

Henry Harrower and the Turbulent Beginnings of Endocrinology

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The emergence of new medical science in the mid-19th century was usually greeted with derision by “practical men” who saw their academic colleagues as elitist intellectuals whose work bore little or no relation to the rough-and-tumble aspects of patient care. This schism, which was nowhere greater than in the field of endocrinology, widened in 1891 when a myxedematous patient was dramatically restored to health after the administration of a thyroid extract. On the one hand, academicians—who saw this result as a triumphal example of the transference of laboratory studies to the bedside—were encouraged to pursue further studies in endocrine pathophysiology and pharmacology. On the other hand, medical practitioners began to believe that crude extracts from glands or other organs, when prescribed as orally administered mixtures, were effective for the treatment of most human ailments.

The organotherapeutic forces were ably championed by Henry R. Harrower, MD, a manufacturer as well as a dispenser of organotherapeutic products. For some years, the claims of the organotherapists remained unchallenged. Finally, in 1921, Harvey Cushing, pioneer neurosurgeon and endocrinologist, launched a crushing assault on the purveyors of pluriglandular therapy. These attacks continued over ensuing years, and organotherapy fell into disrepute. Nevertheless, the assertions of “practical men” have not subsided; rather, we are now confronted by insistent claims for a bewildering array of herbal remedies, over-the-counter hormonal products, and alternative therapies.

“Well, now, Doctor, just in confidence, I’m going to tell you something that may strike you as funny, but I believe that foxes’ lungs are fine for asthma, and T.B. too. I told that to a Sioux City pulmonary specialist one time and he laughed at me—said it wasn’t scientific—and I said to him, ‘Hell!’ I said, ‘Scientific!’ I said, ‘I don’t know if it’s the latest fad or wrinkle in science or not,’ I said, ‘but I get results and that’s what I’m looking for’s results!’ I said.”

Sinclair Lewis, *Arrowsmith* (1925).

On 30 May 1860, Oliver Wendell Holmes, delivered an address titled “Currents and Countercurrents in Medical Science” before the Massachusetts Medical Society (1). In it, he characterized as “Art” the practice of “practical men” who relied on time-honored but unproved empirical remedies. Such practitioners distrusted the newly emerging medical science, which was seen as the product of elitist intellectuals who lacked experience in the rough-and-tumble aspects of patient care.

In contrast, practitioners who adhered to “Nature,” including Holmes, believed in the Hippocratic concept that the physician’s role was to make a diagnosis, offer a prognosis, and then, because many diseases were self-limited, provide a setting conducive to recovery. They were convinced that most drugs were useless or worse. Holmes put it succinctly: “I firmly believe that if the whole *materia medica*, as used now, could be sunk to the bottom of the sea, it would be all the better for mankind—and all the worse for the fishes” (1).

The divergence of these two currents stretches back to ancient Greece and forward to the present day. The path followed by therapeutic reformers, which culminates in today’s randomized, double-blind clinical trials, has been well documented in a recent monograph (2) and need not be reviewed here. The “practical men,” in contrast, found that the narrow advances achieved by medical science were insufficient for their workaday needs. After all, they had history on their side. They were the inheritors of a massive *materia medica* dating back to the dawn of humankind.

This schism in therapeutic approach can be documented in all branches of medicine, but nowhere was it more sharply delineated than in the emerging field of endocrinology. When endocrinologic science began an astonishing expansion at the turn of this century, many medical practitioners, poorly trained

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in a plethora of pre-Flexnerian medical schools (3), hit upon a new panacea. They offered their patients a wealth of crude, mainly glandular tissue preparations touted as effective for any and all ailments.

Sir Humphrey Davy Rolleston (4) summarized the genesis of what came to be called organotherapy: “the administration with medical intent of some substance of the body.” Ancient remedies included such plausible selections as hare’s brain for nervous diseases and “the lung of the long-winded fox for those short of breath.” Inevitably, charlatans prospered, purveying crab’s eyes, fake mummy parts, and that perennial favorite, the unicorn horn.

Ironically, a major development gave impetus to both factions. In 1891, George R. Murray, inspired by the laboratory studies of Sir Victor Horsley, successfully treated a myxedematous patient with an extract of sheep thyroid (5). To the academic community, the patient’s dramatic recovery proved that careful laboratory observations could be applied clinically, but to the organotherapists, Murray’s success was a resounding vindication of their convictions. And the convictions of no less a personage than Charles Edouard Brown-Sequard further advanced the organotherapists’ cause. Brown-Sequard claimed, at 72 years of age, to be rejuvenated by injections of an extract of animal testes. Shortly after this testimonial by one of the century’s leading physiologists, the floodgates of organotherapy opened wide.

