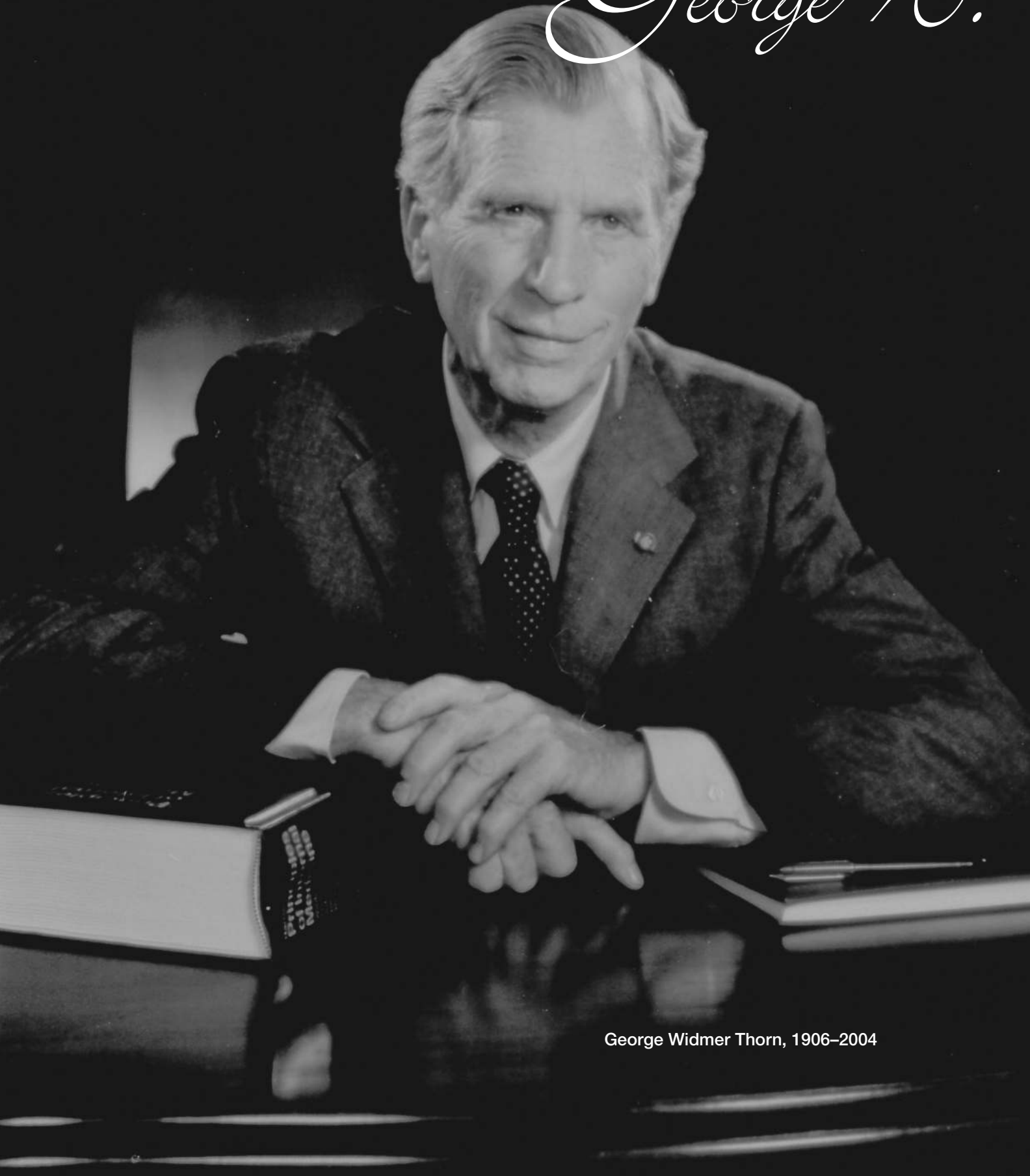


George W.



