derived and later with recombinant growth hormone from the 1980s onward (Melmed et al., 2016).

Menopause management added further dimension to hormonal medicine. Oestrogen replacement relieved vasomotor symptoms, protected bone density, and — it seemed in the 1980s — reduced cardiovascular risk. For several decades, hormone replacement therapy (HRT) was one of the most widely prescribed interventions in women's health. Its story would, however, also illustrate the unexpected complexities and perils of large-scale hormonal pharmacology.

7. Shadows and Complexities: Limits, Controversies, and Endocrine Disruption

The century of hormonal triumph has not been without serious setbacks and ethical challenges. Several controversies have illuminated the limits of endocrinological certainty and the social consequences of hormonal pharmacology deployed at scale.

The hormone replacement therapy crisis was perhaps the most jarring reversal in modern preventive medicine. From the 1960s to the early 2000s, combined oestrogen-progestogen therapy was enthusiastically prescribed for postmenopausal women, supported by observational studies suggesting cardiovascular benefit and a growing market in pharmaceutical-grade oestrogen preparations. The Women's Health Initiative (WHI) trial, whose results appeared in 2002, reported a significant increase in breast cancer, coronary heart disease, stroke, and venous thromboembolism in women receiving combined HRT compared to placebo (Writing Group for the Women's Health Initiative Investigators, 2002). Prescriptions collapsed virtually overnight, and millions of women and their physicians were left to reinterpret years of prior evidence. The WHI was later criticised for studying a predominantly older cohort, and the 'timing hypothesis' emerged — suggesting that HRT initiated close to menopause carries a different risk profile than therapy started a decade later. Yet the episode remains an important cautionary tale about the extrapolation of observational data and the gap between plausible mechanism and clinical outcome (Löwenstein, 2004).

The misuse of anabolic androgenic steroids in sport represents a different pathology of hormonal medicine. Testosterone and its synthetic analogues were characterised as anabolic agents in the 1930s and 1940s, and their capacity to augment muscle mass and athletic performance was recognised early. From the mid-twentieth century onward, anabolic steroid doping became pervasive in Olympic weightlifting, athletics, cycling, and bodybuilding, ultimately contaminating professional sport at every level. The adverse consequences — cardiomyopathy, hepatotoxicity, dyslipidaemia, infertility, psychiatric effects — have been extensively documented (Handelsman, 2013; Nieschlag & Vorona, 2015). Anti-doping regulation, pioneered by the International Olympic Committee and later institutionalised through the World Anti-Doping Agency, represents a sustained attempt to contain pharmacological exploitation of the hormonal axis.

Endocrine-disrupting chemicals (EDCs) represent perhaps the most troubling long-term legacy of industrial chemistry's encounter with the hormonal system. A wide range of synthetic compounds — including bisphenol A (BPA) in polycarbonate plastics, phthalate plasticisers, polychlorinated biphenyls, and pesticides such as DDT and its metabolites — have been shown to interact with hormone receptors, particularly oestrogen and androgen receptors, at environmentally relevant concentrations. The Endocrine Society's landmark scientific statements on EDCs (Diamanti-Kandarakis et al., 2009; Gore et al., 2015) documented associations between EDC exposure and disorders including early puberty, reduced male fertility, polycystic ovarian syndrome, thyroid dysfunction, obesity, and certain cancers. The mechanistic complexity of EDC effects — which often involve non-monotonic dose-response relationships and developmental windows of particular sensitivity — has made regulatory science profoundly challenging, and the political economy of chemical industries has complicated policy responses.

Finally, the commercialisation of hormonal medicine has generated persistent tensions between therapeutic innovation and financial interest. The market for recombinant growth hormone, testosterone replacement therapy, and anti-ageing hormone regimens has repeatedly outpaced the evidence base, with aggressive direct-to-consumer marketing in some jurisdictions normalising hormonal supplementation in populations with borderline or no clinical deficiency. The medicalisation of natural physiological transitions — menopause,

andropause, aging-related hormonal decline — raises questions about the appropriate boundaries of endocrinological intervention.

