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ZANVIL ALEXANDER COHN
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A Biographical Memoir by

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Biographical Memoir

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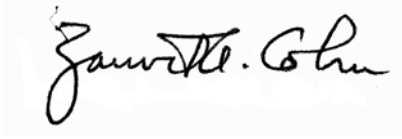

ZANVIL ALEXANDER COHN

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BY CAROL L. MOBERG AND RALPH M. STEINMAN

ZANVIL COHN MAY BE most remembered as the founder of modern macrophage biology and for leading the shift in mid-twentieth-century research from bacterial cells to host-parasite relationships. After graduate studies in microbiology, Harvard Medical School, and a residency at Massachusetts General Hospital, he joined The Rockefeller Institute (now The Rockefeller University) laboratory of René Dubos in 1957. There with James G. Hirsch he discovered that granules in phagocytes are lysosomes that digest microbes. He elucidated how macrophages identify, engulf (endocytose), destroy, and defend the body against pathogens. Zan pioneered the study of cell biological analysis of endocytosis. He unraveled many features of cell-mediated resistance to infection in the laboratory and in clinical studies at the Rockefeller hospital and medical centers around the world. He was an adviser to several institutions of biomedical research and championed programs for the M.D.-Ph.D. degree and clinical scholars to perform research in human disease. He was an incisive editor of *The Journal of Experimental Medicine*. A demanding yet inspiring mentor, he took great pleasure in nurturing graduate students and postdoctoral fellows. He was warm, witty, modest, and fair during his lifelong search for knowledge that could heal the sick.

Zanvil Cohn was the first of two sons born in New York City to David and Esther (Schwartz) Cohn; his brother, Donald, was born three years later. The remarkable name Zanvil, a Hebrew word for Samuel, was a family name, although when asked in later life about it he said the only one he knew with this name was a horse thief in a short story. His father emigrated from Dusseldorf in 1905 at age 19 and went to work in his Uncle Josef's butcher shop in Manhattan. Within a few years he became an owner of Kansas Packing, the largest independent meat packing company in New York and a purveyor to the French shipping lines. Zan's mother was born in the United States of parents who had emigrated from Budapest. Raised in Huntington, Long Island, she was a buyer of women's blouses for Oppenheim, Collins & Co., a specialty clothing store in Manhattan before becoming a partner in a blouse manufacturing company. Zan's parents lived comfortably, traveling each year to Europe; they were founding members of synagogues in both Long Island towns where they lived.

Zan, who spoke German and English as a child, attended public grade schools in Forest Hills before entering the private Columbia Grammar School on Manhattan's Upper West Side. He was less interested in studying than being the star cleanup hitter on the baseball team with a batting average of .415; as captain of the football team, whose games were played in Central Park, he became an All-City tackle on a team that rarely won a game. He was the president of the student government and played the piano at graduation.

Zan's lifelong love of saltwater fishing began in childhood after his parents built a summer house in Amityville on Long Island's Great South Bay. There a charter boat operator, Captain Shard, showed the two brothers how to fish, identify sea birds, and hunt ducks. The boys loved to read about fishing and hunting, one special book setting them to

dream of catching black marlin off the coast of Chile. They would often row their boat across the bay, letting the south wind push them back while they read. Once trapped by a heavy fog, they found refuge in a marsh and read until the fog lifted; the Coast Guard boat sent out to find them got stuck on a sandbar and returned after the boys were safe onshore. When their father became ill, they got up early to catch weakfish for his favorite breakfast. If the weather was too bad, they went to the American Museum of Natural History where they fished vicariously in the dioramas in the Hall of Ocean Life.

No one from either side of the family had a medical or academic background. Even so, Zan was influenced by his maternal grandmother who spoke seven languages while helping immigrants on the Lower East Side adapt to their new country. Two teenage experiences may have stimulated his interest in infectious disease. One was his brush with death from scarlet fever that quarantined the whole family. Another was the caring family physician who looked after his father, bedridden nearly a year following a severe bout of pneumonia that weakened his heart; he died at age 57 as Zan was finishing high school.