George Widmer Thorn, 1906–2004

Thorn, M.D.

Medical scientist, educator, humanist

George F. Cahill, Jr., M.D.

The author (ΑΩΑ, Columbia University, 1952) served on the house staff of the Peter Bent Brigham Hospital from 1953 to 1955, and from 1957 to 1958. He subsequently ended as senior physician and emeritus professor of Medicine at Harvard Medical School. He directed both the Endocrine-Metabolic Unit at the Brigham and the Joslin Research Laboratories at the New England Deaconess Hospital, and succeeded George Thorn (ΑΩΑ, University of Buffalo, 1928) as director of research and later vice president of the Howard Hughes Medical Institute. In the 1990s, he taught undergraduate biology at Dartmouth College. Like his mentor, George Thorn, he also tends a forest.

In the autumn of 2003, my wife and I drove to Beverly, Massachusetts, to visit George Thorn in his retirement complex. On his table were the New England Journal of Medicine, the Lancet, and Science, among others. We had lunch at a local pizza parlor, had a grand time reminiscing, aided by mugs of beer. Hours passed. George had recently received the Lifetime Achievement Award of the Massachusetts Medical Society and, at 97, was as ebullient as ever, and only slightly frail. He had last played tennis only three or four years previously! His intellect, humor, and youthful enthusiasm were still 100 percent of normal.

George Widmer Thorn was born in Buffalo, New York, the son of George W. and Fanny Widmer Thorn. The Thorns were of German and the Widmers of Swiss descent, both families having arrived in upstate New York in the 1840s. George's father was a middle manager in the food industry in Buffalo, and his mother, an excellent musician, was active in church, the temperance movement, and other civic affairs. His sister Catherine was also a musician, and received a Ph.D. in speech

therapy. George played the four-string banjo professionally to help pay his educational expenses, and when he was 15, he contracted with town officers at Keuka Lake, where his family had a summer cottage, to hand dig a mile-long ditch for the town's water supply. At age 17, George entered Wooster College in Ohio. After two years there, he returned to Buffalo as a first-year medical student.

The magic extract for Addison's disease

During his second year as a medical student, Thorn began work with Dr. Frank Hartman in the Department of Physiology. By his senior year, Hartman and he had prepared an extract that maintained the growth of adrenalectomized rats. After graduation and a year as house officer at the Millard Fillmore Hospital, Thorn became research fellow in Physiology with Dr. Hartman.¹ Thorn and Hartman's extract was subsequently found to dramatically return Addison's disease patients to normal or near-normal life. In June 1931, Thorn and Hartman presented their results at the annual meeting of the American Medical Association. The following year, the two received the Gold Medal of the AMA for their accomplishments, an award that Thorn received again in 1939 for his significant contributions to the study of adrenal physiology and disease.

In 1931, Dr. Alan Gregg, then head of the Rockefeller Foundation, heard of this precocious researcher in Buffalo, and awarded him a three-year Rockefeller Fellowship. That year, George Thorn married Doris Weston Huggins, a talented technician in his lab who analyzed urinary electrolytes by the laborious chemical means, and who also served as a normal

subject for several protocols involving hormone/electrolyte relationships.

*“Traveling fellowship” — The MGH,
Ohio State, and then Hopkins*

The first year of Thorn’s fellowship was spent on Ward 4 at the Massachusetts General Hospital with James Howard Means, Joseph Aub, Walter Bauer, Fuller Albright, and exposure to Dean Edsall, Walter Cannon, and others. The following year, Thorn again joined Frank Hartman at Ohio State, where Hartman was assistant professor of Physiology. There, active adrenal extracts were first given to normal subjects, including Thorn and his wife Doris. Thorn spent the third year of the fellowship at Johns Hopkins in the Biochemical Division of the Department of Medicine, which was headed by George Harrop. During that year, sex hormones were found to have effects on mineral metabolism, and an assay for the mineralocorticoid potencies of adrenal extracts was devised, almost 20 years before the discovery of aldosterone. Doris Thorn analyzed urine sodium by the laborious chemical method devised by Alan Butler. Lewis Engel, Ph.D., a young steroid chemist in the laboratory, characterized the potencies of a number of steroid compounds, and at the same time, the Swiss discovered desoxycorticosterone (DOC), which Thorn and others showed corrected the electrolyte abnormalities of the Addisonian patient.

