

OBTITUARY

Alan Randolph Giles, MD (1940–2022): dogged pioneer and esteemed hematologist

Alan Randolph Giles, a pioneer and leader in the field of hemostasis and thrombosis, passed away on September 29, 2022 at the age of 82 (Figure 1. Alan Randolph Giles, MD, circa 2002). Alan was born on August 8, 1940 in Wallasey, Cheshire, England, shortly after the outbreak of the Second World War. He had an older sister Patricia. His father, Randolph Giles, was a manager and mother, Violet (*née* Dawson), a housewife. He was a good sportsman and played rugby for his county school's boys club. Alan enjoyed football and was an ardent Arsenal fan until the end. He also had a brief stint in a band that opened for the Beatles in Liverpool before they hit the big time.



Alan read medicine at St. Mary's Hospital Medical School, University of London, England, from 1959 to 1965, where he also specialized in Pathology/Hematology from 1966 to 1968. He married his childhood sweetheart Hilary (*née* Burnley) in 1964, who remained his lifelong companion. He held various clinical posts between 1968 and 1971, including Medical Assistant in the Department of Haematology, High Wycombe General Hospital and Attending Obstetrician at Stone Maternity Home, Buckinghamshire, England. Spurred by his pioneering spirit and keen interest in hemostasis and translational medicine, he changed course in 1971 and together with Hilary and their two young children, Nicola and Matthew, set off to Amsterdam, where Alan took up a position as Head of Clinical Methodology in the Medical and Anti-Thrombosis Unit in Organon. In 1974, Alan and his family embarked on a grand new adventure, immigrating to Canada where he took up clinical-academic posts at McMaster University in

Hamilton, home to one of the most prestigious hemostasis and thrombosis groups in history, led by Jack Hirsh. Alan became a Fellow of the Royal College of Physicians Canada, in 1977, and was appointed as the Clinical Head of the Hemostasis Laboratory and Assistant Professor in the Departments of Pathology and Medicine at McMaster. He was also a member of the Hamilton Regional Hemophilia Centre and Associate Medical Director of the Canadian Red Cross Blood Transfusion Services. It was during this time that Alan's interest in hemophilia and novel therapies manifested, which continued throughout his career. It was also the time when his clinical-scientific career took off, fueled by cutting-edge research and leading clinicians and investigators he encountered.

As is often the case with big clinical-scientific research groups led by strong, driven personalities, it is either their way or the highway. In 1979, Alan did just that, he hit Highway 401 and headed east, with a new arrival in his family, their youngest son Jeremy. He travelled to the opposite end of Lake Ontario, where he would establish another highly innovative and productive hemostasis and thrombosis group at Queen's University in Kingston. With a sharp eye, sound judgment, and enormous vigor, he quickly started recruiting leading scientists and clinicians in the field. Among them was the peerless biochemist Michael Nesheim from Kenneth Mann's laboratory at the Mayo Clinic in Rochester Minnesota, where he was engaged in pioneering research on factor V and the prothrombinase complex. Another compatriot was a distinguished hematologist-academic David Lillicrap, completing a post-doctoral fellowship in genetics at the University of Wales. The two would become pillars of the local, national, and international hemostasis and thrombosis communities (Figure 2. "The three wise men," David Lillicrap, Michael Nesheim, Alan Giles, Coagulation Research, Queen's University, Canada, circa 1990). Other notable recruits to this Ontario Heart & Stroke Research Program included Marlys Koschinsky from Genentech, studying Lp(a) and coronary heart disease, currently Professor in Physiology and Pharmacology at Robarts Research Institute, Canada; Graham Cote, Professor of Biomedical and Molecular Sciences, Queen's University, Canada, studying alpha-kinases and myosins in Dictyostelium and vascular smooth muscle cells; and Donald Maurice from Richard Haslam's laboratory at McMaster, investigating cyclic nucleotides and phosphodiesterases in vascular endothelial and smooth

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muscle cells, Professor in Biomedical and Molecular Sciences, Queen's University, Canada.