Zan was not serious about academic studies or large institutions on graduating from Columbia Grammar at age 16, but he took a counselor's advice to go to Bates College in Maine. He was the first in his family to attend college. After two years, during World War II, he joined the U.S. Merchant Marine and trained as a hospital corpsman. During 1944-1946, he served as purser-pharmacist on Liberty ships in the Atlantic and Pacific, while sporting a mustache to look old enough for this position. He was occasionally the only medically trained person among the ship's crew and 1,500 soldiers, with responsibility for preventing epidemics, administering vaccines and antibiotics, and treat-

ing wounds. He once saved a soldier's life. An article in a Norfolk, Virginia, newspaper described how Zan diagnosed a ruptured appendix, but not trained to operate, packed the soldier in ice, and administered antibiotics until he could be transferred to a hospital ship for surgery. Other adventures in the Pacific ranged from a terrifying giant typhoon to an almost comic adventure. After a nighttime alert that their ship had been torpedoed, all hands took to life boats; when daybreak revealed the damaged ship was still afloat, they climbed back on board.

When Zan returned to Bates as a junior in 1946, he met Fern Dworkin in an organic chemistry class. They graduated in June 1948 and were married that December.

With a major in biology, he was already thinking of going to medical school, inspired not only by reading Paul de Kruif's *Microbe Hunters* and Sinclair Lewis's *Arrowsmith* but also by the medical experiences on Liberty ships with the newly introduced penicillin. According to David Luck, a medical school classmate and lifelong friend, Zan's grades at Bates were not good enough to get into Harvard Medical School so he entered their graduate program in bacteriology. He did so well that he entered medical school a year later, where he continued independent research, produced a thesis, and published his first paper on the interaction of viruses and chicken eggs. According to another classmate, S. James Adelstein, an early experience in clinical research came in their fourth year. An elective rotation in the arthritis unit, designed principally by Zan, involved analyzing patients' synovial fluid for its nucleic acid content.[1] His M.D. degree in 1953 is one of very few in the medical school's history to have been awarded a summa cum laude for research.

In the introduction to his thesis he announced what would be a lifelong scientific interest, host-parasite relationships. While at Harvard, Zan heard a series of provocative

lectures by René Dubos, the eminent Rockefeller Institute microbiologist.[2] Dubos discussed host-parasite interplay, the microenvironment of inflammation, and the fate of microorganisms in vivo—topics covered in Dubos's 1954 monograph *Biochemical Determinants of Microbial Diseases*, a book Zan called "visionary and provocative" and always kept within reach. After the lecture, Zan approached Dubos about a position in his laboratory where these questions were being actively pursued. Dubos was interested, but in one of his occasional overstatements told him, "Just forget about viruses. They're passé. When you come to Rockefeller we'll work on something important."

After internship and residency at Massachusetts General Hospital, Zan met his military obligations in the Army Medical Corps. With help from Walter Bauer, professor of medicine at Harvard, he served as a captain at the Walter Reed Army Institute of Research in the laboratory of physician and virologist Joseph Smadel. For the next two years he explored respiratory enzymes and the cell wall of the intracellular parasite *Rickettsia tsutsugamushi*.

At the end of army duty Smadel introduced Zan to two eminent researchers. Lewis Thomas invited him to work in pathology at New York University, but Zan was more interested in host-parasite interactions. Since Smadel had worked with Thomas Rivers in the Rockefeller hospital from 1934 to 1946, he arranged an interview for Zan with Dubos, who had forgotten their earlier Harvard conversation. A short time later Dubos sent a rejection letter stating he did not want anyone to work on *Rickettsia*. On the day it arrived James Hirsch,[3] a physician-scientist in Dubos's laboratory, was giving a seminar at Walter Reed. After Zan explained to Jim that his intention was to study the role of white blood cells in disease (not just bacteria), Jim straightened out the

misunderstanding. Zan was appointed research associate and assistant physician to the hospital in October 1957.

Like Jim and many others before him, the environment Zan encountered was similar to the one Dubos found on entering Oswald Avery's laboratory in 1927. No projects were assigned and no training given. Dubos fostered investigators, not mere problem solvers, thus allowing newcomers independence to plan experiments and progress at their own pace. As Zan said in a 1983 interview, Dubos had a habit of talking to newcomers "for the first two days, and if he thought they could get along on their own he would not talk to them again for another year. I was terribly upset, I must say."[4] Once again Zan was on his own, this time to find research projects compatible with his skills and temperament.

For the next 35 years Zan worked at Rockefeller, most of them on the fourth floor of Bronk Laboratory.[5] Previous research on host-parasite relationships in the Dubos Laboratory of Bacteriology and Pathology had focused on the causative agent of tuberculosis, which is ingested and can survive inside phagocytic white blood cells while remaining poised to reactivate disease if disturbed by the physiology or environment of the host. This research included Merrill Chase's studies of cell-mediated immunity; Hubert Bloch, Werner Schaefer, and Samuel Martin's quantitative studies on the fate of tubercle bacilli inside phagocytes; and Jim Hirsch and Russell Schaedler's clinical studies of tuberculosis and sarcoidosis.

