



E. Donnell Thomas

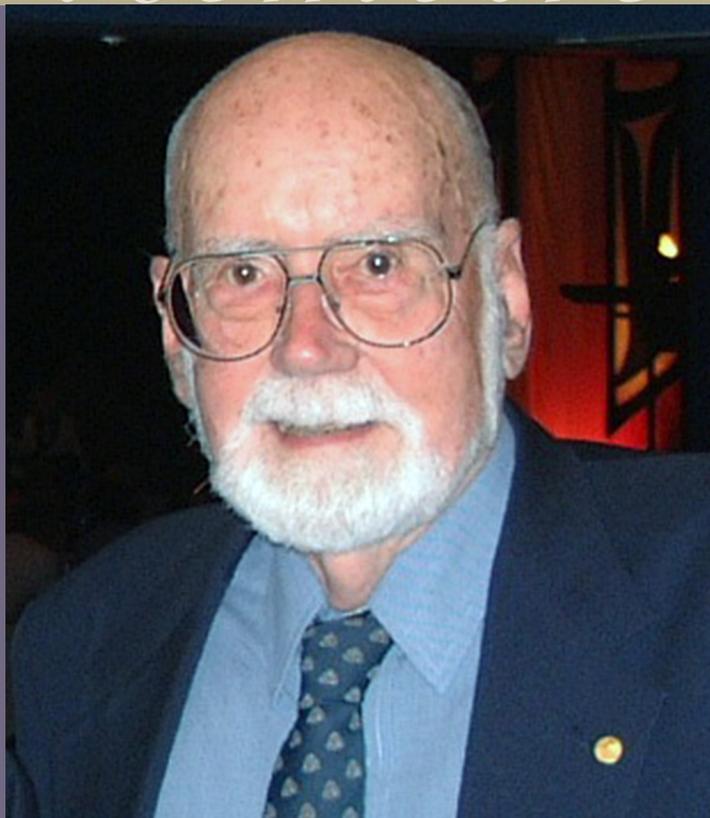
1920–2012

BIOGRAPHICAL

Memiors

*A Biographical Memoir by
Frederick R. Appelbaum*

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EDWARD DONNALL THOMAS

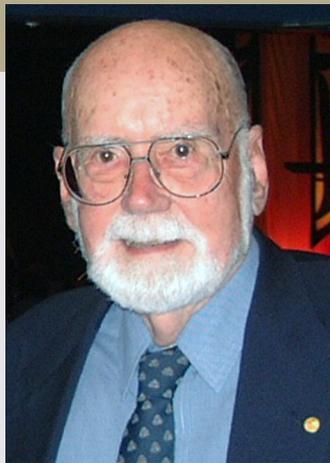
March 15, 1920–October 20, 2012

Elected to the NAS, 1982

From the time he first encountered leukemia patients during his medicine internship, Dr. E. Donnall Thomas became intent on studying that and similar blood diseases in what would become a lifelong crusade to develop cures for these terrible afflictions. Despite seemingly endless setbacks and slow progress, he and like-minded other researchers eventually triumphed, through the perfection of bone-marrow transplantation. Facing and overcoming a series of obstacles—the need to match tissue compatibility between patients and donors (at first limited to identical twins), fatal post-transplant infections, tissue rejections for various reasons, the formidable task of finding vast numbers of people willing to submit to blood testing as possible donors—all were overcome in turn. Thomas's intense focus and intense energy was the force that made bone marrow transplantation a lifesaving cure around the world.

Thomas earned a bachelor's degree from the University of Texas at Austin in 1941 and an M.D. from Harvard. After a three-year stint as an Army internist in Germany and a year at M.I.T., he and a colleague, Joseph Ferebee, began serious research and experimentation with bone marrow transplants in Cooperstown, New York. In 1963 Thomas moved to Seattle and started a transplantation program in affiliation with the University of Washington Medical School, then at the Fred Hutchinson Cancer Research Center, finally retiring at age 82.