Thorn and his colleagues were the first to report an overdose of DOC in a post-nephrectomy patient. The patient had been treated postoperatively with DOC and developed weakness and severe muscle paralysis, hypertension, and hypokalemia. Because intravenous potassium was unavailable in those days, he was treated by reduction in salt intake and the addition of many bananas to his diet. This clinical vignette defined the excessive “mineralocorticoid” effect of adrenal hormones.

Another patient with terminal Addison’s disease was saved by implantation of a pellet of DOC and adrenal extract therapy. A year later, he drove in an ancient car to Baltimore with a just-shot deer on the roof. Venison was served to all on the Osler V service the next day! The original DOC pellets were hand-pressed by Thorn and Harry Eisenberg, the department’s long-serving technician.

In 1938, Thorn was promoted to associate professor and associate physician and director of the Division of Biochemical Medicine at Hopkins. This was the era of the scientific “adrenarche.” Thorn and his colleagues showed that steroids increased glucose production in livers from adrenalectomized rats, the “glucocorticoid effect.” The potencies of corticosterone (Compound B), cortisone (Compound E), and others were characterized, and urinary steroids first systematically isolated by Engel and Thorn.

The steroid “monopoly” of the Hopkins group stemmed partly from an event 10 years earlier. As a second-year medical student, Thorn had accepted a summertime job as “Doc” at a boys’ camp at Lake Erie. He was called to see a couple of vacationers, Dr. and Mrs. Edward C. Kendall, who were suffering from an acute gastrointestinal problem, probably food poisoning. Thorn gave them a potion of some sort and they rapidly recovered, but Dr. Kendall did not forget the reddish-haired kid who had cured them. Thus, samples of the first adrenal compounds, 85 mg of Compound B and 35 mg of Compound E, were sent to Thorn, who gave the full load of each to a single, very well-studied patient with Addison’s disease, and was thus able to characterize the metabolic activities of both. Had Thorn tried to conserve the doses by splitting them into smaller parts, the effects might have been missed! Edward Kendall received the 1950 Nobel Prize for Physiology or Medicine for his work in steroid synthesis.

*The war and Soma Weiss’s death: sad events
leading to opportunity at age 37*



The Peter Bent Brigham Hospital was established in 1911 "for the care of sick persons in indigent circumstances."
Photo courtesy of Brigham and Women’s Hospital.



With the start of World War II, medicine turned to anoxia, high altitude, shock, and other military problems. Thorn was appointed a major in the Army Medical Corps. But the sudden death of Soma Weiss, the young physician-in-chief of the Peter Bent Brigham Hospital created an opportunity for Thorn. Then 37, he gave his last lecture at Johns Hopkins on May 27, 1942, and four days later directed rounds at the Brigham as the Hersey Professor of the Theory and Practice of Physic at Harvard, the oldest chair of medicine in the country.¹ And he was forthwith honorably discharged from the Army!

During the war years, the Brigham's medical and surgical staffs were depleted. The Harvard unit had left for the European theater and many others departed to various other academic medical centers. At times, the service at the Brigham comprised only Thorn, Lewis Dexter, Charles Janeway, James P. O'Hare, Samuel Levine, and several residents and interns.