When Zan arrived, Jim was just beginning to study how the freely moving polymorphonuclear leukocytes, or granulocytes, ingest and kill microbes. At this time the study of leukocytes was still in its infancy and hematology was focused on the erythrocyte. It was also the time when the new science of cell biology was emerging at Rockefeller under the direction of Keith Porter, George Palade, and Philip Siekev-

itz. This was making it possible to explore the world inside cells: electron microscopy for showing cell structures never before observed and centrifugation methods for separating and analyzing cellular constituents. Zan and Jim used these new tools to address the question of whether phagocytes contained preformed bactericidal substances or whether these substances developed after foreign particles were engulfed. They isolated granules from the rest of the cell contents, used phase and electron microscopy to visualize them, and determined chemically that they were lysosomes, the cell organelles recently identified by Belgian biochemist Christian de Duve, who soon joined the Rockefeller faculty. These discoveries, which traced the phagocytic digestive system to the fusion of phagocytic vacuoles and lysosomes, became widely available to the community after Jim and Zan made a remarkable series of films showing living phagocytes discharging their abundant lysosomes to kill bacteria.

In 1966 when Zan was promoted to full professor, he and Jim formed an independent joint Laboratory of Cellular Physiology and Immunology. By this time Zan had decided to explore macrophages, the large, long-lived white blood cells. Their presence in every organ in the body also suggested they were more potent phagocytic scavengers. Yet, little was known about macrophages and there were no systems to study them. His adroit tissue culturing of macrophages made it possible to observe, challenge, and manipulate them to figure out how they worked. His talents were distinctive in cell biology and unusual in cellular immunology at the time, because they included an ability to quantify and identify biochemical mechanisms and to obtain images of subcellular behavior. What he demonstrated is how the cell's outer membrane folds around the captured material, forms a sac or vacuole that is pinched off from the cell surface and

enclosed within the cell, and fuses with the lysosome where the contents are then digested. Exploring the macrophage from these composite approaches greatly expanded the scope of intracellular digestion. Endocytosis then blossomed into a central field of cell biology, because it is pertinent to all cells for extracting from their surrounding environment the nutrients needed for survival as well as for capturing and destroying toxins and pathogens.

Zan also moved from phagocytosis of particles to pinocytosis of fluids and solutes. He showed that lysosome-based intracellular digestion applied equally to pinocytosed proteins and polysaccharides as it did to phagocytosed organisms. He addressed the question of whether the cell's membrane is destroyed in the lysosome and new membrane synthesized or whether it is recycled. These questions were answered in part by a stream of doctoral students, postdoctoral fellows, and junior faculty. An important aspect of subsequent studies was influenced by Seymour Klebanoff, another leader in phagocyte science and a friend of Zan's, who suggested using radiolabeling with iodination by the enzyme lactoperoxidase.

These investigators included Barbara Ehrenreich and Ralph Steinman who used radiolabeled proteins and active enzymes to follow intracellular digestion down to the core amino acids. Ann Hubbard, Zena Werb, William Muller, and Ira Mellman radiolabeled the plasma membrane and endocytic vacuole membrane to monitor their composition and metabolism. Siamon Gordon, Jay Unkeless, and Samuel Silverstein unraveled the composition and function of cell surface receptors and revealed how the captured prey is engulfed. One theme that permeated these discoveries was that the process of endocytosis involves an enormous flow and recycling of vesicle membranes into and back out of

cells at the same time that vesicular contents were delivered to lysosomes for thorough digestion.

Zan was known for keeping his focus on important scientific questions and looking for major changes. His philosophy, influenced by Dubos, was that if you need statistics to know the data are significant, then you are probably not looking at a major event. Consequently, his connective sensibilities enabled him to discover other major functions of macrophages and to demonstrate these cells were more than just "large eaters." He moved beyond endocytosis to the role of macrophages as secretory cells. With others in the laboratory, including William Scott, Alan Aderem, and Siamon Gordon, macrophages were found to manufacture a large repertoire of chemical products. Over the years the laboratory catalogued more than 50 products and found they take active roles in inflammation and immunity. After Richard Johnston and Carl Nathan joined the laboratory, the group discovered that activated macrophages release active oxygen intermediates, such as superoxide and hydrogen peroxide, to destroy bacteria and tumor cells. A further demonstration that macrophages could be activated by lymphokines in vivo was important in the laboratory's subsequent clinical efforts to treat diseases in which macrophages achieve both intracellular and extracellular killing.