In addition to recruiting humans, Alan had the foresight to recruit dogs and establish the second hemophilic dog colony in the world, with founders from Walter Bowie's laboratory at the Mayo Clinic. These animals have been an invaluable asset for the development of novel hemophilia therapies. Despite the tremendous cost and energy required in maintaining such a colony, it proved to be enormously rewarding, leading to major advances in recombinant factor VIII therapy. It also created the foundation for future groundbreaking gene therapy studies conducted by David Lillicrap, generating knowledge, revenue, novel therapies, and hope for those afflicted with severe hemophilia. Managing a hemophilic dog bleed at 2 AM is no small feat, requiring highly skilled and dedicated staff, which Alan hired with the same sense of purpose, selectivity, and urgency, recruiting technicians and administrators. Hugh Hoogendorn remained his steadfast right hand for decades, generating invaluable reagents and assays to measure the effects of thrombin generation *in vivo* and running the show when Alan was busy with clinical and academic responsibilities or on the road, whilst starting a highly successful spin-out company, Affinity Biologicals Inc. in parallel. Shawn Tinlin, "the dog whisperer," Alan's star veterinary technician with the canine "golden touch," accompanied by the multi-talented Sandy Webster, who spent countless days and nights nursing dogs back to health were ably supported in the laboratory by the effervescent Marilyn Garrett. Last, but not the least, the ever-jovial Barbara Saunders, Alan's outstanding administrative assistant, coordinated his hectic schedule, and adeptly "put out fires." These were turbulent times for hematologists and blood transfusions, with AIDS-tainted blood wreaking havoc, which Alan expertly navigated.

An important point to highlight regarding recruitment, be it investigators, trainees, or administrative/technologist support, Alan always looked beyond curriculum vitae, transcripts, and polished veneers in interviews. He took a human approach through casual in-person meetings, word of mouth, and socializing. Once in the fold, his mentoring and dedication were second to none.

Numerous aspiring clinicians and scientists from around the world would train in Alan's laboratory over the years and benefit from his generosity. One example would be Cheng-Hock Toh, Professor of

Haematology at the University of Liverpool, UK, who did his Clinical Master's degree under Alan's supervision and continued a productive collaboration with him following his return to England, investigating the molecular basis of disseminated intravascular coagulation. Alan's final Master of Science student was Yotis Senis, who's passion for the molecular basis of cellular hemostasis continues to this day. Yotis went on to become a British Heart Foundation Senior Basic Science Research Fellow and Professor of Cellular Haemostasis at the University of Birmingham, UK, and is currently Inserm Director of Research at the Etablissement Français du Sang Grand-Est, Strasbourg, France. With the Nesheim laboratory next door and the Lillicrap laboratory nearby, weekly group journal clubs with copious amounts of pizza and drinks financed by Alan and Mike and Friday beers at the Grad Club made it a fabulous place to train. Alan often invited students and trainees to the upscale Faculty Club for lunch and Indian cuisine in town, on special occasions. Highly educational, thought-provoking, and entertaining conversations would meander from science to medicine to football.

Following a year's sabbatical in Gérard Marguerie's laboratory at the Commissariat à l'énergie atomique in Grenoble, France, in 1995, Alan decided to take an early retirement in 1996 and settle down in Herbeys, France, with Hilary and their beloved dog Bennie, an offspring from the hemophilic dog colony. France was a place they both fell in love with while courting and would return to (Figure 3. Hilary and Alan, Herbeys, France, circa 2016). Alan remained intellectually and physically active throughout his life. He was an avid gardener and handyman, impressing guests with his English "victory gardens" wherever he resided.



At times fiery, always respectful and respected, Alan's quintessential English bulldog tenacity, political nous, cutting rhetoric, intellect, and grantsmanship allowed him to forge the world-class hemostasis and thrombosis group at Queen's University. It has spawned numerous clinicians, scientists, and discoveries and continues to this day under the astute leadership and vision of David Lillicrap. Alan is survived by Hilary, their three children, and six grandchildren.

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AUTHOR CONTRIBUTIONS

Y.A.S. wrote and revised the manuscript, and C.H.T. and D.L. revised the manuscript.

DECLARATION OF COMPETING INTERESTS

There are no competing interests to disclose.

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