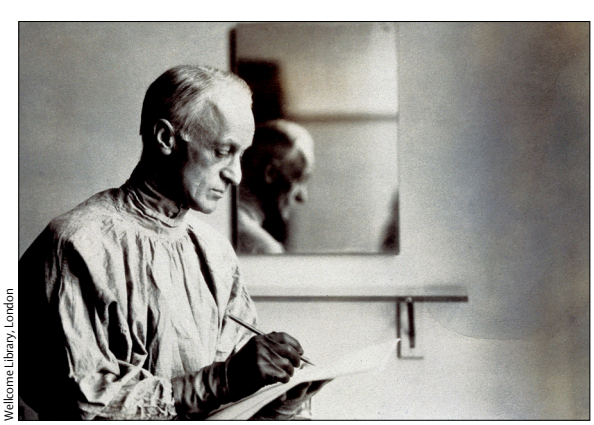
# Case histories
## Cushing's syndrome

Human bodies, like bodies politic, derive their internal stability from complex networks of signalling, feedback, and control. As laboratory science and clinical medicine forged an uneasy alliance in the late 19th century, this metaphorical connection between politics and biology was on the minds of many practitioners. A breakdown of order could mean disease and death for an individual, or chaos and revolution for a nation. Emerging from this tumult of experimental and philosophical reflection, the discipline of endocrinology offered a new frame for disease, and a way to connect laboratory research with the innovations of leading surgeons like Harvey Cushing.

The ambitions and techniques of endocrinology reflected its roots in the rich and powerful industrial societies of late-19th-century Europe and America. Based in laboratories, it demanded complex equipment and sensitive biochemical tests, often based on vivisection, and drew on the technocratic virtues of patience, discipline, and precision. In the 1850s the French physiologist Claude Bernard's notion of a *milieu intérieur* had established a new paradigm for thinking about regulation and control within the body. Half a century later the English physiologists William Bayliss and Ernest Starling showed that, when stimulated with hydrochloric acid, the duodenum secreted an unknown substance into the blood, and this prompted the pancreas to release digestive enzymes. In 1905, Starling borrowed a Greek verb—*hormao*, "to set in motion"—to name a general class of blood-borne chemical messengers or hormones.

Although some glands and tissues seemed to have a single and easily decipherable function, others proved more resistant to elucidation. By the early 20th century clinicians and scientists had attributed what seemed to be a baffling range of functions to the pituitary gland. This tiny nub of tissue, nestling in its own hollow of the skull, appeared to be "the leader of the endocrine orchestra", in the words of the English physician Walter Langdon-Brown. The Lithuanian physiologist Oskar Minkowski noted that acromegaly was associated with pituitary tumours, suggesting that the gland might also have a role in promoting growth. In 1900, his Polish colleague Joseph Babinski described a strange set of symptoms—central obesity, arrested sexual characteristics, hirsutism—in a 17-year-old girl with a pituitary tumour, and in 1911 a near-identical case, a 23-year-old woman known as "Minnie G", walked into Cushing's Boston office.



Wellcome Library, London

**Harvey Williams Cushing (1869–1939)**

Cushing embodied everything that the progenitors of the 19th-century revolution in surgery had hoped to achieve: a hero and a polymath, both an inheritor and a progenitor of surgical myth-making. Born in 1869 into an old Puritan family, he studied at Yale and Harvard Medical School, before a residency at the Johns Hopkins Hospital under the leading American surgeon William Halsted. Cushing moved to Boston in 1911, becoming professor of surgery at Harvard the following year, and gaining a reputation as the world's leading neurosurgeon. In his *The Pituitary Body and Its Disorders* (1912) he argued that Minnie G was suffering from a "polyglandular syndrome" in which "secondary functional alterations occur in the ductless-gland series whenever the activity of one of the glands becomes primarily affected". He noted the difficulty of working out "where the initial fault lay", concluding that the primary lesion might lie in the adrenal glands, the pituitary gland, or the ovaries.

Cushing returned to this puzzling set of symptoms in 1932, in a paper on "pituitary basophilism". Here he argued that a primary pituitary lesion caused secondary adrenal hyperplasia, which in turn produced the symptom-picture of what quickly became known as Cushing's syndrome. Cushing's frame for his new disease was intriguingly hybrid, drawing on ideas from laboratory endocrinology, but also suggesting that the disease could be treated with precise and heroic cutting of the brain.

Others struggled with the difficulty of distinguishing Cushing's syndrome from related forms of adrenal dysfunction, but research in the 1940s showed that it was a distinctive result of excessive cortisone secretion. As synthetic cortisone was taken up as an anti-inflammatory medication, clinicians drew an aetiological distinction between endogenous Cushing's syndrome, most often caused by pituitary adenomas, and an exogenous form resulting from steroid treatment. Since the late 1960s endogenous Cushing's syndrome has been treated effectively with radiotherapy, cortisone synthesis blockers, and surgery to the pituitary gland—precisely the kind of interplay between surgery and science that Cushing seems to have had in mind.

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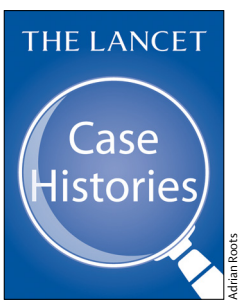


Adrian Roots

For more on **Case histories** see **Comment** *Lancet* 2016; **387:** 211; **Perspectives** *Lancet* 2016; **387:** 217, 737, 1265, 1711, 2082, 2495, and *Lancet* 2016; **388:** 228

**Further reading**

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Welbourne RB. Endocrine diseases. Bynum WF, Porter R, eds. Companion encyclopedia of the history of medicine, volume 1. London: Routledge, 1993: 484–511