Harrower’s Current

Enter Henry R. Harrower, MD (1883–1934), entrepreneurial organotherapist extraordinaire. An audacious, shrewd, articulate, hard-driving, tireless worker with a firm grasp of contemporary endocrinology, he was a formidable protagonist.

Harrower came to prominence by a circuitous route. Born in London, England, he had “common schooling.” At 17 years of age, he began a 3-year stint in Scandinavia studying massage. At 20 years of age, he came to the United States as an expert masseur and worked his way through the American Medical Missionary College, a short-lived Seventh Day Adventist institution in Battle Creek, Michigan. Here he was exposed not to the constraints imposed by scientific principles but rather to the doctrinaire teachings of John Harvey Kellogg, MD, the apostle of clean living (6). Although Harrower was never a Kellogg disciple, he apparently became receptive to the lure of alternative therapies. After graduation, he spent 4 years in Europe, mostly in France and Italy, where he became an ardent advocate of organotherapy.

Returning to the United States, he served in rapid succession as a general practitioner in Kankakee,

Illinois; the head of the research department of the Abbott Laboratories in Chicago, Illinois; and professor of clinical diagnosis at Loyola University in Chicago (7). In 1912, he again sojourned in Europe. During this 2.5-year stay he published a book, *Practical Hormone Therapy*, which discussed organotherapeutic practices in France and Italy and was the first of three volumes dealing with organotherapy (8–10).

Shortly after returning to New York, he moved to what would be his permanent home in Glendale, California. Here he established the Harrower Laboratory and Clinic, which was for some years Glendale’s largest business enterprise. He became a wealthy pillar of his church and community, living in an “English castle” in an exclusive suburb (11).

Harrower was well aware that his views were denigrated by many medical academicians. Regardless, “during the period of enforced professional idleness while awaiting a meeting with the Board of Medical Examiners,” he decided that the time was ripe to establish a national organization of endocrinologists (12). He invited a large number of interested physicians, including prominent figures in academic endocrinology.

The first organizational meeting of the Association for the Study of Internal Secretions (which is known today as the Endocrine Society) took place in 1916. Harrower loomed large in early activities. He was, of course, a member of the organizing committee, and he edited the first two issues of the new journal, *Endocrinology*. However, the “Council soon found that Dr. Harrower’s other business activities were incompatible with the purposes of the Association” (13), and the reins of the fledgling organization were left in the hands of the academicians.

Those who thought that Harrower would fade into obscurity after this naked rejection misread his character. With astonishing vigor, he met his opposition head-on, using techniques that would excite the admiration of today’s spin merchants. He likened the reception of the therapeutic use of animal extracts to the “storm of incredulity with which the first announcement of Roentgen’s discovery was received” (14). He refused to be apologetic for his financial success:

Unfortunately, there is a tendency on the part of the profession to discount any statement made by those who are validly working in this field for their own financial advantage [but] one cannot deny that medicine is indebted to the commercialism of those who have deliberately set themselves to discover something new (15).

Devotees of Sir William Osler should note that Harrower tells of a luncheon with Osler at his Oxford home in 1913. As Sir William gazed across the university cricket grounds, he predicted, “Mark my

words, the internal secretions will be the bat with which the runs are made" (16).

Harrower mounted an effective counteroffensive on other fronts, speaking frequently to audiences of general practitioners. He published 67 papers between 1914 and 1932. In addition to his three books (8-10), he published a monthly review and a quarterly treatise titled "Harrower's Monographs on the Internal Secretions"; he also established an annual essay contest with a \$500 award (17).

The Figure is reproduced from *Practical Organotherapy* (18), which was little more than a catalog of the organotherapeutic armamentarium provided by the Harrower Laboratory. It included extracts not only of familiar endocrine glands but also of the brain, kidney, and mammae. Later, Harrower added extracts of heart and stomach to the list. Although in retrospect it is easy to conclude that the therapeutic effect of these preparations was negligible, it is also a fact that most if not all of these organs do secrete hormones. (Endocrine activity is pervasive; not

even Harrower could conceive that fat cells secrete leptin.)

Although he was astute enough never to challenge the findings of the academic community, Harrower departed from orthodox endocrinology in two important ways. The first, enunciated in 1914 (19), was the principle of homostimulation. By this principle, a patient's depressed thyroid function could be restored to normal simply by administering thyroid extract (20). The second was a construct termed with arresting alliteration—Harrower's hypothesis of hormone hunger (21, 22)—which held that the body has the ability to select from a multiglandular mixture only what is needed to restore health; any excess is harmlessly inactivated.

