Edward Donnall Thomas

(1920–2012)

Immunologist who won Nobel prize for bone-marrow transplants.

Edward Donnall (Don) Thomas has been called the father of bone-marrow transplantation. Until the 1970s, every reported human marrow transplant had failed, and prominent immunologists declared that the barriers between individuals could never be crossed. Thomas persisted and eventually succeeded, sharing a Nobel prize for the feat in 1990. Since 1969, around one million patients with otherwise fatal blood disorders have received bone-marrow transplants.

Thomas died on 20 October 2012, aged 92, of heart failure. He was born in Mart, Texas, and his father was a general practice doctor, whom he often accompanied on house calls. Thomas received his bachelor's and master's degrees in organic chemistry from the University of Texas at Austin in 1941 and 1943, respectively. In 1942, he married fellow student Dorothy (Dottie) Martin. She helped to manage his research and papers throughout his career — the late George Santos of Johns Hopkins University School of Medicine in Baltimore, Maryland, once said: "If Dr Thomas is the father of bone-marrow transplantation, then Dottie Thomas is the mother." The couple had three children, two of whom are physicians.

In 1946, Thomas received his MD degree from Harvard Medical School in Boston, Massachusetts, followed by residency training at the city's Peter Bent Brigham Hospital and then service in the US Army. In 1950, he returned to the area as a research fellow at the Massachusetts Institute of Technology in Cambridge, and then as chief resident and instructor in medicine at Harvard.

In 1955, Thomas was appointed physician-in-chief at the Mary Imogene Bassett Hospital in Cooperstown, New York. Here he became fascinated by the discovery that rodents given a lethal dose of radiation could be rescued by an intravenous infusion of marrow cells from a donor. In 1957, Thomas treated a patient with leukaemia using high doses of total-body irradiation to wipe out the cancer, and then gave them an infusion of marrow cells from an identical twin. The transplant was at first successful, although the patient later died from a recurrence of the leukaemia.

Meanwhile, the medical literature was charting numerous cases of patients with blood disorders who had been treated using marrow transplantation from healthy family members. All the patients died from infections or severe immune reactions that were not predicted from studies in inbred rodents. Many investigators left the field, pronouncing it a dead end.

Thomas did not give up. In 1957 he began experimenting in dogs. Like humans, dogs have unusual phenotypic diversity, a well-mixed gene pool and can develop haematological diseases, including non-Hodgkin lymphoma. In late 1963, Thomas set up his laboratory at the United States Public Health Service (USPHS) Hospital in Seattle, which was affiliated to the University of Washington's medical school.

COURTESY OF DOTTIE THOMAS

When I joined his small band of scientists in 1965 as a research fellow, transplantation was not a widely known concept. Indeed, the university's print shop once produced letterhead stationery for us that read "Division of Hematology and Transportation". A remarkable thing about Thomas's leadership style was that he was happy to give people like me a free hand in innovating, as long as it helped the patients.

Under Thomas's guidance, we spent the 1960s developing high-intensity irradiation treatments to eradicate patients' cancer cells and establishing the importance of tissue matching for transplant outcome. To control and treat graft-versus-host disease, we developed drug combinations to suppress the immune system and produced antibodies against human lymphocytes — which once involved a 1.5-hour chase of an antibody-producing horse. Our total-body irradiation sources were set up in a Second World War underground bunker.

Work with patients began in 1969 at the USPHS hospital. Initial survival rates were low, and unexpected problems required going back and forth between bench and bedside — something that remained a hallmark of Thomas's work. By 1979, after performing a number of transplants, we were able to describe a phenomenon called graft-versus-tumour effects, in which donor lymphocytes help to eliminate residual malignant cells. There are patients who received transplants in 1971 still alive today.

Progress has been slow but steady. Early marrow donors were siblings. In 1979, the first patient with leukaemia was successfully treated with a transplant from an unrelated donor using new immunosuppressant drugs. This success sparked Thomas and others to set up international marrow-donor programmes. Transplant outcomes have improved, with survival rates for some diseases, such as aplastic anaemia, close to 95%.

In 1972, the US government closed the USPHS hospital. This prompted the founding of the private Fred Hutchinson Cancer Research Center (the Hutch), with close ties to the University of Washington's medical school. Thomas headed the medical oncology divisions at both.

Over the years, Thomas's team trained hundreds of young investigators. As one of them put it: "Virtually every major transplant centre in the world got its start by sending someone to train under Don Thomas." Owing to his influence, the Hutch's clinical focus has always been the patient, and its approach, one of teamwork. After retiring in 1989, Thomas continued writing manuscripts, lecturing and serving as an ambassador for the place.

Besides science, Don and Dottie had a passion for fishing and hunting, the fruits of which they shared at intimate dinners with colleagues and friends at their modest home. Reserved, hardworking and uncompromising, Thomas generously attributed much of his success to colleagues, nurses, support staff, patients and their families. ■

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