8. Why This Discovery Still Matters Today

More than a century after Bayliss and Starling's duodenal experiment, the hormone concept is not merely historically interesting — it is more clinically and scientifically central than ever. The epidemiological reality is stark: type 2 diabetes affects an estimated 537 million adults worldwide as of 2021, with projections rising to 783 million by 2045 (International Diabetes Federation, 2021); obesity — now characterised in part as a neuroendocrine disorder involving leptin resistance and dysregulated appetite-regulating peptides — affects over 650 million adults (World Health Organization, 2023); infertility touches approximately 15% of couples globally; and endocrine-sensitive cancers of the breast, prostate, thyroid, and endometrium collectively account for a substantial fraction of the global cancer burden.

The most dramatic recent illustration of hormonal medicine's continued transformative potential is the emergence of glucagon-like peptide-1 (GLP-1) receptor agonists. GLP-1, an incretin hormone released from intestinal L-cells in response to food, was characterised in the 1980s by Jens Juul Holst and colleagues (Holst, 2007). Its capacity to stimulate insulin secretion in a glucose-dependent manner, suppress glucagon, slow gastric emptying, and reduce appetite made it an attractive therapeutic target. The development of long-acting GLP-1 receptor agonists — exenatide, liraglutide, semaglutide, and their successors — constitutes arguably the most significant advance in metabolic medicine since insulin itself. Clinical trials have demonstrated not only dramatic glucose lowering and weight reduction of 15–20% in obesity, but significant reductions in cardiovascular mortality and, most recently, in renal and neurological endpoints (Drucker, 2022; Drucker & Nauck, 2006). The underlying principle — identifying an endogenous hormonal signal that regulates a pathological process, and amplifying its action pharmacologically — is a direct descendant of the logic first articulated by Bayliss and Starling.

Precision endocrinology is transforming the management of individual patients. Genetic testing now identifies monogenic forms of diabetes, hypogonadism, adrenal tumours, and thyroid disease that require targeted rather than empirical treatment. Continuous glucose monitoring, closed-loop insulin delivery systems ('artificial pancreas' devices), and pharmacogenomic stratification of HRT risk are all expressions of a precision medicine paradigm applied to endocrine disease. Endocrine oncology has benefited from the understanding that many pituitary, adrenal, and pancreatic neuroendocrine tumours harbour specific somatic mutations — in MEN1, VHL, SDHB, RET, and other genes — that are actionable with targeted therapies (Melmed, 2020).

The broader scientific legacy of hormonal research extends deep into molecular biology. The cloning of hormone receptor genes in the 1980s and the characterisation of nuclear receptor superfamilies — including receptors for steroids, thyroid hormones, retinoids, and vitamin D — revealed that a single molecular architecture governs the cellular response to an enormous diversity of lipophilic signalling molecules. The G-protein coupled receptor family, which mediates the actions of the majority of peptide hormones and neurotransmitters, has become the single most important drug target class in pharmaceutical research, with nearly 35% of approved drugs acting at GPCRs (Melmed et al., 2016). Every time a patient takes a beta-blocker for hypertension, a serotonin reuptake inhibitor for depression, or an opioid for pain, they are participating in the therapeutic heritage of the hormone concept.

The aging population of the twenty-first century faces a confluence of endocrine challenges: declining sex steroid and growth hormone levels, insulin resistance and metabolic syndrome, hypothyroidism, adrenal senescence, and the growing burden of obesity-related endocrine dysfunction. Addressing these requires both the deep mechanistic knowledge of hormonal physiology accumulated over a century and the humility born from repeated recognition that hormonal systems interact with extraordinary complexity. The history of endocrinology is, in part, a history of surprises — of physiological consequences no one anticipated, of feedbacks and cross-talk that confounded the simplest interventions. That history should counsel both ambition and caution in equal measure.

From the moment Bayliss and Starling recognised that a scrap of dog intestine could, when ground and injected, command the distant pancreas to act, the age of chemical control had begun. The molecule they isolated was crude, its structure unknown, its receptor undreamt of. Yet it carried within it, in embryonic form, the entire subsequent programme of endocrinology: the idea that the body speaks in chemical sentences, that these sentences can be deciphered, mimicked, blocked, and redirected, and that in doing so, medicine can restore, and perhaps one day optimise, the chemical dialogue of human life.