Clinical research at the Brigham during this time also turned to nutrition, shock, and other problems dictated by war. Renal ischemia and subsequent renal failure was a major interest. One young woman at the nearby Boston Lying-In Hospital had renal shutdown postpartum and was transferred to the Brigham on the medical service. One of Dr. Samuel Levine's patients had died the previous night and, with the approval of the patient's physician wife, one of his kidneys was removed and placed on the woman's forearm. Surgical resident Charles Hufnagel made the vascular connections on the ward, using a gooseneck lamp for illumination!² A small amount of urine dripped from the kidney pelvis, but shortly thereafter the patient's own kidneys opened up and she survived, so we'll never know whether the "kidney assist" made a difference! Other help for military medicine at the Brigham was the production of salt-poor albumin by Edwin Cohn and his younger colleague Charles Janeway. It was used in nephrosis and hepatic failure and shock, and contributed greatly to the rather remarkable survival rate of Allied wounded.

After the war, Thorn and his associates returned to the study of the adrenal system. (Other contemporary contributors to the knowledge of adrenal physiology and disease included Robert Loeb and his group at Columbia, Grant Liddle at Vanderbilt, and Jerry Conn at Michigan, to name only a few.) The Armour Company had prepared adrenocorticotrophic hormone (ACTH), and, in 1946, Thorn and his younger colleague Peter Forsham reported the use of ACTH in diagnosing adrenal disorders. Brigham resident Clement Finch found that eosinophils were strikingly depleted by ACTH, and this became a standard test. Direct chemical assessment of adrenal activity using urinary steroids was subsequently reported by Thorn, George Prunty, and Peter Forsham in *Science* in 1947. A number of adrenal-related conditions such as salt-losing nephritis were also characterized. Adrenal hyper- and hypofunction were characterized by stimulation with ACTH or suppression by exogenous steroid.

During World War II, Willem Kolff in the Netherlands had

*Kolff, Carl Walter, John Merrill, and
Holly Smith: collaborators to develop
renal dialysis*

developed a crude renal dialysis system. After the war, Thorn invited Dr. Kolff to the Brigham to discuss his work. With the technical savvy of Dr. Carl Walter, a surgeon at the Brigham, a dialysis apparatus was built in 1948. Thorn recruited cardiac fellow John Merrill to run the program. He was assisted by a young Harvard medical student, Lloyd Hollis "Holly" Smith. Merrill said that "all hands" were literally used in the first patient trials to hold together the many joints of the plastic tubing! Dialysis was not only crucial to the renal-failure population, but led, several years later, to the preparation of patients for renal transplantation.

By the mid-1950s, the Reddy-Nelson-Thorn determination for urinary 17-hydroxycorticoids was in routine use. Hyperaldosteronism had been characterized by Conn at Michigan, but the "escape" phenomenon, the physiologic response to excess mineralocorticoid, was clarified by Thomas August, Don Nelson, and Thorn.

To George Thorn and the endocrine clinic at the Brigham came hordes of patients with real and perceived disorders. Each patient was handled with equal interest, understanding, and compassion. In cases in which an organic component was either lacking or deemed irreparable, modifications to lifestyle were tailored to the patients and their environments. Patients included King Ibn Saud, celebrities like Spencer Tracy, Robert Frost, and Judy Garland, and many others in business, education, and politics. Thorn, still very youthful with his full head of hair, would round with his retinue of visiting physicians, house staff, medical students, ward nurses, and, of course, his personal secretary, who took shorthand notes for the hospital record. Adroit at recognizing functional complaints, Thorn referred one patient to Christian Science mother church. Several months later, the patient told Thorn that she had never felt better.

Thorn also occasionally used a placebo. One well-known matron in Boston society was concerned about her lifelong obesity. She had been on numerous diets, visited health farms on both coasts, and seen behaviorists of various types, all of which had been unsuccessful. After a number of expensive laboratory tests and consultations, Thorn told her that her problem was perhaps slightly low thyroid activity. One grain of thyroid daily was prescribed. The bottle was to be placed on the dining room table in front of her at all meals, not just breakfast. Perhaps unwilling to dine in restaurants with her pill bottle, she lost weight over the next few months, but, as expected, regained most of it.