Because macrophages emigrate into many tissues and respond to local demands to protect the host, Zan identified them as the "versatile element of inflammation." He recognized, however, a delicate balance existed between the nature and the amount of their secreted products. As an important part of the inflammatory process, the secreted substances can lead to wound healing, tissue repair, or destroying microbes and tumors. On the other hand, if macrophages are overstimulated and secrete excessive amounts, they can destroy normal as well as foreign cells and tissues, intensifying such

disease states as rheumatoid arthritis, glomerulonephritis, asthma, and even atherosclerosis.

When Zan moved on to determine the origin of macrophages, he and Ralph van Furth used a radiolabeled isotope to label blood monocytes and trace their production and development. They identified the blood monocyte as the precursor for tissue macrophages and the bone marrow as the source of monocytes. The concurrent electron microscope studies with Jim Hirsch and Martha Fedorko to visualize these precursors further demonstrated the formation and differentiation of these cells.

These experiments led to a redefinition in 1972 of phagocytic mononuclear cells. Replacing the "reticuloendothelial system" of Ludwig Aschoff from 1924, the new classification was called "the mononuclear phagocyte system." This research illuminated a pivotal pathway to host defense and captivated the minds and spirits of innumerable scientists well beyond the confines of The Rockefeller University. Between 1969 and 1991 van Furth organized and published the proceedings of five international conferences on mononuclear phagocytes that were held in Leiden, The Netherlands.

Zan's knowledge of macrophages and their identifying markers in many species of animals and in various tissue sites made it unambiguous for him to appreciate the discovery of the distinct tree-shaped dendritic cells. In 1973 while examining spleen macrophages of mice, Ralph Steinman and Zan found an entirely distinct class of immune cells. They isolated and characterized this cell as different in structure, appearance, and function from macrophages. Since the world was just becoming familiar with Zan's new cell biology of macrophages, it took a decade for these novel white cells to be universally accepted as authentically new powerful initiators of the immune response and major controllers of both innate and adaptive immunity. This modest "novel cell type"

reported in 1973 has become one of the brightest stars in the immune galaxy.

In the early 1980s Zan realized a longstanding goal to direct his bench work to the bedside, as he noted, "taking it to a human problem." The quest was to find out why in certain diseases the macrophages, after ingesting pathogens, not only fail to kill them but instead provide a hospitable environment for them to thrive, multiply, and reactivate disease. Among these diseases Zan and colleagues concentrated on leprosy, leishmaniasis, Chagas' disease, tuberculosis, and eventually AIDS, which are endemic in the developing world.

The idea for Zan to gain firsthand experience with these problems may have been heightened during a special visit to the People's Republic of China in 1977. He and Jim were part of a university delegation, arranged by Rockefeller President Frederick Seitz, to make the first private nongovernmental exchange to China—less than a year following Mao Zedong's death and the end of the Cultural Revolution. The nine professors were selected by Chinese scientists and physicians who had previously visited Rockefeller laboratories to work on mutual research interests. While visiting many Chinese scientific, medical, and educational centers, the Rockefeller scientists observed a severe disruption of academic and intellectual activity. In a report on his return Zan (like the others) noted the rudimentary equipment, few students, and minimal basic scientific research. Yet, in examining the abbreviated medical school curriculum, he was impressed by something else. The Chinese were stressing very practical medical concerns, applying techniques of both Western and Chinese medicine (acupuncture and herbal medicine), and especially training motivated paramedics (the "barefoot doctors") to orient medical care directly toward the welfare of all its citizens, even those in the most remote areas.

A short time later and continuing for the last 15 years of his life, Zan and the motivated medical scientists in his laboratory began traveling back and forth from his laboratory and the Rockefeller hospital to patients in city hospitals and rural mission hospitals in Latin America, Asia, and Africa. Brazil was the first of the laboratory field trips, spurred in part by Nadia Nogueira, a medical intern in Rio who became one of Zan's Ph.D. students. By applying the laboratory's biochemical tools that had been developed for exploring the macrophage to *Trypanosoma cruzi*, the causative parasite of Chagas' disease, she found that when T cells secrete lymphokines, the latter activate macrophages and make them effective killers able to sterilize this intracellular parasite.

