The Quest for Cortisone chronicles the pursuit and successful isolation, synthesis, and clinical use of cortisone. The author, Thom W. Rooke, is a graduate of Johns Hopkins School of Medicine. He completed internal medicine and cardiovascular medicine residencies at the Mayo Clinic, following which, he joined Mayo’s vascular medicine section. Rooke is now Professor of Vascular Medicine at Mayo.

The heroes of the book, complete with their foibles, are Edward C. Kendall and Philip S. Hench, who ultimately (along with Tadeus Reichstein) received the 1950 Nobel Prize in Physiology or Medicine for their investigations into the hormones of the adrenal cortex. The book details the lives of other important figures in Mayo Clinic history, such as Walter Alvarez, and major contributors to steroid chemistry, including Percy Julian, Albert Szent-Györgyi, Lewis Sarett, and Russell Marker. This is not only a story of science, but it is also a human adventure with its share of unusual character traits, successes, and disappointments—all laced with the excitement and rewards of discovery.

The search for cortisone was entwined in the historic development of the Mayo Clinic. The beginning of the famed Mayo Clinic—the opening of a 27-bed hospital in 1889 under the direction of Dr. William W. Mayo—is not well known. The hospital was the result of a friendship established between Mayo, a practitioner in Rochester, MN, USA, and Mother Alfred Moes, who ran a Catholic primary school. In the aftermath of a tornado in 1883, Mayo called on Mother Alfred and her colleagues to provide nursing for the injured under his care. It was Mother Alfred who promoted the idea of a hospital and directed the raising of funds to purchase nine acres of land and build the small hospital. Mayo was joined by his two sons, Will Mayo, an 1883 graduate of the University of Michigan Medical School, and Charlie, who graduated from the Northwestern University Medical School in 1887. They established a basic philosophy in the Mayo Clinic, where in the 1930s and 1940s, scientific innovation was encouraged, failure was tolerated, and “doing the right thing might somehow be more important than maximizing profits”—the right environment for the quest for cortisone to succeed.

Edward C. Kendall, called Nick by family and friends, was a chemist, having obtained his Ph.D. from Columbia University in 1910. His work on the isolation of thyroid hormones made him an attractive candidate to head the department of biochemistry at the Mayo Clinic, where Henry Plummer’s focus on toxic nodular goiter and Charlie Mayo’s interest in thyroid surgery were responsible for the early growth and reputation of the clinic. In 1914, Kendall was the first to isolate thyroxine. By then, his compulsive work ethic and drive to succeed were recognized but so were his flaws: his penchant for making premature announcements of results, his stubbornness, his uneven temperament, and his deficiencies in scientific ability. He often made wrong choices in his lab and took detours down false paths. His successes came from a willingness to work hard and long and his tenacity. Following his successful extraction of thyroxine, he repeatedly failed to synthesize the hormone over the next decade.

Hench, a large man (6 feet, 4 inches, and 220 pounds), had a cleft palate with a speech impediment, but he learned to give effective lectures, innovating with the use of slide projections. With a medical degree from the University of Pittsburgh, he was one of the first to receive postgraduate medical education at the Mayo Clinic. After 2 years of fellowship training, he joined the Mayo Clinic medical staff, becoming head of the department of rheumatic disease in 1926, but he continued his training with 1 year in Germany, followed by a Master’s of Science degree from the University of Minnesota. He returned to his clinical career in 1931.
scene-setting quotation from Sherlock Holmes is featured under the title of each chapter in *The Quest for Cortisone*, a tribute to Hench’s devotion to the scholarly detective, manifested by Hench’s outstanding collection of Holmes’ publications. The author appropriately alludes to Holmes’ thinking throughout the book. Another one of Hench’s pursuits was the life and work of Walter Reed. He intended to write Reed’s accurate and definitive history.

In 1930–1931, Leonard Rowntree was treating Mayo Clinic patients with adrenal insufficiency (Addison’s disease) with extracts of the adrenal cortex. The impressive improvement in his patients prompted Rowntree to urge Kendall to pursue the identification of “cortin,” the unknown, life-preserving component of adrenal extracts. At the same time, Hench observed a remission in his arthritic patients during an attack of jaundice, leading him to conclude that jaundice induced the production of an antirheumatic substance X. For the next 20 years, Kendall pursued the magical cortin, and Hench searched for his substance X.

Kendall obtained hundreds of pounds of adrenal glands every week from Parke-Davis Pharmaceutical Company by agreeing to extract the profitable adrenaline for the company. For 10 years, Kendall used his adrenal extracts to pursue the identity of cortin but at the same time, produced millions of dollars’ worth of adrenaline for Parke-Davis. He prematurely announced that he had identified cortin but belatedly realized that the adrenal cortex produced many products and the one he had identified failed to keep adrenalectomized animals alive. According to the author, behavioral traits such as recklessness and improvisation, regarded as Kendall’s shortcomings, may have deliberate actions to keep his laboratory open and funded in times of the Great Depression.

By 1936, Kendall had isolated five separate compounds produced by the adrenal cortex, and he simply labeled them alphabetically; thus, cortisone became Kendall’s Compound E. Kendall and Hench together named Compound E “cortisone,” a name derived, at Hench’s suggestion, from the long-pursued magic substance cortin.

