Victor Herbert died in New York City on 19 November 2002 at the age of 75 of a malignant melanocytoma. He was a former president of the American Society for Clinical Nutrition (1980–1981) and a winner of the McCollum Award in 1972 and of the Herman Award in 1986. As an established Veterans Administration investigator, he won that agency’s prestigious Middleton Award in 1978 for “outstanding achievement in medical research for his work on developing scientific tools to diagnose nutrient deficiencies.” He received the Food and Drug Administration Commissioner’s Special Citation in 1984 for “outstanding and consistent contributions against the proliferation of nutrition quackery to the American consumer.” In 1993 Herbert was elected a Fellow of the American Society for Nutritional Sciences for his “outstanding lifetime research and teaching in nutrition.” During his professional career, he was the epitome of the physician-scientist and probably the most interesting and compelling person many of us were privileged to know. During the many years I knew him, I, like many in the folate and vitamin B-12 field, never knew what was really true about him and what was fascinating “Victor lore.” To find out, I researched his website (www.victorherbert.com), articles written about him, and articles written by him, and I obtained invaluable insights from many others who knew him.

Herbert was born in New York City on 22 February 1927 and was named after the Irish-American composer, who was a distant cousin. When Victor was 10 y old, his father was killed while fighting in the volunteer Abraham Lincoln Brigade during the Spanish Civil War; Victor’s mother, a Russian émigré and lawyer, died 3 y later. After several years in an orphanage, Victor lied about his age and in July 1944 enlisted at age 17 in the US Army “to get Hitler before he killed all the Jews” (1). He served as a Private First Class paratrooper in the 82nd Airborne Division during the last year of World War II. On discharge from active duty in 1946, he enrolled in Columbia University, from which he received a BS in chemistry in 1948 and a medical degree in 1952.

After internship and residency at Walter Reed Army Medical Center, Dr Herbert began his academic career as a physician-scientist at the Albert Einstein and Mount Sinai hospitals in New York City (1955–1959), where he made his first forays into vitamin B-12 and folate research. It was there that he discovered that vitamin B-12 requires both calcium and intrinsic factor to bind to the ileal mucosa (2) and that he developed the first microbiological assay for serum folate (3). In 1959 he was invited by William Castle to become his research associate and an assistant physician at the Thorndike Medical Laboratory on the Harvard medical service at Boston City Hospital. Describing his new environment as one of “scientific and emotional intensity and exhilaration” (4), Dr Herbert made seminal discoveries about the clinical effects of folate deficiency and continued his studies of vitamin B-12 physiology during his 5 y at the Thorndike Lab (1959–1964). In the early 1960s, the medical ward provided the most common “laboratory” for the observant physician-scientist, and great scientific discoveries in clinical nutrition were made through well-planned and well-executed studies of patient volunteers who exhibited classic features of poorly understood diseases. True to the best tradition of the physician-scientist, Dr Herbert, with a fellow, Ralph Zalusky, demonstrated the clinical relation of folate deficiency to megaloblastic anemia by studying a man who lived on coffee, doughnuts, and hamburgers and responded to minute (50-mg) daily doses of folic acid (5). At about the same time, Herbert and Zalusky made the first observations of what later came to be known as the “methyl trap” theory of the integral relation of vitamin B-12 to folate metabolism in the setting of isolated B-12 deficiency in patients with pernicious anemia. In careful and reproducible experiments, they showed that serum folate concentrations were typically normal.

In Memoriam

Victor Herbert, MD
1927–2002
or even high in these patients and that the concentrations fell with vitamin B-12 injections, whereas the clearance of injected folic acid, measured by the microbiological *Lactobacillus casei* serum folate assay over time, was prolonged and often on a plateau. Because *L. casei* measures methyltetrahydrofolate, Herbert proposed that this metabolically active folate is unavailable for normal metabolism, including correction of DNA and anemia, and that it “piles up” in the serum because vitamin B-12 is required for its normal utilization (6). This classic clinical study spawned the vast and still ongoing field of research on the importance of the B-12–regulated transmethylation pathway for folate, homocysteine, and methionine metabolism.

To prove the link between inadequate diet and folate-deficient megaloblastic anemia, in October 1961 Herbert began his most famous prospective experiment, with himself as the only subject, in which he consumed for the next 5 mo a diet that consisted mainly of thrice-boiled vegetables. As he described in his classic publication (7) and related to a *New York Times* reporter 2 decades later (8), during these 22 wk, he had his fellow Louis Sullivan perform 8 separate subternal bone marrow aspirations as well as multiple venipunctures to carefully catalog the progression of folate deficiency to its endpoint of megaloblastic anemia. Midway through the experiment, Herbert awoke on Christmas Day 1961 unable to walk. Realizing that potassium could be leached out of his diet by its bizarre preparation and that muscle weakness could be caused by potassium deficiency, he downed as much saturated potassium iodide cough syrup as he could find at home until the diagnosis could be confirmed and treated by a colleague (4). This experiment set the stage for the vast literature on human folate metabolism and deficiency that appeared over the next 40 y. While conclusively proving that megaloblastic anemia can indeed be caused by improper diet, Herbert’s study showed how to interpret diagnostic tests during the sequential clinical stages of the development of folate deficiency. Because the amount of folate in human liver was generally known, Herbert’s self-experiment established a reasonable estimate of the minimal daily folate requirement and hence the daily loss in a healthy man (9), which has been validated several times since by others with the use of sophisticated isotopic studies.