Don Thomas liked to point out that his life spanned the period from horse-and-buggy house calls to genetically engineered T cells. His father, Dr. Edward E. Thomas, was born in 1870 and moved to what was then frontier Texas with his family in a covered wagon in 1874. Growing up with almost no formal education, Edward still managed to attend the University of Kentucky and earn an M.D. degree. He returned to Prairie Hill, a small Texas village in the Brazos River Valley, and set up shop as a solo practitioner. His first wife died of tuberculosis. He remarried, and when he was 50 years old, on March



By Frederick R. Appelbaum

15, 1920, his second wife, Angie Hill Donnall, gave birth to Edward Donnall “Don” Thomas, her only child.

According to Don, his father was a remarkable man. “Despite his rather limited education, he was a scholar. He knew Latin; he knew Greek. He was familiar with most of the world’s great literature. When I was a graduate student in chemistry, I found that he knew almost as much organic chemistry as I did, and it was all self-taught.” His father enjoyed having Don accompany him on house calls, first in a horse and buggy, and later in a Model T Ford. Don recalled seeing patients with measles, mumps, tuberculosis, and, occasionally, smallpox. After each visit, his father would turn it into their private teaching conference. “In Texas at the time, you were old enough to drive when your legs were long enough to reach the pedals, for me that was about age 12. I would go with my father if he had a baby to deliver. I would sleep in the car while he finished the delivery and he would sleep in the back seat while I drove us home.” Don spent so much time trailing his father he became known as “Doc” even before he entered high school.

His high school class consisted of only 15 students and Don, by his own admission, was not outstanding even in this small group; while he enjoyed science, he had less interest in the liberal arts. He attended the University of Texas in Austin and in his first year of college he made only B’s. But in subsequent years, as he focused on chemistry and chemical engineering, his grades improved dramatically, and he graduated Phi Beta Kappa in 1941.

Although successful as a physician, Don’s father was an unlucky businessman, investing the family savings in land purchases that he promptly lost in the stock market crash of 1929. When Don got to college, he had almost no money, so during his undergraduate years he worked several odd jobs, including waiting tables at the girls’ dormitory. One January morning in 1940, there was a freak snowstorm, and as he left the dormitory, he was accidentally hit by a snowball thrown by an attractive young woman. Don chased down his assailant and that is how he met Dorothy Martin, who would become his wife and life-long partner, Dottie. Three years after they met, Don and Dottie married, in December 1942.



Don and Dottie Thomas, Boston, 1944.
(Photo Credit: Hutch Library Archives.)

Although Don badly wanted to go to medical school, he couldn't afford it and so began working on a Ph.D. in chemistry in Austin, where he received a nominal salary as a teaching assistant. But then, in response to the acute shortage of physicians caused by World War II, the U.S. Army created a Specialized Training Program that covered the cost of medical education. With support from this program, Don was able to attend Harvard Medical School, where he was elected to both Alpha Omega Alpha and the Boylston Medical Society (two academic honorary groups), before graduating in 1946 near the top of his class.

During his internship, at Peter Brent Brigham Hospital, he cared for several patients with leukemia, and that experience changed his life. "Looking back on it, I just found leukemia inherently interesting. It was an alarming, frightening disease. The diagnosis was a death sentence, usually within just weeks or months. I felt I owed it to the patients to try and do something about it," Don said. "What really attracted me was that you take a cubic centimeter of blood from a vein and that's equivalent to a biopsy of a tumor. So, it seemed to me that this was an important opportunity for research, and working with a disease where you had ready access to the cells just made sense." Having decided that leukemia was his target, after finishing his internship in 1947 he began a year of hematology training under Dr. Clement Finch at Harvard.

During his year with Finch, Don had an opportunity to work with Dr. Sidney Farber and was fortunate to see the first child with acute lymphoblastic leukemia whose remission was induced with an anti-folate drug. He also was exposed to the work of another Brigham researcher, Allan Erslev, who was attempting to identify erythropoietin. These experiences reinforced Don's interest in leukemia and the factors that influence normal and abnormal marrow function. Following his year with Finch, Don spent three years as an internist in Germany, paying back the Army for supporting his education, and then returned to Boston, spending a year at the Massachusetts Institute of Technology in John Loofborough's laboratory, studying stimulating factors released from radiated yeast. It was during that year (1950) that Don first began thinking about the possibility of bone marrow transplantation.