The search for cortisone received a major boost during World War II when the U.S. National Research Council established, as the number one priority, the identification and synthesis of the hormone of the adrenal cortex, cortin. Kendall was included in a committee of 14 internationally recognized chemists to direct this search. Hench was still pursuing the beneficial effects of jaundice, inducing jaundice in his patients with various substances—an experimental practice that would be impossible to do today. In 1941, Hench sought out Kendall for multiple discussions regarding various agents to induce jaundice—conversations that led to a consideration of other possibilities, including the use of Kendall’s Compound E. The two men decided to try Compound E once it was available in sufficient amounts.

For their initial clinical studies, Hench’s group used cortisone supplied by Merck. Lewis Sarett, working at Merck, had developed, at the young age of 26 in 1948, a method of producing cortisone from ox bile. The final step in the conversion process—the insertion of a double-bond in ring A—was developed in Kendall’s lab.

The first patients with rheumatoid arthritis were treated by Hench’s group at Mayo in 1948, using cortisone obtained from Kendall but manufactured by Merck (the first patient received her first injection on September 21, 1948). The detailed descriptions of these patients and the step-by-step responses are as captivating as a good mystery story. Critical decisions were made in a group effort, answering questions, such as: What form of the drug should be administered? What is the appropriate dose? How should the drug be administered (intravenously, intramuscularly, or orally)? The responses were dramatic, but Hench insisted that secrecy be maintained until adequate numbers and results could be presented publicly. The first presentation of 14 patients, complete with a movie record of the remarkable responses, occurred on April 20, 1949, to a packed house of the regular staff meeting of the Mayo Clinic, and on May 3, 1949, Hench received a standing ovation after his talk at the annual meeting of the Association of American Physicians. Merck insisted that Hench conduct a clinical trial using patients and clinicians in scattered parts of the United States. This was accomplished, and cortisone became commercially available from Merck in 1949.

In 1950, Kendall, adhering to the Mayo principle at that time—that staff should not benefit from the exploitation of drugs used in the practice of medicine—assigned his patents on thyroxine and cortisone to the Mayo Clinic. Will Mayo presented the thyroxine patent as a gift to the American Medical Association; the cortisone patents were assigned to Mayo’s Research Corporation. Also in 1950, Kendall and Hench received both national and international acclaim and went to Stockholm.

Life after the Nobel Prize was not as exciting and for Hench, problematic. Hench’s mental and physical health deteriorated; he developed diabetes but refused insulin treatment. He died at age 69 on March 30, 1965. His Sherlock Holmes collection was bequeathed to the University of Minnesota. He never wrote his book on Walter Reed, and the Reed collection was given to the University of Virginia.

Kendall retired from the Mayo Clinic at the mandatory age of 65 in 1951, just 1 year after he received the Nobel Prize. He spent the next two decades in a program at Princeton University founded for displaced former Nobel Prize winners. Working in a small lab, he focused on isolating other adrenal compounds without success, but he did complete his memoirs. On a visit to Merck on May 1, 1972, at age 86, Kendall was staggered with chest pain when he went to the blackboard to write a chemical formula. He died 3 days later.

There is a nagging uncertainty regarding the scholarship in this book. Although it is probably a sign of the times, a significant number of the references are Inter-
net websites (even Google is referenced!). A check of these websites reveals some unreliable resources. Examples can be found in the story of Russell Marker. Marker’s ultimately successful search for an inexpensive method to produce progesterone is interspersed throughout the book at the appropriate chronologic times in this history. Unfortunately, many of the reported details are not correct.

The author reports that Russell Marker “withdrew all of his savings from the bank—and got an indefinite separation from his wife.” The documentation for this is a website that is a syllabus for a course taught at University of California, Los Angeles—a syllabus without references. Marker did not return to Mexico City “with a suitcase full of progesterone.” His initial contact was with Frederick Lehmann, not Emeric Somolo, and he did not come to the first meeting “with a couple of loosely wrapped bundles in his arms.” The accurate details of these events can be found in an autobiographical article by Marker (1) and a 2-h recorded interview with Marker preserved at the Chemical Heritage Foundation in Philadelphia. Early in Rooke’s book, Russell Marker is introduced as “a bit of a madman,” and in the penultimate sentence in the book, Marker’s last years are described as those of “a happy, crazy old man.” Marker was a cantankerous iconoclast, to be sure, but there is no evidence that he was ever mentally unstable. Another referenced website turns out to be a marketing site for “bioidentical progesterone,” and yet another website cannot even be found. However, the details and personal reactions in the last 10 chapters of the book have a ring of authenticity, as they are derived from the papers, documents, and unpublished notes in the Mayo Archives.

The book suffers from the lack of an index, and there are no illustrations—an absence sorely missed when Thomas Addison is described as having “a physical appearance that was alleged to strike terror into his students.” Photos of the principal characters and diagrams of key steroids would have added to the enjoyment of the book.

Overall, the book is informative, entertaining, and easy-to-read, written in the style of Charles Dickens—not to the degree of Dickens’ cliff-hangers but with paragraphs and chapters ending with dangling questions and hints of the future. Interesting anecdotes are abundant, and the lives of the two heroes are effectively tied to historical events.

The Quest for Cortisone stands as excellent testimony for the fruits of collaboration between clinicians and basic scientists. It is also an account of the inexorable progress of science, albeit slow, measured in years and often hampered by circumstances and human errors and follies. The facts in the historical record of the search for cortisone are well-known landmarks; this book effectively and enjoyably provides the human stories behind those facts.

REFERENCE

The Quest for Cortisone by Thom Rooke (2012) Michigan State University Press East Lansing, MI, USA
Leon Speroff

FASEB J 2012 26: 4385-4387
Access the most recent version at doi:10.1096/fj.12-1101ufm

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