The first field trips studied patients with leprosy, chosen because it was a major scourge having a spectrum of forms, from virulent to mild, and it could be studied in easily accessible skin lesions. Since the disease was so widespread and new cases were being admitted to hospitals all the time, the patients' cells could be studied before they were modified by treatment. Zan's first innovation was to look directly in the skin lesions, whereas previous immunologic changes in leprosy had been based on analyzing blood cells. Working with the local physicians, this group compared blood and tissue samples using a variety of biochemical, morphological, and biological assays. What they found was the lymphocytes in skin lesions were not representative of those in blood: at one end of the spectrum of lesions were those containing bacteria-filled macrophages along with many suppressor T cells, while at the other end were lesions dominated by more helper T cells. This observation led to Zan's next innovation to inject purified lymphokines into the skin of leprosy patients. They tested two lymphokines, interleukin-2 and interferon-gamma, and observed that each one boosted T-cell responsiveness and reduced the number of bacteria in

the macrophages. These treatments restored some of the patients' immune function at both the local and systemic level, although they did not cure the disease.

These clinical trials confirmed Zan's belief that the study of disease in patients stimulates new insights that could not have been anticipated at the bench. They also brought new attention to infectious diseases as clinical models to study the cellular basis of immunity and gave Zan high expectations that lymphokines and other agents interacting with macrophages would someday enter the physician's armamentarium to fight disease. As the leprosy work progressed, Zan and colleagues, particularly Gilla Kaplan, transferred attention to other diseases in which macrophages play a role. Studies in the Rockefeller hospital evaluated the intracutaneous effects of interleukin-2 in HIV-1-infected patients and showed these individuals mobilized a cell-mediated reaction in the skin and a systemic boost in responsive killer T cells. At his death Zan was organizing an expanded program to enhance the immune system of immune-compromised individuals with AIDS and tuberculosis.

Zan's professional activities extended to many other spheres of academic medicine. One of his great pleasures was to nurture the development of students and young faculty. He personally helped train nearly 200 young scientists and 40 doctoral students, many of whom are now professors and heads of their own laboratories all over the world. He immensely enjoyed these bright, hardworking people who were good with their ideas and their hands. "Progress in cell biology," he once said, "demands busy work, because it deals with the behavior of living cells and consequently differs from finite studies on inanimate macromolecules." Cell biology studies, he recognized, took numerous interdisciplinary and interlaboratory collaborations around the world.

Zan never imposed any model or edict that might detract from a person's individuality or creativity. There was always a quiet but profound sense of mutual respect in his interactions with everyone. He kept an open door and an open mind. Brief in his discourses, he got to the heart of the matter in a few words, exercising an impressive memory and analytical skills. Gentle, but firm and self-assured, he defined and organized complex research problems into simple, intelligible terms that were rooted in practicality of execution.

Zan believed it was not enough to do science; to become an independent investigator meant writing and speaking clearly and succinctly. Part of his mentoring of graduate students involved going over their first papers, discussing every sentence, removing most punctuation, and smoothing rough data into seamless, well-reasoned arguments. Once fledged from his tutoring, they were treated like the postdoctoral fellows and would find their drafts of manuscripts bore only cryptic suggestions such as expand, shorten, or more focus. Brevity did not mean he was in a hurry or impatient; brevity was to convey and preserve the main points.

These qualities carried over to his editorial roles for many journals, particularly his 20-year tenure as an editor of *The Journal of Experimental Medicine*. Following in the footsteps of retiring editor René Dubos, Zan insisted its pages provide sufficient space to document conclusions adequately and to pursue mechanisms in detail; he looked for papers with novelty, clarity, and a mechanistic analysis that was quantitative, direct, and multifaceted.

His own approach to the writing of a few hundred scientific papers, reviews, and lectures was quite amazing. He first thought long and hard about the topic, saying his best thinking was done while commuting by car from home on Long Island or on his fishing boat. Then he sat down with sharpened pencils and a yellow lined pad and wrote straight

through from beginning to end, without correcting, changing, or rewriting a sentence.

Zan had a distinct way of running a large laboratory; he managed by walking around. Rather than assume the role of boss, he would visit each person in every laboratory at least once a week to follow the progress of their experiments. Clad in a white lab coat with a pocket full of pencils and pens, and without any formalities, he arrived quietly, exchanged a few pleasantries about birds, children, or the weather, then inquired about a few experimental details and offered pithy insights or suggestions, and left just as silently. Without writing a single note he managed to keep track of the ongoing work and life of nearly 60 people. In turn, this personal attention encouraged special diligence on the part of the researchers who avoided unnecessary work and achieved astonishing progress in the whole laboratory. These visits, as remembered by Samuel Silverstein, "were always stimulating and challenging, and often led me, at least, to formulate a few sensible experiments out of the inchoate morass of ideas at play in my mind."