In 1949 Leon Jacobson, of the University of Chicago, and colleagues had reported that a mouse could be protected from otherwise lethal irradiation by shielding the spleen. Jacobson assumed that the spleen's function was to produce a hormonal factor that stimulated marrow growth. But then in 1950, Egon Lorenz and colleagues at the National Cancer Institute (NCI) published results suggesting that the radiation protective effect

of the spleen and marrow might be due to the transplantation of cells rather than a hormone. This led Don to speculate that if you could destroy a normal marrow with radiation and replace it, perhaps you could do the same for an abnormal marrow. While at Loofborough's lab, Don attended the American Society of Clinical Investigation meeting in Atlantic City and made it a point to attend Jacobson's talk describing his spleen shielding experiments. After his talk, Don approached Jacobson as they left the room. "We sat on a bench on the boardwalk and discussed the possibilities of bone marrow transplantation. Jacobson was convinced the spleen's role in radiation protection was hormonal and explained how he was going to try and identify the hormones involved. He was skeptical about Lorenz's findings."

Following his year at M.I.T., Don returned to the Brigham to complete his clinical training and then to serve as a staff hematologist. During that time, he became acquainted with the efforts of Dr. Joseph Murray and his team to develop kidney transplantation. In fact, Don helped Murray care for Robert Herrick, the twin who was the first successful recipient of a kidney graft. This experience further deepened Don's interest in the broad topic of transplantation, although he was thinking about marrow, not kidneys. Thirty-six years later, Don and Murray would again be together, this time in Stockholm sharing the Nobel Prize.

While Don was keen to begin pre-clinical experiments in marrow transplantation, there were neither space nor resources at the Brigham to allow him to proceed. Dr. Joseph Ferrebee, a previous colleague of Don's in Boston who had since moved to the Mary Imogene Bassett Hospital in Cooperstown, New York, shared many of Don's thoughts about the potential for human transplantation in general and marrow transplantation specifically. The two had kept in touch after Ferrebee left Boston, and in early 1955 Ferrebee convinced Don to join him in Cooperstown, explaining that there was ample room and start-up funds for them to begin to explore their shared vision.

Within months of his arrival in Cooperstown, several papers were published that were of enormous interest to Don and Ferrebee. The first, from Joan Main and Richmond Prehn at the NCI, showed that a mouse protected against lethal irradiation by marrow infusion



Joe Ferrebee, Don Thomas, and James Bordley (left to right) in Cooperstown, 1956. (Photo Credit: Hutch Library Archives.)

would then become tolerant to skin grafts from the marrow donor. The second was from Charles Ford and colleagues in Harwell, England, who used cytogenetic markers to prove beyond doubt that the radiation-protection effect of marrow transfer was due to the long-term engraftment of the transplanted marrow. As Don wrote, “Ferrebee and I spent a number of long evenings studying these reports. On the wards of the Bassett Hospital were patients dying of leukemia. These patients inspired us to speculate that it might be possible to destroy leukemia cells and normal marrow by lethal whole-body irradiation, with reconstitution of marrow by marrow transplantation.”

In 1957 Don and Ferrebee published their first paper, in the *New England Journal of Medicine*, describing their initial attempts at marrow grafting in six patients. The patients were prepared for transplantation using either low doses of alkylating agents or low-dose total body irradiation. No efforts were made to match the donors with the recipients. They found that they could infuse large amounts of properly prepared marrow intravenously without apparent harm but saw only one transient graft of donor marrow. As Don stated, “we found that allogeneic marrow grafts in human patients were going to be difficult indeed to achieve.”

In 1959 they reported their first two identical twin marrow transplants for children with end-stage acute lymphocytic leukemia and showed that the intravenous infusion of twin marrow readily restored marrow function after total body irradiation, but in both patients the leukemia recurred within a few months. After a few other attempts at allogeneic transplants in humans using higher doses of total body irradiation also failed, by the late 1950s Don and Ferrebee called a halt to their human studies. Attempts at marrow transplantation by others were similarly unsuccessful. According to available medical literature, between 1958 and 1962, allogeneic marrow transplantation was attempted in 154 patients with aplastic anemia or leukemia without a single long-term survivor. Not surprisingly, most investigators left the field.