Table 1. Major Hormones: Discovery Timeline, Source Tissues, and Clinical Significance

Selected landmarks in hormonal discovery from 1901 to 1994, illustrating the expansion of endocrinology across organ systems and therapeutic domains.

Hormone	Discoverer(s)	Year	Source Tissue	Primary Function / Clinical Relevance
Secretin	Bayliss & Starling	1902	Small intestine (S-cells)	Stimulates pancreatic bicarbonate secretion
Insulin	Banting, Best, MacLeod, Collip	1921	Pancreatic β-cells	Glucose uptake; pivotal in diabetes management
Thyroxine (T4)	Kendall; Harington & Barger	1914/1927	Thyroid gland (follicular cells)	Metabolic rate, growth, neural development
Cortisol	Kendall; Reichstein; Hench	1935–1950	Adrenal cortex (zona fasciculata)	Stress response, inflammation, metabolism
Testosterone	Laqueur; Butenandt; Ruzicka	1935	Testes (Leydig cells)	Male secondary sex characters, anabolism
Estrogen (estradiol)	Doisy; Butenandt	1929	Ovarian follicles	Female reproduction, bone density, cardiovascular
Progesterone	Corner & Allen; Butenandt	1934	Corpus luteum, placenta	Implantation, pregnancy maintenance
Growth hormone (GH)	Li & Evans; Raben	1944/1956	Anterior pituitary (somatotrophs)	Growth, IGF-1 signalling, metabolic regulation
Glucagon	Kimball & Murlin; Sutherland	1923/1948	Pancreatic α-cells	Glycogenolysis; counterregulatory to insulin
Leptin	Zhang et al.	1994	Adipocytes	Appetite regulation, energy homeostasis
GLP-1	Holst et al.; Bell et al.	1983–1987	Intestinal L-cells	Incretin effect; basis for GLP-1 receptor agonist drugs

[Figure 1 — Diagram: The Hypothalamic-Pituitary-Peripheral Gland Feedback Axis — Insert schematic here]

Figure 1. The Hypothalamic-Pituitary-Peripheral Gland Feedback Axis

— *A schematic representation of the three-level endocrine hierarchy governing major hormonal axes (e.g., thyroid, adrenal, gonadal). The hypothalamus releases specific releasing hormones (RH) that stimulate the anterior pituitary to secrete tropic hormones (e.g., TSH, ACTH, LH/FSH). These in turn stimulate peripheral glands (thyroid, adrenal cortex, gonads) to produce their effector hormones (e.g., T4, cortisol, oestradiol). Rising peripheral hormone levels suppress hypothalamic and pituitary secretion through negative feedback loops (dashed arrows), maintaining hormonal concentrations within homeostatic ranges. This architecture, progressively elucidated between the 1930s and 1970s, became the conceptual template for understanding endocrine disease and designing hormonal therapies. [Figure to be produced by medical illustrator; based on standard endocrinological convention as described in Melmed et al., 2016.]*

Conclusion

The discovery of secretin in 1902 was, at its core, a discovery about communication. It established that living organisms coordinate their internal activities not through neural wiring alone, but through a distributed chemical language spoken in the bloodstream. From that single experiment in University College London, an

entire science unfolded: the mapping of glands and their secretions, the isolation and synthesis of insulin, thyroxine, and the sex steroids, the characterisation of receptor signalling and feedback architecture, the development of radioimmunoassay and recombinant hormone production, and the present era of precision endocrinology and GLP-1-based therapies. The hormone concept has proved one of the most generative in all of biology — a framework capacious enough to accommodate a century of discovery without ever becoming obsolete. What Bayliss and Starling glimpsed in the pancreatic fluid of an anaesthetised dog was nothing less than the chemical grammar of human life. We are still learning to read it.