It would follow, then, that a pluriglandular mixture would repair both primary and secondary endocrinopathies by homostimulation. Moreover, in accordance with Harrower's hypothesis, the organotherapist need not concern himself with the risk for overtreatment. Finally, to complete the organotherapeutic rationale, because endocrine dysfunction is seen as a component of all human disease, pluriglandular mixtures, which are never contraindicated, may be widely prescribed.

To his credit, Harrower succeeded admirably in his efforts to keep abreast of the explosive growth of endocrinologic literature. The sections of *Practical Endocrinology* (10) that dealt with mainline clinical endocrinology were accurate and up-to-date. Furthermore, he was capable of yielding ground. By 1930, he conceded readily that adrenalin, oxytocin, and insulin were most effective when administered parenterally, but he was not ready to abandon his long-held view that oral therapy was efficacious as well. When "the 'destroyed-in-the-stomach-with-the-exception-of-thyroid' idea" was scorned, Harrower counterattacked with the novel notion that the efficacy of oral preparations was enhanced because "endocrine extracts do in fact have to be digested before their active principles can be separated by the intestines, and to interfere with this digestion is absurd" (23).

Harrower continued on course, although with diminishing success. With his death in 1934, the leading voice of organotherapy was stilled and support for this form of treatment rapidly decreased. The hypothesis of hormone hunger became Harrower's sole claim to fame; it was noted as recently as 1986 in a medical dictionary (24).

Cushing's Countercurrents

With the rapid advance of medical science, it became evident that a laboratory was an essential component for state-of-the art medical practice.

2. DOSE TABLE

Preparation	Aver. Dose t. i. d.	Rel. Dry to Fresh	Compar. Cost
Adrenal (total)	1/2-2 gr.	1:6	2
Adrenal Cortex	2-5	1:15 1/2	9
Adrenal Medulla	3-10 m.	1:20M	1200
Amylopsin	2-10	1:8	1-5
Bile Salts	1-5	1:40	1
Bone Medulla	1-2 dr.	3
Brain Substance	5	1:6	1
Corpus Luteum	2-5	1:5	10
Duodenal Scrapings	5-10	1:12	1
Hemoglobin	3-5	2
Kidney	5-15	1:8	2
Lecithin	1/2-3	3
Liver	5-15	1:6	1
Lung	10-20	1:10	1
Lymphatic	1-5	1:5	3
Mammary	3-10	1:4 1/2	2
Nuclein	1/8-1/2	3
Ovary (total)	2-5	1:6 1/2	2
Pancreas (gld.)	2-10	1:5	1
Pancreatin	2-5	1:8	1-5
Parathyroid	1/50-1/20	1:5-5	60
Parotid	2-8	1:5	1
Pepsin	3-10	2-5
Pineal	1/10-1/2	1:7	40
Pituitary (anterior)	1-5	1:5	7-5
Pituitary (total)	1/4-1	1:4 1/2	9
Pituitary (posterior)	1/10-1/2	1:4	15
Pituitary (post. prin.)	3-15 gt.	800
Placenta	3-5	1:6 1/2	3
Prostate	3-5	1:6	3
Spermin (Leydig cells)	2-3	1:9	5
Spleen	3-10	1:4 1/2	1
Steapsin	2-5	4
Submaxillary	2-5	1:8	3
Testes (orchid)	3-10	1:7 1/2	1-5
Thromboplastin	4
Thymus	3-5	1:6 1/2	2
Thyroid	1/12-1/2	1:6	2-5
Tonsil	1/2-1	1:7	5
Trypsin	1-5	5

Figure. Dose table of extracts. The dose is given in grains. The second column shows the weight ratio of whole organ to extract, and the third column shows relative cost (1 = least expensive).

Lewellys F. Barker, professor of medicine at Johns Hopkins University, pointed out in a long discourse (25) that laboratories were indispensable for training physicians, for the practice of medicine, and for research. At the same time, Richard Cabot, the exemplary clinician and medical scientist (26), cautioned physicians that diagnosis and treatment still required excellence at the bedside as well as in the laboratory (27). Academic endocrinologists, committed to the scientific method, felt threatened by the popular success of Harrower and his supporters. The initial response to Harrower's preachments was to ignore him, thereby adhering to the admonition of the American Medical Association (AMA): "Never . . . denigrate one's fellow physicians" (28).

However, the young endocrine association soon made it clear where its interests lay. The second presidential address, delivered by Barker, set the tone. The title, "Remarks on the Function of Suprarenal Glands as Revealed by Clinicopathologic Studies of Human Beings and Experiments on Animals" (29), reflected the establishment's view of what the field of endocrinology should encompass.