That first kidney transplant

The Brigham, in spite of its small size, was a hubbub of activity in the 1950s and 1960s. Francis D. “Frannie” Moore, the “father” of surgical metabolism, was surgeon-in-chief. Cardiologists Lewis Dexter and Samuel Levine referred many patients to cardiac surgeon Dwight Harken. The first successful renal transplant was performed by urologist Hartwell Harrison and plastic surgeon Joseph Murray, with preparation of the patient by nephrologist John Merrill, as Thorn and Moore stood proudly in the wings. Murray received the Nobel Prize for this accomplishment, along with Donnall Thomas, who had been a Brigham chief resident from 1952 to 1953.

Large numbers of fellows rotated through the Metabolic Unit on the third floor of the old Brigham hospital, as well as the Joslin Research Laboratories, a unit at the New England Deaconess Hospital under the direction of Albert E. Renold that was devoted to studies of diabetes mellitus. The medical service of the Brigham was spawning-ground for many researchers and academic practitioners, including 20 chairs of departments of medicine and most of the directors of endocrine-metabolic units in the United States and abroad.

During the early 1960s, Thorn addressed the problem of outpatient medical care in a university/research hospital setting. The Brigham’s Outpatient Department was not functioning well either for the patient or for medical education. The specialty clinics had skimmed off the interesting patients, leaving the General Medical Clinic the elderly with their minor problems. Thorn assembled a number of medical groups, each with either a senior or junior faculty member from the medical specialties, so that consultation was immediately available, obviating the need for a subsequent patient visit. Thus began a “total health” approach in an academic setting, soon adopted by the Harvard (prepaid) Community Health Plan, and embraced by other Boston hospitals. Thorn retired from the Brigham in 1972, becoming the Emeritus Hersey and Samuel A. Levine Professor of Medicine, Emeritus, Harvard Medical School.

HHMI—superb private funding for biomedical research

Howard Robard Hughes, Jr., needs no introduction.³ A multimillionaire from the time he was 19, he inherited the Hughes Tool Company, which held a patent for an oil drill. He was a year younger than George Thorn. After a near-fatal

plane crash in 1946, Hughes discussed with his personal physician, Hopkins graduate Dr. Verne R. Mason, the possibility of founding a medical research institute. Mason enlisted several distinguished colleagues to form an advisory group, including Dean George Berry of Harvard, Hugh Morgan of Vanderbilt, and Alan Gregg of the Rockefeller Foundation. They subsequently asked Thorn to join the group and, in 1950, they began to meet with Hughes. In December 1953, Hughes placed the Hughes Aircraft Corporation, founded in the 1930s and a principal defense contractor during World War II, into a trust with himself as sole trustee. Thus began the Howard Hughes Medical Institute (HHMI) and the inception of “Investigators” hired to work at a small number of major medical centers.

There were problems, however. The Internal Revenue Service challenged the institute’s tax exempt status in 1955. After much legal haggling, the HHMI was given the exemption in 1957. After Hughes’s death in 1976, the exemption was again challenged and was not completely settled until a decade later.⁴ In 1956, Thorn was appointed the institute’s director of research, as well as a member of the Medical Advisory Board, which was chaired by Mason until his death in 1965. Thorn then succeeded to the chair. By 1977, the institute’s annual budget was \$18 million, with 75 Investigators in 12 medical centers. Trustees were Hughes lawyer, Chester Davis of New York, and the executive director of the non-aircraft Hughes holdings (the Summa Corporation), F. William Gay of California. The two elected Thorn to be the third member of the executive committee and the institute’s president.