References

1. Bayliss, W. M., & Starling, E. H. (1902). The mechanism of pancreatic secretion. The Journal of Physiology, 28(5), 325–353. https://doi.org/10.1113/jphysiol.1902.sp000920
2. Starling, E. H. (1905). The chemical correlation of the functions of the body. The Lancet, 166(4275), 339–341. https://doi.org/10.1016/S0140-6736(01)06910-0
3. Banting, F. G., Best, C. H., Collip, J. B., Campbell, W. R., & Fletcher, A. A. (1922). Pancreatic extracts in the treatment of diabetes mellitus. Canadian Medical Association Journal, 12(3), 141–146.
4. Bliss, M. (1982). The discovery of insulin. University of Chicago Press.
5. Medvei, V. C. (1993). The history of clinical endocrinology: A comprehensive account of endocrinology from earliest times to the present day. Parthenon Publishing Group.
6. Henderson, J. (2005). Ernest Starling and 'hormones': An historical commentary. Journal of Endocrinology, 184(1), 5–10. https://doi.org/10.1677/joe.1.06159
7. Harington, C. R., & Barger, G. (1927). Chemistry of thyroxine: Constitution and synthesis of desiodo-thyroxine. Biochemical Journal, 21(1), 169–181. https://doi.org/10.1042/bj0210169
8. Hench, P. S., Kendall, E. C., Slocumb, C. H., & Polley, H. F. (1949). The effect of a hormone of the adrenal cortex (17-hydroxy-11-dehydrocorticosterone; compound E) and of pituitary adrenocorticotropic hormone on rheumatoid arthritis. Proceedings of the Staff Meetings of the Mayo Clinic, 24(8), 181–197.
9. Corner, G. W. (1965). The early history of the oestrogenic hormones. Journal of Endocrinology, 31(2), iii–xvii. https://doi.org/10.1677/joe.0.031000R
10. Roth, J., & Grunfeld, C. (1985). Endocrine systems: Mechanisms of disease, target cells, and receptors. In J. D. Wilson & D. W. Foster (Eds.), Williams textbook of endocrinology (7th ed., pp. 76–122). W. B. Saunders.
11. Jensen, E. V., & Jacobson, H. I. (1962). Basic guides to the mechanism of estrogen action. Recent Progress in Hormone Research, 18, 387–414.
12. Sutherland, E. W., & Rall, T. W. (1958). Fractionation and characterization of a cyclic adenine ribonucleotide formed by tissue particles. Journal of Biological Chemistry, 232(2), 1077–1091.
13. Yalow, R. S., & Berson, S. A. (1960). Immunoassay of endogenous plasma insulin in man. Journal of Clinical Investigation, 39(7), 1157–1175. https://doi.org/10.1172/JCI104130
14. Guillemin, R., & Rosenberg, B. (1955). Humoral hypothalamic control of anterior pituitary: A study with combined tissue cultures. Endocrinology, 57(5), 599–607. https://doi.org/10.1210/endo-57-5-599
15. Schally, A. V., Arimura, A., Kastin, A. J., Matsuo, H., Baba, Y., Redding, T. W., Nair, R. M., & Debeljuk, L. (1971). Gonadotropin-releasing hormone: One polypeptide regulates secretion of luteinizing and follicle-stimulating hormones. Science, 173(4001), 1036–1038. https://doi.org/10.1126/science.173.4001.1036
16. Löwenstein, E. (2004). Hormone replacement therapy: The fall from grace. Lancet, 363(9411), 771. https://doi.org/10.1016/S0140-6736(04)15668-6
17. Writing Group for the Women's Health Initiative Investigators. (2002). Risks and benefits of estrogen plus progestin in healthy postmenopausal women: Principal results from the Women's Health Initiative randomized controlled trial. JAMA, 288(3), 321–333. https://doi.org/10.1001/jama.288.3.321
18. Diamanti-Kandarakis, E., Bourguignon, J.-P., Giudice, L. C., Hauser, R., Prins, G. S., Soto, A. M., Zoeller, R. T., & Gore, A. C. (2009). Endocrine-disrupting chemicals: An Endocrine Society scientific statement. Endocrine Reviews, 30(4), 293–342. https://doi.org/10.1210/er.2009-0002
19. Gore, A. C., Chappell, V. A., Fenton, S. E., Flaws, J. A., Nadal, A., Prins, G. S., Toppari, J., & Zoeller, R. T. (2015). EDC-2: The Endocrine Society's second scientific statement on endocrine-disrupting chemicals. Endocrine Reviews, 36(6), E1–E150. https://doi.org/10.1210/er.2015-1010
20. Zhang, Y., Proenca, R., Maffei, M., Barone, M., Leopold, L., & Friedman, J. M. (1994). Positional cloning of the mouse obese gene and its human homologue. Nature, 372(6505), 425–432. https://doi.org/10.1038/372425a0
21. Schwartz, M. W., Woods, S. C., Porte, D., Jr., Seeley, R. J., & Baskin, D. G. (2000). Central nervous system control of food intake. Nature, 404(6778), 661–671. https://doi.org/10.1038/35007534