During this time, Herbert found that folate deficiency was widespread among derelict alcoholics, who are notorious for poor diet (10), a finding that set the stage for a whole body of literature by himself and others on the relation of alcohol consumption and folate metabolism. An intriguing and yet unexplained finding resulted from an experiment in 3 alcoholic patients with megaloblastic anemia in which Sullivan and Herbert (11) showed that an initial positive response to minute doses of folic acid could be completely and reproducibly suppressed by whiskey or wine in their typically excessive amounts. In a brief autobiographical sketch (4), Herbert described how one of the patient-volunteers “leapt like a cat” on a National Institutes of Health inspector who came to Boston to find out why this research group was spending so much government money on Hiram Walker Imperial Whiskey.

On his departure from the Thorndike Laboratory, Dr Herbert became the associate director of hematology at Mount Sinai Hospital in New York. After short forays to several other institutions, in 1970 he settled into a 32-y career as chief of the Hematology and Nutrition Research Laboratory at the Bronx Veterans Administration Hospital and professor of medicine at Mt Sinai School of Medicine. Over these 3 decades, he trained many future academic scientists and continued to make vast contributions to our understanding of the basic biochemistry, clinical diagnosis, and significance of vitamin B-12 and folate deficiency. A nonexhaustive list of seminal findings emanating from his laboratory includes refinements of assays for serum and red cell folate (12, 13) and vitamin B-12 (14), the usefulness of the deoxyuridine (dU)-suppression test to distinguish vitamin B-12 from folate deficiency (15), demonstration of the essentiality of intrinsic factor for ileal absorption as well as gastric binding of vitamin B-12 (16), the complex transfer of vitamin B-12 from R binder to intrinsic factor (17), the clinical importance of vitamin B-12 analogues (18), and the significance of low transcobalamin II as an early marker of vitamin B-12 deficiency (19).

Much of this work is summarized in his 1986 American Society for Clinical Nutrition Herman Award lecture on the folate and vitamin B-12 paradigm (20).

Yet, amazingly, his scientific work was paralleled by a second career as a quackbusting physician-attorney. Well before *alternative medicine* crept into the lexicon of medical practice, Dr Herbert obtained a law degree from Columbia University in 1974, and with that and his expertise as a nutrition scientist, he challenged the “health food” and “phony drug” industries. From then on, his curriculum vitae is fertilized with a seemingly endless barrage of scientific papers, letters to the editor, and columns in the lay press on the dangers of phony drugs and vitamins such as laetrile (21, 22) and panagamic acid or “vitamin B-15” (23), on the wastefulness and dangers of megavitamins (24), and on the burgeoning herbal and health food industry (25). He was chair of the Committee on Life Sciences of the American Bar Association for 5 y, a board member of the National Council Against Health Fraud (www.ncahf.org), a frequent witness to Congress on health and nutrition, and the author of numerous books that debunked the health-supplement industry (26, 27). At the same time, he also provided sensible and accurate nutritional advice to laypeople (28).

Although accomplished in all things scientific and legal, Victor was most proud of his career as a young paratrooper in World War II and later as a medical officer during the Korean (1953–1954), Vietnam (1964–1966), and Gulf (1991) wars. Even while he was establishing his academic career at Mt Sinai, he reenlisted at age 37 in the US Army, this time in the Special Forces (Green Berets), and served 122 d on active duty during the Vietnam War. After his discharge from the Army as a Lieutenant Colonel in 1987, a compulsion to reenlist yet again, at age 64, for a brief stint during the Gulf War in 1991 was facilitated by the intervention of his former Fellow and then Secretary of Health and Human Services, Louis Sullivan (1).

All who knew Victor or saw him in action share indelible memories. Who can forget his impromptu star performances at each and every Experimental Biology meeting? He was always the first to the microphone with the most incisive and provocative questions that nearly always brought a level of excitement and set a higher tone for the discussions that followed. Just as he had described encounters with his first mentor, William Castle, if you were the target of Victor’s questions, “You realized the enormous range and depth of his knowledge and his ability to communicate it in such a way that he made you not only think but remember” (4). Who can forget his favorite slide in his phony-diploma-mill talk—his cat Charlie’s PhD? Or his brilliance, as when he summarized in handwritten but, unfortunately, unpublished poetry an
entire workshop on folic acid (29), with intimate details of every speaker’s contribution? To those who knew him well, he was much more than a complete repository of knowledge of vitamins and of health fraud. He was a true and generous friend, supportive of the careers of those who came after him and always available with informal legal advice or specific scientific suggestions. He knew the best deals on hotels and restaurants in every city you were likely to visit, and his storehouse of jokes and stories—mostly unprintable—was legendary. While almost always controversial, he will be remembered fondly by his friends and as a scientific inspiration to all who followed in his footsteps into clinical nutrition research.

I am indebted to Mrs Marilynne Herbert, who provided me with a true copy of Victor Herbert’s military record and confirmation of several details of his life, and to many friends and colleagues who shared their memories with me during the preparation of this article. There were no financial or other conflicts of interest associated with this work.

Charles Halsted

American Journal of Clinical Nutrition
3247 Meyer Hall
University of California, Davis
One Shields Avenue
Davis, CA 95616
E-mail: ajcn@ucdavis.edu

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