Another problem was Hughes’s will, or, rather, lack of a will. Hughes’s family, led by Mr. William Lummis, a distinguished Houston attorney who was Hughes’s first cousin, challenged the institute’s ownership in federal court in Las Vegas. A settlement was arranged in 1984 by the appointment of eight trustees by the chancellor of the State of Delaware, in which the institute was incorporated. The group included Thorn; Gay (Davis had died); the institute’s vice-president, Donald S. Fredrickson, a previous director of the National Institutes of Health; William Lummis, Hughes’s cousin; Irving Shapiro, the chairman of DuPont; Hanna Gray, president of the University of Chicago; James Gilliam, a distinguished Delaware lawyer; and Helen K. Copley, newspaper owner and publisher from San Diego. The eight elected a ninth, a successful New York banker, Frank Petito. Thorn was unanimously appointed first chairman of the board.

Thorn’s role in the resolution of the legal disputes was pivotal, and was related to his stature, his international reputation, and, most importantly, his contacts with both sides of the suit. The new trustees decided to sell the institute’s 75,000 shares of stock to General Motors for \$2.7 billion and 50 million shares of General Motors at a guaranteed \$60 per share. The new funding for the institute allowed the creation of new programs, including the refurbishing of a cloister on the NIH campus for some four dozen medical students to spend a

year in one of the NIH labs. Other unique activities included construction of an *Aplysia* farm at Woods Hole to accommodate Eric Kandell's snails, a "public" port at the Brookhaven synchrotron, the first world genomic meeting held at the NIH, and the founding of the Human Genome Project. HHMI's budget is over \$500 million, and, in addition, a \$600 million research facility, the Janelia Project, is under construction on the Potomac River in Virginia. It will bring together investigators both to pool research and to allow access to the latest major instrumentation. The Institute is currently directed by Nobelist Thomas Cech.

Beginning of the Harvard / MIT collaboration

Before he retired from the Brigham, Thorn had become a life member of the corporation and executive committee of the Massachusetts Institute of Technology (MIT). This facilitated the formation of the Harvard Medical School/MIT Life Sciences Program directed by Irving London, enabling medical students to take their basic science at MIT rather than at Harvard. Thorn also became vice president of the Whitaker Health Science Fund, which is devoted to biology and engineering; in 1979 he became chairman of its Scientific Advisory Board. A formal resolution by MIT Chairman Dana G. Mead and President Charles M. Vest honoring Thorn (adopted by the corporation in October 2004) described some dozen committees on which Thorn sat, beginning in 1956, when then President Killian appointed Thorn to join the Medical Visiting Committee.⁵ The following quote from the MIT resolution, accurately describes George Thorn:

Despite his professional distinction and world-class stature, knowing George Thorn was like being in the company of an old friend. He was a fixture in the front row at Corporation meetings during his forty years of membership: an interested and intelligent observer, a warm and generous colleague, a brilliant analyst, an innovative educator, a dedicated public servant, and a humorous and humble human being. He shared his many personal gifts and his extraordinary talents wholeheartedly and in full measure with everyone he encountered.

A West Campus House was named for Thorn in 1981, when he retired from the Executive Committee. George Thorn played what is perhaps the most significant role in bringing together three academic colossi: Harvard University, Harvard Medical School, and the Massachusetts Institute of Technology. The HHMI today supports outstanding scientists

at all three locations, bonding these institutions even more tightly.

Recognition . . . well deserved

George Thorn received many awards from around the world, including over a dozen honorary degrees, one given by Harvard. Included are the Public Welfare Medal of the National Academy of Science, the John Phillips Award of the American College of Physicians, the George M. Kober Award of the Association of American Physicians,¹ twice the Gold Medal of the American Medical Association (the first time at age 27), and many others. Thorn was elected president of every academic medical organization of which he was a member. His last recognition was the Lifetime Achievement Award of the Massachusetts Medical Society, given in 2003 at a luncheon attended by a multitude of guests, including several colleagues yet alive.

One of Thorn's major academic contributions was "the book," *Harrison's Principles of Internal Medicine*. He was on the board for a number of editions and was editor-in-chief of the eighth edition in 1974.⁶ Thorn was also consultant to the Surgeon General of the Army, the Bureau of Medicine and Surgery, the U.S. Navy, the Public Health Service, and other government agencies.