But Don and Ferrebee persisted. Instead of continuing human studies, they turned to a canine model. They chose dogs because, unlike inbred genetically identical mice, dogs are, like humans, outbred and genetically diverse. Further, like humans, they come in families allowing for transplant studies between related pairs, and are large enough to receive clinical care much like human patients. Using this model, they found that dogs could routinely survive four times the lethal dose of irradiation if given autologous marrow, that canine marrow could be cryopreserved in glycerol or DMSO for months or years and still function normally, and that peripheral blood could substitute for marrow if sufficient numbers of cells were given. But

when allogeneic rather than autologous marrow was used, recipients invariably died from graft rejection or graft-versus-host disease (GVHD).

When animals were given methotrexate as an immunosuppressant in the early post-grafting period, as first suggested by the NCI's Delta Uphoff, the severity of GVHD was lessened, but all recipients of marrow from unrelated dogs still died. However, when canine littermates were used as donors, an occasional methotrexate-treated animal became a long-term survivor with genetic markers proving engraftment of donor marrow. Those rare survivors indicated to Don that marrow transplantation was possible but left unanswered how to choose appropriate donor-recipient pairs.

Late in the summer of 1960, Don was invited by Clement Finch, who had since moved to Seattle, to give a talk about his experience with transplantation. In his talk, Don outlined the problems of GVHD and leukemic relapse. Immediately after his talk, a pediatrician in the audience, Moreno Robins, came up to the podium and explained that he had an ideal patient for Don, a 7-year-old girl, Nancy Lowry, with severe aplastic anemia and an identical twin. Under Don's supervision, Nancy was transplanted with her twin sister's marrow, and two weeks later, her blood counts began to rise, reaching normal levels a little more than a month post-transplant. While genetic markers were not available to prove it, Nancy Lowry is almost certainly the first individual ever to be cured with marrow transplantation. More than 30 years after the transplant, working as a school nurse for children with special needs, she contacted Don to congratulate him when she read that he had received the Nobel Prize.

During Don's visit to Seattle, Finch and Dr. Robert Williams, the first chair of the Department of Medicine at the University of Washington, began conversations attempting to convince him to leave Cooperstown and move to Seattle. Williams, like Finch, had been a colleague of Don's back in Boston. While the leadership of the Bassett Hospital in Cooperstown was supportive of Don and his work, the opportunity to join a large academic center with old colleagues, along with the physical beauty of the Pacific Northwest, eventually persuaded Don to make the move, which he did in 1963. With grant support from the NIH and the NCI, laboratory space at the Seattle Public Health Service Hospital was remodeled for Don, and an irradiation facility was created in an unused former military facility in West Seattle, about seven miles away.

Don was soon joined by two research fellows, Bob Epstein from Chicago and Rainer Storb, a Fulbright scholar visiting from Germany. Don asked them to work on the problem of donor selection for marrow transplantation using the dog model. During



Paul Neiman, Alexander Fefer, Don Thomas, Dean Buckner, and Rainer Storb (left to right), Seattle, 1988.

(Photo Credit: Hutch Library Archives.)

the early 1960s Jean Dausset, Rose Payne, and Jon van Rood were developing serologically based techniques to define tissue compatibility among human family members. Using similar techniques, Epstein, Storb, and Don developed typing sera that enabled them to identify matched donor-recipient pairs among canine littermates. After several years of work, they were able to show that dogs given supra-lethal total body irradiation (12Gy) that were then infused with marrow from a matched littermate followed by post-transplant methotrexate almost always became long-term survivors, with stable donor marrow engraftment. These studies convinced Don that it should be possible to carry out grafts between

matched human siblings, and that it was time to return to the clinical and human trials. Dean Buckner, a former hematology fellow at the University of Washington, returned from the NCI to join the team. Together, they wrote a grant that included funding to remodel a ward at the Public Health Hospital into eight single isolation rooms and hire a dedicated nursing and support staff. The grant was site-visited in 1967 and awarded in 1968.