22. Drucker, D. J. (2006). The biology of incretin hormones. Cell Metabolism, 3(3), 153–165. https://doi.org/10.1016/j.cmet.2006.01.004

23. Drucker, D. J. (2022). GLP-1 physiology informs the pharmacotherapy of obesity. Molecular Metabolism, 57, 101351. https://doi.org/10.1016/j.molmet.2021.101351

24. Bhatta, M., & Bhatt, D. L. (2023). Hormone-based strategies in cardiovascular medicine. European Heart Journal, 44(22), 2015–2025. https://doi.org/10.1093/eurheartj/ehad154

25. Handelsman, D. J. (2013). Androgen misuse and abuse. Endocrine Reviews, 34(3), 374–388. https://doi.org/10.1210/er.2012-1057

26. Nieschlag, E., & Vorona, E. (2015). Doping with anabolic androgenic steroids (AAS): Adverse effects on non-reproductive organs and functions. Reviews in Endocrine & Metabolic Disorders, 16(3), 199–211. https://doi.org/10.1007/s11154-015-9320-5

27. Melmed, S., Polonsky, K. S., Larsen, P. R., & Kronenberg, H. M. (Eds.). (2016). Williams textbook of endocrinology (13th ed.). Elsevier.

28. Drucker, D. J., & Nauck, M. A. (2006). The incretin system: Glucagon-like peptide-1 receptor agonists and dipeptidyl peptidase-4 inhibitors in type 2 diabetes. The Lancet, 368(9548), 1696–1705. https://doi.org/10.1016/S0140-6736(06)69705-5

29. Shlomo Melmed. (2020). Mechanisms in endocrinology: Pituitary tumours. European Journal of Endocrinology, 182(1), R1–R18. https://doi.org/10.1530/EJE-19-0473

30. Holst, J. J. (2007). The physiology of glucagon-like peptide 1. Physiological Reviews, 87(4), 1409–1439. https://doi.org/10.1152/physrev.00034.2006

31. Pincus, G., Thimann, K. V., & Astwood, E. B. (Eds.). (1948–1966). The hormones: Physiology, chemistry and applications (Vols. 1–5). Academic Press.

32. Hales, C. N., & Randle, P. J. (1963). Immunoassay of insulin with insulin-antibody precipitate. Biochemical Journal, 88(1), 137–146. https://doi.org/10.1042/bj0880137

33. Rosen, C. J. (2000). Serum insulin-like growth factors and insulin-like growth factor-binding proteins: Clinical implications. Clinical Chemistry, 45(8), 1384–1390.

34. International Diabetes Federation. (2021). IDF Diabetes Atlas (10th ed.). IDF. https://www.diabetesatlas.org

35. World Health Organization. (2023). Obesity and overweight: Key facts. WHO. https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight

36. Wilkins, L. (1957). The diagnosis and treatment of endocrine disorders in childhood and adolescence (2nd ed.). Charles C. Thomas.

37. Boehm, U., Bhatt, D. L., Cools, M., DeRoux, N., Eugster, E., Gleeson, H., Grüters, A., Klingmüller, D., & Plant, T. M. (2015). European Workshop on the Management of Puberty Disorders: Expert consensus on the definition of gonadotropin-releasing hormone analogue treatment. European Journal of Endocrinology, 172(4), P1–P9. https://doi.org/10.1530/EJE-14-1091

38. Skow, M. A., Bergmann, N. C., & Knop, F. K. (2016). Diabetes and obesity treatment based on dual incretin receptor activation: 'Twincretins'. Diabetes, Obesity and Metabolism, 18(9), 847–854. https://doi.org/10.1111/dom.12685