

OBITUARY

Geoffrey Peter Herzig, MD (1941–2013): *Transplant Pioneer*

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Smart lad, to slip betimes away
From fields where glory does not stay,
And early though the laurel grows
It withers quicker than the rose

AE Housman, *Ode to an Athlete Dying Young*

Young people in the transplant field may not realize how much they are indebted to Geoff or Jeff Herzig (he was neutral on how you addressed him). He once told me (RPG): call me whichever you like but don't call me late for dinner.

Geoff was part of an outstanding group of physician-scientists who developed many aspects of modern cancer therapy at the National Cancer Institute beginning in the late 1960s. The NCI team included Robert Graw Jr, Nicholas Rogentine, Ronald Yankee, Brigid Leventhal, Jacquie Whang-Peng, Roger Halterman, Richard Root, Edward Henderson, John Ziegler, David Poplack, Philip Pizzo, Frederick Appelbaum and others who spread across the US to establish important leukemia and transplant programs. Geoff had a central role in many of their accomplishments. He figured out how to viably freeze dog, monkey and human BM cells; the cell dose we use for transplants today, 3×10^8 , was determined by him (he simply multiplied the LD_{10} (lethal dose to 10% of the population) dose in dogs, 3×10^7 by $1 - \log$). Geoff, with Seymour Perry and Emil Freireich, developed techniques to collect granulocytes and platelets from single donors using the NCI-IBM blood cell separator, the prototype of today's apheresis machines. The IBM was the Gladys the Tart or Galloping Centrifuge aka *Gallop Gertie* of our day (for those too young to recognize this, see Arrowsmith, the book, not the vocal group although Geoff would likely have preferred the latter). To put this instrument in perspective, the collection procedure took 4–6 h or more and, as there was no disposable software; the centrifuge bowl had to be sterilized overnight in what is best regarded as an elaborate version of a Betty Crocker crock pot (trust me, I also had an IBM centrifuge, a gift of John Fahey (RPG)). Whether the team made pot roast with the sterilizer on off-days is unclear. More on Geoff's epicurean

adventures later. And with Professor Paul Terasaki, the team proved the value of HLA matching of platelets for transfusion.

In 1973, Geoff published an important study where he described attempts to rescue rhesus monkeys from early acute GVHD by destroying the graft and infusing frozen autologous bone marrow. What he and his colleagues showed was that, if performed early this approach worked but once GVHD was advanced, it evolved to a nonspecific phase such that destroying the graft no longer prevented death from GVHD. We would do well to remember this today in our efforts to prevent and treat GVHD in humans.

Many people forget Geoff was a co-author of a 1976 seminal report with Vincent DeVita, John Ziegler and others on the use of combined-modality therapy and autotransplants to treat Burkitt lymphoma. He and his colleagues further developed this concept of using high-dose therapy to eradicate cancer and then rescuing the person with frozen blood or BM cells (see *The Emperor of All Maladies* for details). Different from people who promoted throwing drugs together in a sort of bouillabaisse, Geoff insisted on a more rigorous approach of finding the maximum tolerated dose of each component before combining them. If you know what STAMP-5 used for autotransplants is (not a philatelic issue), you can trace its origin to Geoff. And we could go on. Simply put, many cancer therapies and interventions that we take for granted today were developed by Geoff Herzig and his colleagues at the NCI in the 1970s and advanced during his time at Washington University (with Nate Berger). Clearly, the right people at the right places at the right times!

Moving to AML, we also owe our current regimens of high-dose cytarabine to Geoff and his colleagues at Washington University and elsewhere including his younger brother Roger, Joseph Fay, Gordon Phillips, Steven Wolff, Hillard Lazarus and others. After Robert Capizzi reported encouraging phase-1 data, Geoff and colleagues decided to work out the optimal dosing scheme for high-dose cytarabine. They did, and this is the schedule we use today as the backbone of post-remission therapy of AML. (Sadly we have not gotten much further since their 1985 report.) When Geoff was at Roswell Park Cancer Institute, he worked closely with Clara Bloomfield to define the predictive role of cytogenetics and molecular abnormalities in predicting AML therapy outcomes. He was also an important contributor to our concepts of how to best treat Hodgkin lymphoma including novel drug regimens and autotransplants.