That same year, Robert Good and his team at the University of Minnesota were referred an infant, David Camp, with X-linked lymphopenic immunodeficiency. With the assumption that the patient's immunodeficiency would prevent him from rejecting foreign cells, Good treated him with an intraperitoneal injection of bone marrow from his partially matched sister with no pre-transplant conditioning. The patient rejected the first graft but a second one took, and Camp went on to become the first long-term survivor of an allogeneic bone marrow transplant. Don and his team began conducting transplants for patients with acute leukemia and aplastic anemia in March of 1969.

Don's first series of patients all had end-stage disease and were within weeks of death. Don and his team went to extraordinary lengths to support these already debilitated patients through the severe toxicities of the high-dose preparative regimens and the resulting profound immunosuppression of the early post-transplant period. Patients were housed in laminar flow rooms and fed food that had been radiated to sterilize it. Staff members donated platelets, and granulocytes were collected from patients with chronic myeloid leukemia. Don worked with Robert Hickman to develop an indwelling catheter for intravenous alimentation. Among the small number of patients they transplanted in

1970 and 1971, most died, often within weeks of transplantation, but a few survived. As supportive care measures improved, the small number of patients surviving transplantation slowly increased.

In 1972 the Public Health Hospital was threatened with closure, and Don temporarily housed his program at Providence Hospital before moving in 1975 to the program's permanent home in the newly constructed Fred Hutchinson Cancer Research Center, soon nicknamed "the Hutch." By this time, Don had recruited additional faculty to join his team, including immunologist Alex Fefer, molecular biologist Paul Neiman, gastroenterologist George McDonald, infectious disease expert Joel Meyers and other specialists, all focusing on the general problem of bone marrow transplantation. By the end of 1974 the Seattle group had transplanted over 100 patients, and the following year they published their results in a landmark paper in the *New England Journal of Medicine*.

Among the patients included in the paper were 37 with severe aplastic anemia, of whom half were alive with normal functioning grafts more than one year post-transplant, the first group of patients cured of aplastic anemia using allogeneic transplantation. Among 70 patients with acute leukemia, 20 were alive in remission, 10 of whom were more than four years from transplant, the first patients cured of leukemia by transplantation.

While these cures of patients with otherwise fatal diseases were gratifying, most patients were still dying, often from complications of the procedure. Over the next decade, Don and his group led the way in overcoming many of the barriers to a successful outcome. Fatal infections were common. Don's group conducted the first randomized trials demonstrating that cytomegalovirus infections could be prevented by selecting appropriate blood products for sero-negative patients or using pre-emptive ganciclovir for those with latent virus. They found that *Pneumocystis* infections could be prevented with trimethoprim-sulfamethoxazole, and that prophylactic fluconazole decreased the incidence of fungal infections. Despite HLA-matching of donor and recipients, GVHD was a major killer. Don's group showed that anti-thymocyte globulin was sometimes effective in treating the disease, and once cyclosporine became available, they conducted the first trials demonstrating the effectiveness of the combination of methotrexate and cyclosporine in preventing GVHD, which rapidly became the standard of care.

With these improvements in supportive care, the safety of the procedure improved, and with increased safety, Don and his team took the controversial step of transplanting patients while in first remission. In 1979, they published their results in the *New England Journal*, reporting that over 50 percent of a small number of patients

transplanted in first remission were cured, more than doubling what was seen without transplant. This paper drew considerable criticism from chemotherapists complaining about selection bias and lack of controls, but numerous subsequent controlled studies conducted at the Hutch and elsewhere repeatedly confirmed Don's conclusion that for younger patients with acute myeloid leukemia and an HLA-matched sibling, transplantation provides the best chance for long-term survival.

With the demonstration that allogeneic marrow transplantation offered curative therapy for patients with end-stage leukemia, Don and his team began studying transplantation as treatment for other hematologic diseases. They published the first series demonstrating the curative potential of allogeneic transplantation for myelodysplasia, myelofibrosis, non-Hodgkin's lymphoma, and Hodgkin's disease. Don and his team also reported the first cure of thalassemia using marrow transplantation.