The George Thorn away from medicine

Those who had the privilege to be associated with George Thorn as a fellow board member, a scientific collaborator, a friend, a house officer, a medical student, a tennis partner, or particularly, as a patient, were struck by his gentle, warm, patient, and understanding ways with people. When you were with him, he was 100 percent with you, no matter who you were. He was an excellent musician, expert on the four-string banjo, and played with the "Malady Boys," a Brigham group with Frannie Moore on the piano, John Merrill on the clarinet, and several others. They played at Brigham and other social events.

Thorn learned navigation to improve his sailing abilities and played bridge (with Mr. Vanderbilt himself). He took a six-month sabbatical while physician-in-chief to work in the biophysical facility of Bert Vallee as a research fellow. Everything he did was a challenge, both physical and intellectual. Once, while vacationing in Switzerland with family,

he climbed a mountain with his then young son, Weston. Another time, in Greece, he explored the cone of an active volcano, which erupted the very next day.

But other than family and science, tennis was Thorn's passion. He was a good, not excellent, country-club player and every point was a very important to him. Tennis was a glue that helped hold together the Hughes Institute during its formative years. Every trustee meeting was held where there was a nearby tennis court. The late Chester Davis, Hughes's lawyer and a co-trustee of HHMI, had a "failure" of eyesight as Thorn lobbed a ball over his head. Davis called "out" before the ball bounced. It was the only time I ever saw Thorn speechless with anger. Thorn continued to play tennis doubles through his mid-90s at either the Brookline Country Club or the indoor Badminton and Tennis Club in Boston. He played in the summer at the Essex Country Club or on the Coolidge family court near his home in Manchester-by-the-Sea. Once, he enlisted a woman, a one-time national player, to be his partner in the club men's senior doubles. They cleaned up. It is doubtful that the tournament committee knew of her credentials. Another major hobby was horticulture, working with his trees around his summer house. He planted several hundred, including several exotic species. He commented frequently that it was a superb pastime, since the trees mainly took care of themselves, and if he was too busy they could always wait.

The most significant part of Thorn's life was his wife Doris, an ebullient, socially vivacious, and most gracious woman. She was his major support in his role as chief of Medicine and she knew the first names of all the house staff members and their spouses. Their son, Weston, is a leading expert and auctioneer of antiques and fine arts. Two grandsons, Nicholas, now assisting his father, and Tyler, in his second year in law school, were the pride of their grandfather.

Doris Thorn died in 1984, and Thorn later married Claire Steinert, the widow of Alan Steinert, Sr., who had played a major role as chairman of the board of the Brigham. During the five years they had together until her death, their relationship held much joy for both.

George Thorn died quietly on June 26, 2004. He was 98. He has gone down in history as a major national and international leader in medicine. A resolution passed by the trustees of the HHMI said this of him: "He left a legacy that will continue to inform and reshape the medical and scientific landscape in successive generations." A remarkable man!

Acknowledgment

Except as noted, all photos are courtesy of the author.

References

1. Cahill GF Jr. Presentation of the George M. Kober Medal to



George W. Thorn. *Trans Assoc Am Physicians* 1976; 89: 39–52.

2. Tilney NL. *Transplant: From myth to reality*. New Haven (CT): Yale University Press; 2003.

3. Thorn GW. Howard Hughes Medical Institute. *N Engl J Med* 1978; 299: 1278–80.

4. McCook A. What The Aviator left out: Visionary Howard Hughes Medical Institute had trouble taking off in its early days. *Scientist* 2005; 19: 52.

5. Mead DG. Resolution of the Corporation of the Massachusetts Institute of Technology on the Death of George Widmer Thorn. 2004 Oct 1.

6. Thorn GW, editor. *Harrison's Principles of Internal Medicine*. 8th edition. New York: McGraw-Hill; 1977.

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