Geoffrey Herzig was born in 1941, the day before the Japanese attacked Pearl Harbor. Nevertheless, he loved sushi, udon and other Japanese foods. He and Roger grew up in Cincinnati and Cleveland and attended the University of Cincinnati where Geoff graduated with honors in chemistry and Phi Beta Kappa. He attended medical school at Case Western Reserve University in Cleveland and his internship and residency were at Albert Einstein College of Medicine in New York where he developed his love for *The City*. He trained in hematology and oncology at the NCI and Washington University in St Louis where he joined the faculty and developed leukemia and transplant programs 1975–1991. While there he further developed his concept of using high doses of anticancer drugs whose dose-limiting toxicity was BM suppression that he could overcome with an autotransplant. To accomplish this, he built his own cryopreservation device using refrigerator and car parts (he was terribly handy). Geoff was a radical thinker in

a conservative environment but was admired for his fearlessness of university administrators (names redacted by the NSA). Geoff then joined Clara Bloomfield, at Roswell Park Cancer Institute to concentrate on clinical trials of acute leukemia, especially AML, his special interest. In 2000, he moved to the University of Louisville School of Medicine to co-direct the BMT program with his brother and close scientific collaborator, Roger.

Geoff was active in many professional societies and research organizations including the American Society of Hematology, the American Society of Clinical Oncology, International Society of Experimental Hematology, the Cancer and Acute Leukemia Group B, the International Bone Marrow Transplant Registry and later the Center for International Blood and Marrow Transplant Research and others.

Geoff was exceptionally honest when it came to science. In 1972, he published an article in the *New Engl J Med* asserting the effectiveness of granulocyte transfusions in persons with leukemia with infection. But he did not hesitate to co-author a report of a randomized trial in the same journal in 1981 (with both of us) that showed no efficacy. (The studies used different collection techniques.) Geoff called the plays as he saw them, one reason he was considered a superb clinical investigator and clinician.

Geoff had many colleagues, friends and protégés including Gordon Phillips, Hillard Lazarus, Donna Reece, Michael Caligiuri and others, but sometimes preferred to be alone. He could be aloof at times and demanding with mentees but underneath had a warm heart and was prone to random acts of kindness. He lent his only car to Gordon Phillips for a month for no special reason other than because Gordon's was under repair.

Geoff loved 'precision' cooking and provided complex dishes for family Thanksgivings and other holidays, and recently developed

the perfect hamburger. (Paradoxically, it must be admitted he had a weakness for White Castle hamburgers, perhaps because he developed 'tolerance' at an early age in Cincinnati.) He loved fine cigars (Cohiba preferred; provenance unquestioned), Burgundy wines and South Indian food. He had an extraordinary collection of vinyl records (remember these?) and CDs, and several stereo systems with 2-m high speakers and power requirements that could tax the output of the Tennessee Valley Authority. Your dream stereo system was Geoff's Walkman. He had >400 songs of every type on his mobile phone that he played while writing in medical charts after clinic. Geoff loved sailing and rowing, and kept a boat in NY harbor for a while, not the friendliest sailing venue.

In a recent conversation with Geoff one of us (RPG) discussed the correlation between most high achievers and a constant need to be in the limelight. I suggested drugs like Prozac might help a modest, self-effacing but highly productive person like Geoff seek public accolade. He said it was I who needed drugs. Imagine that!

Geoff is survived by his dear brother Roger, his son Andrew and grandchildren. We and the tens of thousands of people who benefited from his innovations will miss Geoff Herzig. A memorial will be held in Louisville soon.

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