Up until the late 1970s, marrow transplantation was restricted to those patients with an identical twin or closely matched family member available to serve as a donor. Transplants using donors mismatched for two or more HLA antigens resulted in an unacceptably high incidence of graft rejection or GVHD. Since there is a one-in-four chance that any two siblings will be HLA identical, given the average size of the American family, this meant that the possibility of transplantation was limited to the one-third of patients with an appropriate family member match.

In 1979, Bob Graves, a veterinarian from Colorado, approached Don and his colleague John Hansen about the possibility of conducting a matched unrelated transplant for his daughter Laura, who had recurrent acute lymphocytic leukemia. Don and Hansen agreed, and Laura became the first patient transplanted for leukemia using a matched unrelated donor. The transplant itself went smoothly, but sadly Laura's leukemia recurred two years later. Nonetheless, Graves remained committed to helping others find unrelated donors. Given the enormous polymorphism in HLA, Graves and Don realized that a very large number of volunteers would have to be HLA-typed and consent to donate marrow for this to be a realistic option.

Graves started a foundation to help support the development of a registry, but initial attempts fell far short of what was needed. Then in 1986, with the aid of Admiral Elmo Zumwalt, Jr., whose son had undergone a transplant, Don and Graves were able to convince the Navy to award a contract to support the National Marrow Donor Registry. Similar efforts were developed in other countries, and today, over 35 million people have

volunteered to be HLA typed and serve as a donor. With this large registry and subsequent advances that allow for the use of mismatched donors and cryopreserved cord blood, an acceptable source of allogeneic stem cells can be found for almost every patient in need.

Thanks to Don's pioneering work, hematopoietic cell transplantation is available worldwide, with over 100,000 patients receiving the treatment annually. Transplantation has become the treatment of choice for patients with severe aplastic anemia and is the only curative therapy for thalassemia and sickle cell anemia. Autologous transplantation is used as first-line therapy for multiple myeloma and for patients with recurrent non-Hodgkin's lymphoma and Hodgkin's disease. Allogeneic transplantation is standard therapy for most patients with acute myeloid leukemia and advanced myelodysplasia, and for selected patients with acute lymphocytic leukemia.

In addition to its therapeutic importance, Don's extended exploration of marrow transplantation has had broad scientific influence on hematology, immunology, and oncology. By showing that it is possible to transplant the entire lymphohematopoietic system from one person to another by transferring a limited number of marrow cells, Don helped define the nature of human hematopoiesis and stimulated efforts to identify factors that control its growth and development. He found that with correct donor selection and the proper use of post-transplant immunosuppression, life-long bidirectional immunologic tolerance between adults is achievable, an observation that has led to decades of basic and applied research in immunogenetics.

Perhaps most significant was Don's team's observation in 1978 that the chance of leukemia recurring after transplantation was lowest in patients in whom GVHD developed, was higher in recipients of allogeneic transplants who did not develop GVHD, and was higher still in identical twin transplant recipients or if T cells were removed from the transplanted marrow. This observation provided the first and best evidence that the human immune system can eradicate a disseminated cancer. Appreciation of this graft-versus-tumor effect led to the development of preparative regimens that are less intense than those initially used, allowing transplantation to be safely conducted on an outpatient basis and in patients even in their seventh and eighth decade of life. More importantly, Don's demonstration of the immunologically based graft-versus-tumor effect provided the impetus for subsequent efforts to develop effective cell-based immunotherapeutic approaches culminating in today's new breakthrough treatments.

Don was a quiet man, “spending words like a miser spends money,” according to his wife, Dottie. While not saying much, he still projected an aura of authority. When he did talk, people listened. He had an unusual ability to motivate those of us who worked with him. He could be a strict taskmaster. Papers and proposals were expected to be on time and carefully done. Shoddy work or sloppy thinking was not acceptable. While authoritative, he was also modest and quick to deflect praise to his co-workers. And he was loyal to those who worked with him.