With the third presidential address, in 1921, a direct assault was mounted by no less an authority than Harvey Cushing. Cushing railed against organotherapy and its practitioners. He referred to Brown-Sequard as the "Ponce de León of our predecessors." He emphasized that, aside from the thyroid, knowledge of endocrinology was in a primitive state, and when so little is known of uniglandular disease, "What is there to say of a pluriglandular complex except to acknowledge an abysmal ignorance?" He refuted Harrower's key tenets: "It has been claimed that the body picks out the substance it needs and will discard the others, but this has the familiar sound of the gunshot doses of earlier days We have very little evidence that glandular extracts [other than thyroid] have any action when given by mouth." He summarized his views bluntly:

Surely nothing will discredit the subject in which we have a common interest so effectively as pseudoscientific reports which find their way from the medical press into advertising leaflets, where, cleverly intermixed with abstracts from researchers of actual value the administration of pluriglandular compounds is promiscuously advocated for a multitude of symptoms, real and fictitious.

This presidential diatribe was published not in *Endocrinology* but in the *Journal of the American Medical Association*, where it would receive the widest attention (30).

Four years later, Leonard G. Rowntree of the Mayo Clinic, in his presidential address, also spoke of the problem of organotherapy: "There are still certain so-called pharmaceutical firms engaged in a most fraudulent exploitation of the medical profes-

sion and the public in their greed for money. They squeeze gold out of human heartaches." As for hormone hunger, "The practice of administering such mixtures constitutes a disgrace to 20th-century medicine, a menace to our profession, and a betrayal of our patients" (31). The AMA administered the coup de grâce in a pamphlet in which a panel of endocrine specialists summarily dismissed what they saw as the unfounded claims of organotherapists (32).

In this manner, the battle over endocrinology in the United States ended. Similar struggles took place in England and on the continent. Conservative endocrinologists such as Swale Vincent (33) and A.J. Clark (34) damned organotherapy outright; others, such as Ivo Cobb (35), equivocated; and still others championed pluriglandular therapy. The eminent Harley Street endocrinologist Leonard Williams had had enough of Vincent's "scoldings." Williams sighed, "It is a pity that he should be tiresome as well as tireless" (36). In Spain, Gregorio Marañon, the leading endocrinologist, agonized over the conservatives' rejection of his organotherapeutic transplant procedures (37). A more thorough discussion can be found in the comprehensive text of Medvei (38).

Present-day endocrinology has become a vital, intellectually challenging branch of medicine that has ramifications throughout biological science. It has recovered from its precarious beginnings—Herbert Evans, in 1933, said that "endocrinology suffered obstetric deformity at its very birth" (39)—but the rift between "practical" Art and "contemplative" Nature persists. In 1993, a group of dissident, assertive clinicians who believed that their interests were being neglected broke away from the Endocrine Society to form the American Association of Clinical Endocrinologists.

Today's Currents

Today, few if any physicians prescribe organ extracts. Such extracts are usually available only in a few multivitamin mixtures that contain raw adrenal and gonadal concentrates. Nevertheless, for many patients, the lure of unproved over-the-counter remedies has been irresistible (40). We are told of the advantages of natural phytoestrogens, the muscle-building potential of creatine, and the prostate-shrinking properties of the extract of the saw palmetto berry. An advertisement notes that colostrum, "life's first food . . . the ultimate anti-ageing weight loss and immune supplement," is available from "pasture-fed cows." And Harrower's old friend, homostimulation, survives as a homeopathic variant: Thyroid extract with kelp is recommended to stimulate a sluggish thyroid.

It is unsettling to see the ease with which putatively pure and potentially toxic hormones have been welcomed into the realm of natural remedies. Writing of dehydroepiandrosterone, a major adrenal androgen, an advertising writer states without blushing, “A new shining star has made its way into the *natural* health industry” (*italics added*). Another even more potent unregulated adrenal steroid, androstenedione, made headlines when it was revealed that the record-breaking home-run hitter Mark McGwire used it to “bulk up” his impressive musculature.

So, Henry Harrower can look down benignly on the proliferation of innumerable products available for use by “practical men” and the insistent claims to legitimacy of other alternative therapies (41). Harvey Cushing, too, would be pleased by the emergence of paracrine and autocrine functions and the rapidly proliferating array of growth factors, neurotransmitters, and cytokines.

Currents and countercurrents flow on. They may twist and turn, but despite optimistic predictions (41), they are unlikely to merge; they reflect long-held antithetical views of what constitutes the proper domain of health care.

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