Cohn was deeply committed to scientific medicine. Throughout his career he served as adviser or trustee of Harvard University, Massachusetts General Hospital, Max Planck Institute, Trudeau Institute, Roswell Park Memorial Institute, the National Institute of Allergy and Infectious Diseases, the New York Blood Center, and Bates College. His many awards included election to the National Academy of Sciences (1975), the first Henry G. Kunkel Professorship (1986), and honorary degrees from Bates College (1987), Oxford University (1988), and Rijksuniversiteit, Leiden, The Netherlands (1990).

Zan's belief in the unique role of the physician-scientist is reflected in the programs he helped establish at Rockefeller. In 1972 with Jim Hirsch and Alexander Bearn, he organized

with Cornell University Medical College one of the first medical scientist training programs for the combined M.D.-Ph.D. degree. When he was appointed vice president for medical affairs by President Torsten Wiesel in 1992, Zan's priorities were to increase the role of the Rockefeller hospital and clinical research. In particular he fostered interactions of young people with physicians at Rockefeller, Weill Cornell Medical College, and Memorial Sloan-Kettering Cancer Center, the three biomedical research and educational institutions across the street from one another. One activity was establishing the Tri-Institutional Biomedical Forum, an informal sherry-and-lecture series reminiscent of his happy 1988 sabbatical at the Dunn School in Oxford, where young scientists could get to know their counterparts at these three institutions. Another activity was invigorating the Clinical Scholars program to support and train new physicians to care for patients on a daily basis while conducting bench research to better understand their diseases. In 1989 on the 50th anniversary of René Dubos's discovery of the antibiotic gramicidin, Zan organized and chaired a symposium on "Launching the Antibiotic Era." Ever mindful of the environment that fostered his own career, he spoke about the importance of "supporting young investigators and global research, the opportunities afforded single investigators working in small laboratories, the efficacy of personal involvement at the bedside, and a moral climate that led to patents for the general good."[6]

When asked about his outside interests, Zan invariably replied, "I'm a fisherman on the end of Long Island in Montauk." An office wall was covered with an enormous nautical survey map of all these waters where he fished from his boat *Davess III* and it inspired him to plan the next fishing adventure. His favorite fish to catch was the bluefish, but his favorite to eat was bonito tuna, for which bottles of soy sauce were kept on board. Until the end of his life Zan took

great pleasure in saltwater fishing and watching birds and shared these passions with his wife, Fern, a newspaper editor; son, David, an interventional radiologist; and daughter, Ellen, editor in chief of *The Papers of Benjamin Franklin*. When asked "What is your favorite bird?" he would fall into a long dreamy pause and say eventually, "shearwater." Why? "Well, the way it flies across the top of the water, and because it indicates schools of tuna just below." It was known he could be enticed to give lectures and attend conferences around the world when fishing, birding, or collecting nomadic rugs were a planned part of the visit.

With an imposing stature and warm demeanor, Zan exuded an air of equanimity and quiet authority. This image only served to heighten the shock and disbelief that followed his sudden death from an aortic dissection on June 28, 1993. During a memorial service two days later, attended by hundreds, Rockefeller President Torsten Wiesel expressed a sentiment felt by all: "Zan was a prince of a man who inspired everyone fortunate enough to have known him. He was an eminent scientist, a caring physician, and a great human being guided by a clear philosophical stance." He was one of the worthies of experimental medicine.

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NOTES

1. Personal communication, letter dated Mar. 21, 1994, from S. J. Adelstein to C. Moberg.
2. J. G. Hirsch and C. L. Moberg. René Jules Dubos, 1901-1982. In *Biographical Memoirs,* vol. 58, pp. 132-161. Washington, D.C.: National Academy Press, 1989.
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4. F. Bardossi and J. N. Schwartz. Unpublished transcript of interview with Zanvil A. Cohn for *Research Profiles*, spring 1983.
5. This memoir presents a general survey of Zan's scientific contributions. A comprehensive survey with a complete bibliography of his nearly 400 publications appeared in R. M. Steinman and C. L. Moberg. Zanvil Alexander Cohn, 1926-1993. *J. Exp. Med.* 179(1994):1-30. Full text at http://jem.rupress.org/cgi/reprint/179/1/1
6. C. L. Moberg and Z. A. Cohn, eds. *Launching the Antibiotic Era.* New York: The Rockefeller University Press, 1990.

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