Perhaps Don’s most important characteristic was his single-mindedness. He truly believed in transplantation and was willing to bet the house on it. In the early and mid-1970s, while other cancer centers were developing “comprehensive” clinical programs addressing every major cancer type, Don focused the entire clinical effort of the Fred Hutchinson Cancer Research Center on marrow transplantation. He specifically designed the clinical facilities at the Center to care for transplant patients. For well over a decade, every recruit to his clinical division was dedicated to some aspect of that topic. Don understood that it would take a team to achieve his vision. The group he assembled included nurses, administrators, lab techs, and medical subspecialists focused on the spectrum of complications of marrow transplantation. The single mission of his program created a unique family-like culture in which everyone, from nurse to dietician to social worker contributed. Don was quick to acknowledge that it was the group that was responsible for his success. When he arrived at work that morning in 1990 when he got the call about the Nobel prize, the first place he went to was the nursing station on the transplant ward to thank the nurses, whom he often called “his secret weapon.”

Dottie was Don’s partner in everything they did. She was an English major in college, but once they arrived in Boston, she trained to become a laboratory technician to earn enough money for their rent. When they moved to Cooperstown, her training proved invaluable, as she took over directing the laboratory, performing all the assays supporting the transplant experiments. In Seattle, Dottie functioned as Don’s lead administrator. She organized grant applications, managed the budgets, kept his calendar, and proofread every paper. It’s often been said that if Don was the father of transplantation, Dottie was the mother.



Don and Dottie Thomas with a large steelhead trout.

(Photo Credit: Hutch Library Archives.)

While austere at work, Don and Dottie were warm and gracious hosts once out of the office, regularly welcoming new recruits and visiting scientists to their home. The dinners on those occasions were invariably salmon, duck, venison or elk, courtesy of their rod or rifle, none of it store bought, ever. The Thomases loved the outdoors, and, throughout their lives, spent almost every vacation camping, hunting, and fishing. Don was, by all accounts, an outstanding fly fisherman and wing-shot, tying his own flies and loading his own shotgun shells. He and Dottie became ardent conservationists, supporting organizations like Ducks Unlimited.

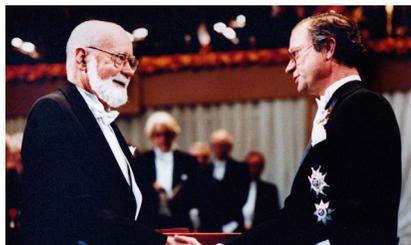
While the outdoors was one of the Thomases's two great passions outside of work, the other was their family. Together Don and Dottie raised three children, Don Jr., Jeff, and Elaine. Don Jr. became an internist and writer who has authored more than 20 books on the outdoors and conservation. Jeff became an accountant, and Elaine is an infectious disease expert at the University of New Mexico, with a special interest in the health problems of Native Americans. All three remember Don and Dottie as great parents. According to Don Jr.,

Some of my earliest memories are sitting in the floor of our canoe while my father paddled and smoked his pipe in the stern and my mother sat in the bow with a shotgun cradled across her lap, eager to see what lay "waiting around the next bend in the creek."

Jeff remembers "a million years" of family camping, hunting, and fishing trips, with his father using every opportunity to teach, either the physics of a campfire, or the anatomy of a fish being gutted. According to Elaine, work and family was their entire life, and whatever Don and Dottie did, they did together.

For his contributions, Don received almost every possible award in his profession, including the Kettering Award, the Stratton Award from the American Society of Hematology, the Karnofsky Award from the American Society of Clinical Oncology, and the Presidential Medal of Science. In 1990, Don and Joseph Murray shared the Nobel Prize "for their discoveries concerning organ and cell transplantation in the treatment of human disease."

The same year he won the Nobel, Don stepped down from his position as head of the transplant program; he



The Nobel Prize ceremony, 1990.
(Photo Credit: Hutch Library Archives.)

finally retired completely in 2002 at the age of 82. According to his daughter, Elaine, until peripheral vascular disease started limiting his mobility, he seemed to enjoy retirement, puttering around the house, working his hunting dog, and taking the occasional hunting or fishing trip. Don died in 2012 at age 92. Dottie died two years later, at the same age. Together, their shared legacy is a field of clinical research and treatment that has saved the lives of untold thousands of patients.

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